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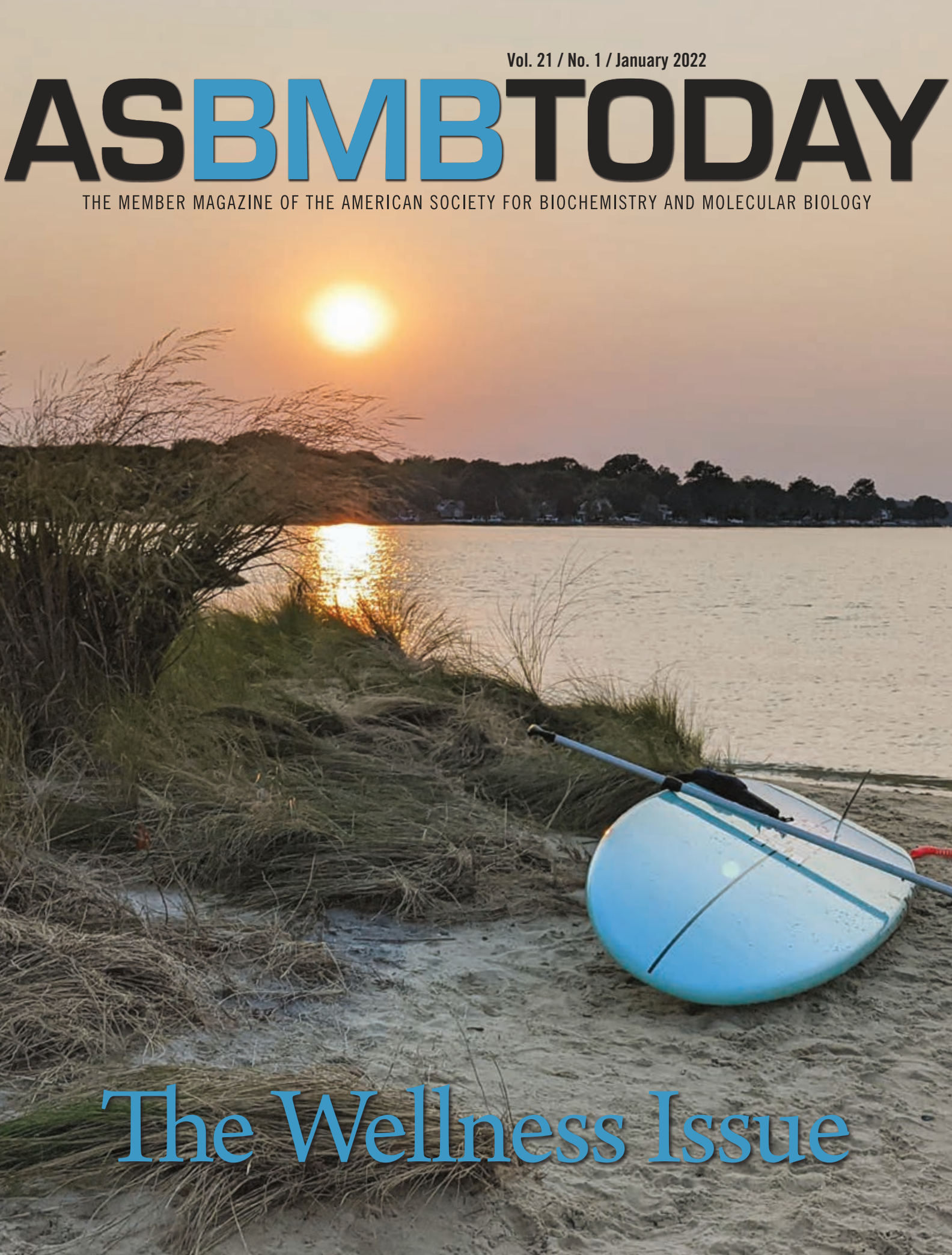
ASBMB TODAY

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



The Wellness Issue

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CONTENTS

NEWS

FEATURES

PERSPECTIVES

The Wellness Issue

Cover photo by Allison Frick.

ASBMB 2022 ANNUAL MEETING

ASBMB TODAY

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Moving forward together

By Toni M. Antalis

Another year has come and gone. Though the pandemic continues and hardships remain, this is a good time to reflect on the bright spots and, the wins of the past year — and to take note of what lies ahead.

In 2021, we shared new ways of meeting and teaching students where they are. We advocated for support for early-career scientists. We stood up for international collaborations and in opposition to racial profiling. We weighed in on various pieces of legislation and a proposal to create a new U.S. health research agency.

We elected new society leaders, celebrated our inaugural class of fellows, doubled our diversity scholarships and wrapped up a full year of open-access publishing.

Thanks to wide availability of effective COVID-19 vaccines, we were able to slowly and carefully return to some in-person activities.

2022 will be my last year as president of the ASBMB, and I'm excited about what's to come. I recently presided over a meeting of the society's governing Council, at which we discussed how wonderful it will be to finally have the entire community in one place in April: to share experiences and to attend lectures and poster sessions in person. For the health and safety of our members and community, we are requiring that all attendees be fully vaccinated for COVID-19, and we will be taking into consideration state and local guidelines for mask requirements. This in-person ASBMB annual meeting in Philadelphia is sure to be a memorable event that you won't want to miss! After so long apart, we've all been longing for company and connection.

The Council also discussed all the opportunities having a standalone meeting in 2023 will offer: more flexible scheduling, more time for specialized sessions, and more networking events designed to strengthen our relationships, invigorate our research and advance the careers of our students and postdocs. I can't wait to share the details for this first-of-its kind meeting later this year.

I hope you'll take time to browse this year's annual report (asbmb.org/2021-in-review) highlighting the society's programs and impact. Our advocacy efforts, education and diversity initiatives, professional-development events and publications are all made possible thanks to your support. I think you'll be as proud as I am of the important work being done to advance our field and support the researchers in it.

I wish you all a safe and happy 2022.

Toni M. Antalis (TAntalis@som.umaryland.edu) is a professor of physiology at the University of Maryland School of Medicine.

CORRECTION:

In the December issue, the profile of Joe Provost, winner of the 2022 ASBMB Exemplary Contributions to Education Award, contained several errors. The corrected profile is republished in this issue on page 74.

Special Lasker award for Baltimore

David Baltimore, a Nobel laureate and distinguished professor at the California Institute of Technology, has received a Lasker~Koshland Special Achievement Award in Medical Science, a recognition of his 60 years of achievements in biomedical research.


BALTIMORE

Baltimore earned his Ph.D. at the Rockefeller University and completed postdocs at the Massachusetts Institute of Technology and Albert Einstein College of Medicine. He went to the Salk Institute to work with Renato Dulbecco as a research assistant for several years and then joined the faculty at MIT as an associate professor in 1968.

There, while studying RNA viruses that can cause cancer, Baltimore discovered the enzyme reverse transcriptase, which does the opposite of RNA polymerase; it uses an RNA template to synthesize DNA. It was a groundbreaking finding and provided insight for later understanding the human immunodeficiency virus that causes AIDS. Reverse transcription is also important in telomere maintenance and has been used widely as a laboratory tool to study RNA — for example, in generating cDNA libraries for RNA sequencing. Baltimore shared the 1975 Nobel Prize in physiology or medicine with Howard Temin and Dulbecco.

A postdoc in Baltimore's lab discovered the transcription factor nuclear factor kappa-light-chain-enhancer of activated B cells, or NF-κB, while studying how cells control the expression of antibody genes; later, the lab outlined how genetic recombination leads to the diversity of those antibodies. The lab also studied the role of microRNA in the immune system and the possibility of treating HIV and cancers with gene therapy.

After founding the Whitehead Institute at MIT and serving for some years as its director, Baltimore joined the faculty at CalTech, where he was president from 1997 to 2006. He continued to run his lab at CalTech until 2019. The cofounder of three biotechnology companies and holder of 100 patents, he now serves on the boards of directors of two companies and the scientific advisory boards of three.

Baltimore's honors, in addition to the Nobel, the National Medal of Science and a long list of honorary degrees, include a 2.1 kilometer asteroid that bears his name.

Markussan wins cross-cultural award

Kia Markussen, a graduate student at the University of Kentucky College of Medicine, has received the university's scholarship for cross-cultural understanding.

Markussen, who is from Denmark, studies neuronal metabolism and protein glycosylation and how they change in neurodegenerative diseases. In a paper last year on Lafora disease, a genetic disorder of glycogen synthesis that causes seizures and neurodegeneration, she and colleagues in Matthew Gentry's lab showed that the mutations behind the disease disrupt oxidative glucose metabolism but have different effects on neurons than on astrocytes, another type of brain cell. She earned her undergraduate degree at the University of Copenhagen, where she also studied neurometabolism in health and disease.


MARKUSSEN

In addition to her research, Markussen serves as the co-chair of an international students' committee on the university's graduate student congress. The scholarship announcement also lauds her "commitment to building cross-cultural understanding through work in her department."

Collins receives innovation award from Sigma Xi

James Collins, a professor at the Massachusetts Institute of Technology who is also affiliated with the Wyss Institute and the Broad Institute, has received the 2021 Walston Chubb Award for Innovation from the scientific research honor society Sigma Xi.


COLLINS

Collins' lab at MIT studies synthetic biology and systems biology, applying large-scale computational techniques to come up with novel antibiotics and other tools. In recent years, his lab has published on synergistic drugs to treat COVID-19, using CRISPR-based biosensors to detect pathogens including malaria and SARS-CoV-2, and applying deep learning to such problems as dermatological diagnoses based on images and identifying synergistic drug combinations.

The lab has investigated ways to use complementary antibiotics, some dependent on metabolic activity and others independent, to kill bacteria without causing harm to human cells. In 2020, with colleague Regina

Barzilay's team, they published a neural network–based study that surveyed thousands of compounds and identified one, a c-Jun N-terminal kinase inhibitor called halicin, that could slow the growth of numerous bacteria, including some that can resist other antibiotics.

Collins earned his doctorate in medical engineering at the University of Oxford, where he was a Rhodes scholar. He then joined the faculty at Boston University, where he remained until moving to MIT in 2014. Among his many honors are a MacArthur fellowship, a National Institutes of Health director's Pioneer Award, and a Sanofi–Institut Pasteur Award. He is a member of the National Academy of Sciences, the National Academy of Engineering, the National Academy of Medicine, the National Academy of Inventors, and the American Academy of Arts and Sciences.

Marnett to step down as Vanderbilt dean

Lawrence Marnett, the dean of Vanderbilt University's school of basic medical sciences, has announced that he will step down from that role on June 30.

Marnett has led the school since 2016, when the university separated from Vanderbilt University Medical Center. As dean, he led the creation of the school of basic medical sciences in 2016, aiming to give a new home to basic science departments including biochemistry, cell and developmental biology, molecular physiology and biophysics, and pharmacology.

MARNETT

Marnett earned his Ph.D. at Duke University and conducted postdoctoral research at the Karolinska Institute and Wayne State University. He was a professor at Wayne State for 14 years before joining the faculty at Vanderbilt in 1989. Since then, he has helped to launch or lead numerous other groups and centers on the campus; he served as director of basic research at the Vanderbilt–Ingram Cancer Center for five years, directed the Vanderbilt Institute of Chemical Biology and served as associate vice chancellor for research and senior associate dean for biomedical sciences at the medical center.

After stepping down as dean, Marnett plans to focus on his cancer research. His lab, which has trained nearly 100 doctoral students and postdocs, studies the enzyme cyclooxygenase-2 and how its activity contributes to cancer and inflammation. They also investigate how normal metabolism contributes to DNA damage and how cells respond to damaged proteins.

Marnett has received awards for excellence in teaching from Vanderbilt, and he is a fellow of the American Chemical Society, the American Association for the Advancement of Science, and the Society for Redox Biology and Medicine.

Horton joins Draupnir advisory board

Jay Horton, a professor and director of the Center for Human Nutrition at the University of Texas Southwestern Medical Center, will join the scientific advisory board of the biotech company Draupnir.

Draupnir, based in Denmark, uses small-molecule therapeutics to lower low-density lipoprotein cholesterol. Its principal target enzyme, PCSK9, controls the level of LDL receptor expressed on cells in the liver, thereby altering liver cholesterol metabolism. Injectable drugs that block PCSK9 activity using monoclonal antibodies and RNA interference have provided new treatment options for people with high cholesterol or heart disease whose cholesterol levels do not respond to statin drugs. Draupnir aims to push that advancement into molecules that can be delivered as pills, which are easier to administer and usually more affordable.

HORTON

Fifteen years ago, Horton's lab was the first to show that mice without PCSK9 have lower plasma cholesterol, confirming observations of humans with PCSK9 mutations; his group also determined the mechanism by which PCSK9 decreases LDL receptor level. He continues to study the molecular bases of metabolic disease, including how nonalcoholic fatty liver disease develops and how sterol- and cholesterol-responsive transcription factors can go awry in disease.

Horton is an associate editor of the Journal of Lipid Research and a consulting editor for the journal Arteriosclerosis, Thrombosis and Vascular Biology. He serves on the board of the Deuel Conference on Lipids.

Department chair for Schiffer

Celia Schiffer has been named chair of the newly renamed Department of Biochemistry and Molecular Biotechnology (formerly biochemistry and molecular pharmacology) at the University of Massachusetts Chan

Biophysical Society fellows named

The Biophysical Society, a 7,500-member international organization founded in 1958, has named seven members as its 2022 class of fellows. The honorees are recognized for demonstrating sustained excellence in science and contributing to the expansion of the field of biophysics, according to the BPS Bulletin.

Four of the new fellows are also members of the American Society for Biochemistry and Molecular Biology: Karen Fleming, Angela Gronenborn, Stephen Kowalczykowski and Carol Robinson.


FLEMING

Karen Fleming, a professor of biophysics at Johns Hopkins University and an associate editor of the Journal of Biological Chemistry, is honored "for her rigorous and incisive contributions to our understanding of the thermodynamics of membrane protein folding and for her tireless devotion to promoting gender equity in science."


GRONENBORN

Angela Gronenborn, the University of Pittsburgh Medical Center Rosalind Franklin chair and distinguished professor of structural biology at the University of Pittsburgh School of Medicine, is honored "for her pioneering work in the use of nuclear magnetic resonance to probe the structure and function of macromolecules in biology and for her outstanding commitment to and impact on the biophysics community as a whole." Gronenborn won the ASBMB's Mildred Cohn Award in 2019.


KOWALCZYKOWSKI

Stephen Kowalczykowski, a distinguished professor of microbiology and molecular genetics at the University of California, Davis, is honored "for his seminal biophysical and biochemical studies, including advancing 'visual biochemistry,' that have contributed to our understanding of the complex protein-DNA interactions involved in DNA recombination and DNA replication."


ROBINSON

Carol Robinson, a professor of chemistry and director of the Kavli Institute for Nanoscience Discovery at the University of Oxford, is honored "for advancing the field of native mass spectrometry of proteins and protein complexes."

Also named BPS fellows are Roger Cooke, Martin Karplus and Pernilla Wittung–Stafshede. The seven honorees will be recognized in February during the Biophysical Society's 66th annual meeting.

Medical School, effective Oct. 1.

Schiffer's research has helped define the field of drug resistance and develop frameworks to avoid drug resistance. She discovered that drug resistance occurs when mutations in the target enzyme alter the balance of substrate recognition to inhibitor binding to favor the substrates. Mechanistically, she has demonstrated that resistance mutations either occur where drugs physically contact regions of the drug target that are not essential for substrate recognition or alter the ensemble dynamics of the drug target.


SCHIFFER

Schiffer defined the substrate envelope, and her lab designed inhibitors that minimize the likelihood for resistance in structure-based drug design. She delineated a strategy of parallel molecular dynamics to capture how mutations equate with alterations in inhibitor potency. She is applying these strategies to the viral proteases of SARS-CoV-2.

After earning her Ph.D. at the University of California, San Francisco, in biophysics, Schiffer pursued post-

doctoral research at ETH Zurich and at Genentech in South San Francisco. She joined the faculty of the UMass Medical School in 1998. In 2009, she established the Institute for Drug Resistance at the medical school, which she continues to direct.

Last year's recipient of the ASBMB William C. Rose Award, Schiffer is also a fellow in the American Academy of Microbiology, received the 2016 Chancellor's Award for Excellence in Mentoring from UMass Chan Medical, and was named educator of the year by the Massachusetts Society for Medical Research.

Bryant receives ASM award

Don Bryant, a professor of biotechnology and of biochemistry and molecular biology at the Pennsylvania State University, has received the American Society for Microbiology's 2022 Award for Basic Research.

BRYANT

Bryant studies chlorophotrophic bacteria. For 50 years, he has been interested in two contrasting taxa: cyanobacteria that photosynthesize and produce oxygen like plants, and green sulfur bacteria, which are killed by oxygen and light. In 2005, his team discovered Chloracidobacterium thermophilum, the first characterized phototrophic acidobacterium, while analyzing microbes that dwell in the hot springs in Yellowstone National Park.

Bryant's group discovered that some terrestrial cyanobacteria can adapt and grow using only far-red light by synthesizing chlorophyll variants that absorb far-red light. Biotechnologists hope these findings might help engineer crops that can produce higher yields by using sunlight more efficiently.

Bryant grew up on a dairy farm in Kentucky. After studying chemistry and biology at the Massachusetts Institute of Technology, he earned his Ph.D. in molecular biology at UCLA, studying cyanobacterial light-harvesting proteins, and conducted postdoctoral research at the Pasteur Institute in Paris and then Cornell University. He joined the faculty at Penn State in 1981 and since has worked concomitantly as a visiting professor at Montana State University and Nanyang Technological University in Singapore.

Among Bryant's recognitions are the Kettering Award, which he received last year from the American Society of Plant Biologists. He is a fellow of the American Association for the Advancement of Science and the American Academy of Microbiology. He has served on the editorial board of the Journal of Biological Chemistry twice, as editor-in-chief of the journal Frontiers in Microbial Physiology and Metabolism, and as an associate editor for other journals.

Zuk named deputy director of NIGMS

Dorit Zuk was promoted to deputy director of the National Institute of General Medical Sciences in October.

Zuk had been serving as acting deputy director of the institute for almost a year while also serving as director of its Division of Genetics and Molecular, Cellular and Developmental Biology.

Zuk earned her undergraduate degree in biology at Tel Aviv University and both a master's and Ph.D. in cell biology at the Weizmann Institute of Science, also in Israel. She completed postdoctoral training at the University of Massachusetts Medical School in Allan Jacobson's lab.

ZUK

She began her career in scientific publishing as deputy editor of the journal Cell and later editor of Molecular Cell.

She joined the National Institutes of Health in 2007 while participating in the American Association for the Advancement of Science's science and technology policy fellowship program. After a year at the American Academy of Arts and Sciences, she spent five years as a science policy adviser at the NIH before being selected to direct what was then called the Office of Policy, Communications and Strategic Alliances at the NIH's National Center for Advancing Translational Sciences. She joined the NIGMS in 2016.

Zuk served on the society's Education and Professional Development Committee from 2005 to 2014.

Coorssen is Proteomes co-editor-in-chief

Jens Coorssen, a professor of health sciences and biology at Brock University in St. Catharines, Ontario, has been elected to serve jointly as editor-in-chief of the

journal Proteomes with Matthew Padula, a senior lecturer and head of the proteomics core at the University of Technology, Sydney.

The editors plan to focus on all aspects of proteome analysis and on rigorous scientific approaches, with complementarity of methodologies being of particular interest.

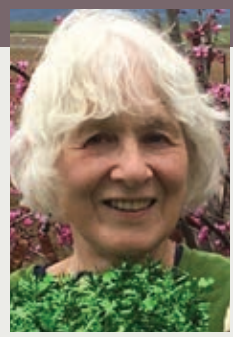
Coorssen's research involves both proteomic and lipidomic analyses of samples, seeking to understand underlying molecular mechanisms of different diseases. He has studied the role of lipids and phosphoproteins in calcium-triggered exocytosis, which is important for synaptic transmission, sought biomarkers for preterm labor in pregnant women's serum and looked into demyelination in a mouse model of multiple sclerosis.

COORSSEN

After earning his Ph.D. at McMaster University in Hamilton, Ontario, Coorssen did postdoctoral research at the Max Planck Institute for Medical Research in Heidelberg, Germany. He was a fellow and then visiting professor at the National Institutes of Health before returning to Canada as a research scholar of the Alberta Heritage Foundation for Medical Research while at the University of Calgary. In 2008 he moved to Australia to establish the Molecular Physiology Unit and head the Molecular Medicine Research Group at Western Sydney University.

Coorssen's return to Canada in 2016 to join the Brock University faculty was something of a homecoming; he earned his bachelor's and master's degrees at Brock.

Catherine L. Squires



Catherine L. Squires, a microbiologist whose research reflected her lifelong interest in how bacterial ribosomes work, died Aug. 3 at her home in Winters, California.

Born April 9, 1941, in Sacramento, Squires grew up visiting dairy and chicken ranches owned by members of her family, and there she gained a lifelong appreciation of nature and agriculture, according to her obituary; in an autobiographical article, she described taking water samples from her father's chicken coop to school for show and tell. She received bachelor's and master's degrees at the University of California, Davis.

While earning a Ph.D. in molecular biology and biochemistry at UC Santa Barbara, Squires determined the structure of several transfer RNAs in E. coli. During a postdoc with Charles Yanofsky at Stanford University, she investigated transcription and translation of genes in the trp operon, which became a famous model system for biosynthetic feedback because its activity is high when its product, tryptophan, is low and vice versa.

Squires began her career as an assistant professor at Dartmouth University and then moved to Columbia University, where she became a professor of biology. In 1994, she was appointed professor and chair of the department of molecular biology and microbiology at Tufts University School of Medicine, serving until her retirement in 2007. She returned to California and completed her teaching and research career as a visiting professor at Stanford.

As an independent researcher, Squires was interested in how ribosomal RNAs were transcribed and in transcription antitermination, which occurs when a polymerase reads through what ordinarily would be recognized as a stop site. In one study, published in Cell in 1984, her lab identified "the antitermination system involved in E. coli ribosomal RNA transcription." She continued to work on ribosomal RNA operons and what controlled their transcription, expanding into an interest in why bacteria have so many rRNA operons. In the late 1990s, she and colleagues generated an E. coli strain that had no RNA operons and depended on plasmid-derived ribosomal RNA to survive. The strain enabled researchers to study bacterial evolution and horizontal gene transfer; Squires' lab also used it to reorganize genes from an rRNA operon and demonstrate that transcription order was not very important for ribosome assembly.

In addition to more than 35 years as an American Society for Biochemistry and Molecular Biology member, Squires was a member of Sigma Xi, the American Association for the Advancement of Science, and the American Society for Microbiology.

Alexander Glazer

Alexander Glazer, a renowned biochemist and environmentalist, died July 18. He was 86.

Glazer was born in Poland on July 7, 1935, and immigrated to Australia with his mother after World War II. He earned his bachelor's and master's degrees in biochemistry from the University of Sydney.

While working toward his master's degree, Glazer attended a lecture given by biochemist Emil Smith from the University of Utah. Glazer moved to Utah for his doctoral degree and researched the physiochemical properties of proteins under Smith until 1960. He completed postdoctoral fellowships at the Weizmann Institute of Science in Israel and under Frederick Sanger at the Medical Research Council Laboratory of Molecular Biology in England. Smith recruited him to UCLA as faculty in 1964, and he subsequently moved to the University of California, Berkeley, in 1976. He retired from research in 1994 but served as co-chair of the department of molecular and cell biology and as a professor in the graduate school until 1997.

Much of Glazer's early research focused on chemical modifications of proteins and the properties of enzymes including proteases and hydrolyses. With collaborators, he helped determine the structure of phycobiliproteins — light-harvesting structures found in photosynthetic cyanobacteria and certain algae. Through these studies, they were able to describe how light energy is transferred to the reaction center in the cell. Glazer then demonstrated how these proteins could be used as fluorescent tags, which now are used to mark and sort living cells in the laboratory.

Glazer's career took a turn when he was hired as the director of the University of California Natural Reserve System, which encompasses a network of field stations and protected natural lands. As director, he focused on issues of environmental science such as nitrogen fixation, contamination of freshwater sources, and the repercussions of oil production and use. He served as the system's director for 11 years.

Glazer received numerous awards and honors throughout his career, including two Guggenheim fellowships, the Endeavor Prize from the British Association for the Advancement of Science, and election to the American Academy of Arts and Sciences and the National Academy of Sciences.

— Courtney Chandler

Richard Duncan Dallam

Richard Duncan Dallam, a member of the American Society for Biochemistry and Molecular Biology since 1958, died July 2. He was 95.

Born Dec. 12, 1925, in Kansas City, Missouri, Dallam enlisted in the Army Air Force Cadet Corps at the age of 17. According to an obituary, as a B-29 tail gunner, he flew his final mission on Aug. 14, 1945, the day the U.S. dropped atom bombs on Nagasaki and Hiroshima; the B-29s continued the attack for 24 hours until Japan surrendered — the largest and last bombing mission of World War II.

Dallam did undergraduate studies at William Jewel College and Rockhurst College before earning a Ph.D. in biochemistry from the University of Missouri. He did postgraduate work at the Massachusetts Institute of Technology and the Rockefeller Institute and then joined the faculty at the University of Louisville School of Medicine, where he taught and did research for 40 years, retiring as professor emeritus in 1993.

After early research in the chemical composition of cell nuclei, Dallam's main interest into the 1960s was the complex biochemistry of oxidative phosphorylation, the process by which energy derived from sugar or other nutrients is used to make ATP. He studied the role of quinones, or K vitamins, which we now know act as lipid-soluble electron shuttles between steps in the electron transport chain. He was also interested in the role selenium plays when incorporated into cytochrome proteins — finding that it was incorporated in selenocysteine and seleniomethionine. In later years, he published on the impact of acid rain on sulfate metabolism in crop plants.

In 1961, the American Heart Association designated Dallam an established investigator for his work on intermediary metabolism. He was a founding member of the Biophysical Society.

Dallam and his wife, Ginny, owned farms in Lagrange and Simpsonville, Kentucky, where for 25 years they raised cattle and quarter horses. For several years, they showed their ponies hitched to an Amish farm wagon in the Kentucky Derby's Pegasus Parade.

Edmond H. Fischer (1920–2021)

By Élyse S. Fischer & John D. Scott

Cosmopolitan, cultured, creative and caring. These characteristics were embodied in the life of Edmond (Eddy) Fischer — Nobel laureate, musician and globetrotting scientific celebrity — who died Aug 27, age 101, in Seattle, Washington.

Eddy was born April 6, 1920, in the French Concession of Shanghai, son of a French mother and an Austrian father. Until the age of 7, he attended l'École Enfantine Française in Shanghai. During the summers, because Shanghai was crushingly hot and humid, his family would go to Hakone Lake in Japan via boat from Shanghai to Yokohama. Thus, from an early age, he experienced a multicultural lifestyle that shaped his perspective, relationships and science in the years to come.

In 1927, the family left for Europe, traveling by the Trans-Siberian Railway. In Switzerland, Eddy was educated at La Châtaigneraie International School, where he became fascinated with science and the emerging field of biological chemistry. His curiosity was sparked by a childhood admiration of bacteriologist Louis Pasteur and the fortuitus gift of a research-grade microscope. This scientific instrument allowed him to conduct experiments and first experience the adrenaline of discovery.

Eddy's cosmopolitan upbringing fostered a love of history, music and art. At age 14, just after moving to Geneva to attend the Collège Calvin, he attended a performance of Beethoven's Emperor Concerto by Swiss maestro Johnny Aubert, a piano professor at the prestigious Conservatoire de Musique de Genève. The next day, Eddy approached the director of the conservatory and asked to become Aubert's student. In the ensuing audition, Eddy impressed Aubert by playing Chopin's Polonaise in A major and Mendelssohn's Rondo Capriccioso. Eddy studied with Aubert for 7 years, and they became good friends. From then on, Eddy regularly entertained friends and colleagues by playing the piano.

COURTESY OF ÉLYSE FISHER

The Fischer family in Shanghai, China, in 1926. From left to right: Oscar (father), Edmond, Georges, Renée (mother) and Raoul.

Graduating from high school weeks before the outbreak of World War II, Eddy remained in neutral Switzerland. After receiving a B.S. in organic chemistry from the University of Geneva, he earned a Ph.D. under the supervision of Kurt Meyer on the structure of polysaccharides and alpha-amylases, enzymes that catalyze hydrolysis of starch into sugars. In 1953, Eddy joined the biochemistry department at the University of Washington, where he remained an active faculty member until his death. Shortly after arriving in Seattle, Eddy teamed up with UW biochemist Edwin G. Krebs; the two embarked upon a lifelong friendship and a remarkable collaboration.

Fischer and Krebs investigated glycogen metabolism in skeletal muscle. They focused on how glycogen phosphorylase, the enzyme that catalyzes the rate-limiting step in glycogenolysis, is regulated. They knew that the phosphorylase a form was active without the addition of adenosine monophosphate, or AMP, and that the phosphorylase b form was inactive without AMP. Through a series of ingenious and occasionally serendipitous experiments, they concluded that

COURTESY OF ELYSE FISHER

Eddy Fischer plays the piano at the wedding of his oldest son, François, in 1984.

interconversion of the phosphorylase a to the b form occurs as "a direct phosphorylation of the enzyme." This heralded the advent of the study of protein phosphorylation as a major mode of cellular regulation. Since then, protein kinases have become the pharmaceutical industry's most important class of drug targets to combat cancer and inflammation. Many kinase-inhibitor drugs are approved for clinical use, and hundreds more are undergoing clinical trials. Fischer and Krebs were awarded the 1992 Nobel Prize in physiology or medicine "for their discoveries concerning reversible protein phosphorylation as a biological regulatory mechanism," the Nobel Assembly wrote.

Eddy's scientific contributions far exceeded the discovery of protein phosphorylation. He was a wonderful mentor whose scientific lineage includes world leaders in cell signaling. In the 1970s, '80s and '90s, he was at the forefront of phosphatase research, the debatably more important reverse step of protein phosphorylation. Luminaries passing through his lab included Philip Cohen (University of Dundee, Scotland), who went on to classify the protein phosphatase family and define subcellular targeting as a vital signal termination mechanism; David Brautigan (University of Virginia), who discerned mechanisms of protein phosphatase 1 action; and Nicholas Tonks (Cold Spring Harbor Laboratory), who discovered protein tyrosine phosphatases, enzymes that frequently counteract oncogenes. Each trainee benefitted from creative and considerate conversations with Eddy. These precious touchpoints garnered an unparalleled loyalty and pride in being part of the Fischer (and Krebs) scientific family tree.

Eddy's first and favorite tongue was French. His French–Swiss flamboyance often contrasted with the Midwestern sensibilities of Ed Krebs. Their linguistic interface was something to behold. In Eddy's own words, "I remember the amused expressions of my colleagues seated in the back row of the class listening to my fractured English when lecturing the medical students. I also remember Ed Krebs' broad smile whenever I lapsed into French. What Ed didn't realize, though, is that within two years, while my English didn't improve very much, his deteriorated completely!"

Publishing is at the core of scientific discovery. Working with Fischer and Krebs on manuscripts was an absolute joy but not without challenges. The scientific world knew this pair as Eddy and Ed. Yet while Fischer always addressed Krebs as Ed, Krebs invariably referred to Eddy as Ed. Most correspondence began with the greeting "Ed" and ended with the salutation "Ed" — often leaving the confused reader uncertain of whether the message was from Fischer to Krebs or from Krebs to Fischer. This befuddling banter made "Ed-iting" manuscripts a daunting prospect.

Both Eds were superb writers and confident of their own grammatical prowess. Fischer was a section editor for the journal Biochemistry, and Krebs was an associate editor for the Journal of Biological Chemistry. Hence, a first author sitting between the two during editing sessions frequently took on the mantle of a tennis umpire as scientific and grammatical points were served diplomatically across the table and courteously returned. On rare occasions, the first author would venture into the fray, offering their own syntactic suggestion, only to be rebuffed with the politeness and precision of a JBC rejection. Thus, each trainee got not only a superb scientific education but also invaluable linguistic instruction at the feet of Fischer and Krebs. As was often said, "Two h-Ed's are better than one."

Eddy's dedication to science did not detract from his devotion to his family. Whether it was a family Christmas dinner or a reunion of friends, he always insisted on hosting, even though he never had enough table space or chairs. He loved to cook traditional Swiss meals, including endives au jambon, fondue and aspic, which always were drowning in fat and often devoid of vegetables. Even at the age of 101, he

liked to cook for everyone.

Eddy was particularly close to his granddaughter and family protege, Élyse Fischer (an author of this Retrospective). He was proud that she attended the University of St. Andrews in Scotland. He always had valued his diverse education and upbringing and thought the experience would be good for her. As a native of Scotland, I (John Scott, an author of this Retrospective) remember being quizzed by Eddy about the benefits of a St. Andrew's education and the value of Élyse's proximity to the city of Dundee, the home of his protege Philip Cohen and Cohen's wife Tricia, both of whom became important mentors to Élyse. I enthusiastically concurred.

COURTESY OF ÉLYSE FISHER

Eddy plays the piano with family at his grandson Leo's wedding on July 31, 2021. Élyse Fischer is on the far left.

Eddy was even more gratified when Élyse chose to study protein structure determination for her Ph.D. with David Barford at the Medical Research Council Laboratory of Molecular Biology at the University of Cambridge. Perhaps fated by genetics, Élyse succeeded in unveiling a molecular mechanism of cell cycle regulation by phosphorylation.

Eddy's enthusiasm for science, music, friends and family never diminished. In June 2021, he participated in the 70th Lindau Nobel Laureate meeting over Zoom, inspiring young scientists and playing piano for the virtual Lindau symphonic orchestra. Less than a month before his death, he played piano at his grandson's wedding as groom and bride walked down the aisle.

We close with Eddy's own words: "As to what has always attracted me toward scientific research ... I believe it's the systematic way one has to proceed in science, the kind of logic one has to apply to solve a given problem. Science builds on science, where every result obtained suggests a number of questions, and every question asked suggests the next experiment. One must follow those leads just like a detective follows different leads to solve a murder mystery, never knowing whether it will lead you to a dead end or to the next big breakthrough. Because in science, one cannot order at will a great discovery, or buy it at any cost because there is no way of predicting when and from where it will come."

The two Eds in 1992 at the annual Fischer and Krebs lab retreat in Pack Forest, Washington. This photo was taken soon after they won the Nobel Prize.

COURTESY OF ÉLYSE FISHER

Élyse S. Fischer (elyse.s.fischer@gmail.com) recently completed her Ph.D. at the University of Cambridge, studying cell cycle regulation with David Barford at the MRC Laboratory of Molecular Biology. Follow her on Twitter: @ElyseFischer7.

John D. Scott (scottjdw@uw.edu) is the Edwin G. Krebs–Speights Professor of Cell Signaling and Cancer Biology and chair of the pharmacology department at the University of Washington.

Making science the focus

By Courtney Chandler

Nicki Nouri didn't grow up with a passion for science. While she knew she didn't share the same interests as some of her friends — like art or film — she wasn't set on one field of study.

That changed the summer before her senior year of high school. After cold emailing researchers at the nearby University of Illinois at Chicago, she ended up connecting with Gonzalo Izaguirre, a research assistant professor in the college of dentistry. Because she was a minor, Nouri couldn't participate in lab research, but Izaguirre created a makeshift mentorship program that exposed her to the world of biochemistry through research using scientific databases and the literature.

"It was very eye-opening for me and just fascinating," Nouri said. "He really inspired me to want to pursue science and opened the door for me."

After high school, Nouri chose to attend the University of Illinois at Chicago to pursue a degree in predental biology. She reached out to Izaguirre again, and he told her to think about starting an American Society for Biochemistry and Molecular Biology Student Chapter at the school.

"We (had) a lot of pre-professional clubs, but nothing for specific topics of science or biochemistry," she said.

It began as a daunting task — Nouri was starting completely from scratch, without a blueprint from a previous president or past members. She asked people that she'd barely spoken to in her classes if they'd be interested in joining the executive board and slowly built a team.

"I really wanted to make sure it wasn't just something that goes on a résumé," she said. "I had to figure out how to have meetings be meaningful and be something that students could come out of and feel like they gained something."

The chapter started having meetings in spring 2019 and was formally recognized in the fall. Meetings highlighted research opportunities and potential career paths and provided professional development, including guest speakers sharing their own career journeys.

The chapter also has hosted blood drives, organized biology experiment demonstrations with children at a nearby school, raised funds to provide lunches for frontline workers, and hosted a virtual symposium with high school students about the importance of mental health and well-being (with a biochemistry spin focusing on the neurological details of depression and anxiety).

COURTESY OF NICKI NOURI

Nicki Nouri, who led the ASBMB student chapter at the University of Illinois at Chicago, on a hike.

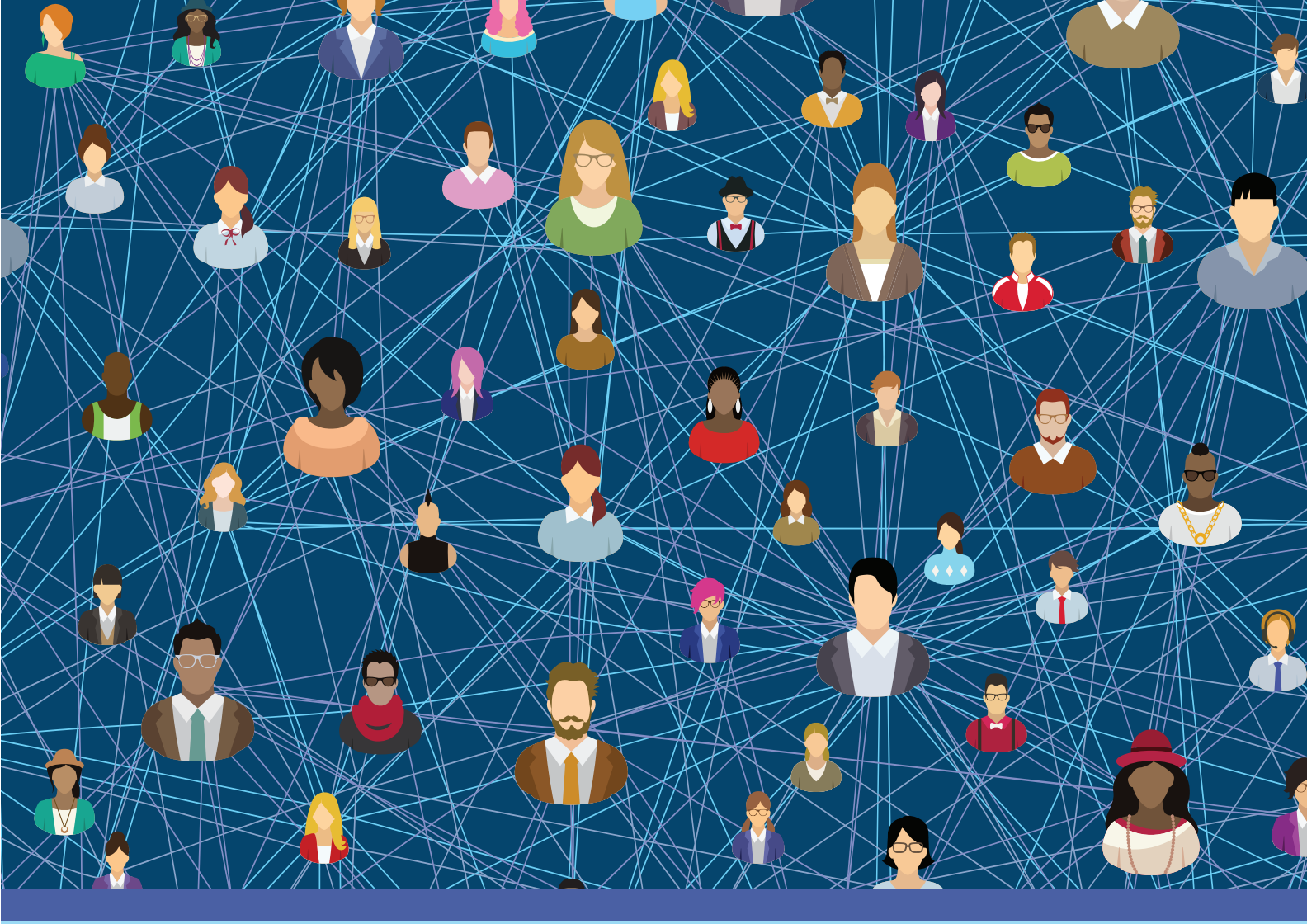
Nouri remained chapter president until she graduated in December with a biology major and entrepreneurship minor. She then passed the reins to her co-presidents, Sona Fokum and Simi Sharma (Izaguirre remains the chapter's faculty adviser).

Nouri said her time as an ASBMB Student Chapter president helped prepare her for a career in research.

"Founding and participating in ASBMB has significantly improved my time management and has allowed me to grow as a leader over the years," she said. "But most importantly, it really opened my eyes to what biochemistry is and what a career in that field can look like."

Nouri plans to pursue research positions with the ultimate goal of enrolling in a D.D.S./Ph.D. program. She hopes to combine a professional career focused on biochemical research with the dental care and patient interaction she has come to enjoy during her undergraduate studies.

Courtney Chandler (courtneyec19@gmail.com) is a postdoctoral researcher at the University of Maryland, Baltimore, and an industry careers columnist for ASBMB Today. Follow her on Twitter: @CourtneyCPhd.



Connect with colleagues at an ASBMB meeting

The ASBMB organizes virtual and in-person events that cover scientific research, educational best practices, the funding environment and more.

Upcoming ASBMB events and conferences

Deuel conference on lipids
March 1–4, 2022 | Monterey, Calif.

2022 ASBMB Annual Meeting
April 2–5, 2022 | Philadelphia

ESCRT biology
May 17–20, 2022 | Madison, Wis.

O-GlcNAc regulation of cellular physiology and pathophysiology
July 7–10, 2022 | Athens, Ga.

Evolution and core processes in gene expression
July 21–24, 2022 | Kansas City, Mo.

Mass spectrometry in the health and life sciences
Aug. 14–18, 2022 | Cambridge, Mass.

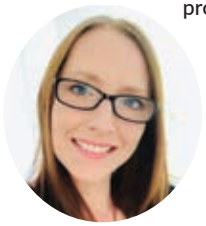
The interplay between epigenetic regulation and genome stability
Sept. 28–Oct. 2, 2022 | Seattle

Transcriptional regulation: Chromatin and RNA polymerase II
Sept. 29–Oct. 2, 2022 | Snowbird, Utah

Explore all upcoming events at asbmb.org/meetings-events.

ASBMB
American Society for Biochemistry and Molecular Biology

New meetings manager



Ann Brameyer joined the society's meetings department in November. She has two decades of professional events experience. She earned her bachelor's at American University and event-management certificate at George Washington University. She can be reached at abrameyer@ASBMB.org.

Nominations for the ASBMB Honor Society due Jan. 31

Student Chapter members are eligible for election into the ASBMB Honor Society, XΩΛ. The honor society recognizes juniors and seniors demonstrating exceptional achievement in academics, research and science outreach. For more information and to apply, visit asbmb.org/education/student-chapters/honor-society.

ASBMB HONOR SOCIETY XΩΛ

Send us your news!

Have you recently been promoted or honored? Do you have good news to share with your fellow ASBMB members? Email it to us at asbmbtoday@asbmb.org and include a photo!

Give the gift of ASBMB membership

Give a colleague, student or friend a full year of exceptional resources and enriching experiences. Visit asbmb.org/gift-membership.

It's certification exam registration time

The 2022 ASBMB degree-certification exam registration window runs from Jan. 5 through Jan. 31. The certification exam is open to all undergraduate students enrolled in ASBMB-accredited programs and is designed to test students' knowledge and understanding of the core competencies in biochemistry and molecular biology developed by the ASBMB and its members. Find out more about the exam and the accreditation process at asbmb.org/education/certification-exam.

Summer research funding for Student Chapter members

The ASBMB supports the development of new scientific minds. Student Chapter members may apply for the Undergraduate Research Award, which grants $1,000 to support the awardee's summer research projects.

The deadline for this year's award is March 1. Applicants must submit a research statement that includes details of the methods used for data collection and a clear summary of the proposed project. Additional requirements can be found at asbmb.org/education/student-chapters/awards/undergraduate-research.

Nominations for Outstanding Chapter Award due Feb. 14

Each year, the ASBMB recognizes a Student Chapter that excels in its leadership, scholarship and service in the areas of biochemistry and molecular biology.

ASBMB STUDENT CHAPTERS

A winning chapter, selected for its demonstrated track record of accomplishments at both the chapter and the individual level over the past year, will be honored at the 2022 ASBMB annual meeting in Philadelphia. All active chapters are eligible to apply. More information at asbmb.org/education/student-chapters/awards/outstanding-chapter.

Veteran staffer Maher retires

Longtime American Society for Biochemistry and Molecular Biology staff member Ned Maher, who served as the society's first controller and went on to handle a variety of accounting and membership matters over the years, retired Dec. 31.

Maher joined the society in 1994. Before his appointment, the ASBMB outsourced its financial affairs. The chief executive at the time, Chuck Hancock, recruited Maher to develop internal accounting systems and controls.

"When I was first hired at ASBMB, they were just implementing their first societywide computer network and standardizing programs across departments," Maher said. "Up to this point, the society still did much of the record keeping manually, and the various computer applications that were in use were not interconnected."

Of course, in those days, the society had fewer journals and less programming. It made sense then for Maher to work at the headquarters in Bethesda, Maryland, part time.

"My position with the ASBMB has changed a lot over the years, and the society has been very flexible with work hours and duties," he said. "I have been the primary parent — Mr. Mom — for my three children, and my employment at ASBMB provided me with the flexibility to raise my children and still have a challenging and rewarding career."

Cindy Whalen, a staffer on the membership team, has worked with Maher since 2008.

"Ned has been a pleasure to work with," she said. "He has always been very helpful, knowledgeable and has been my go-to for problem-solving or when I simply needed an extra hand to complete a task."

Other staffers describe Maher as a man with an unassuming manner. But, they noted, it was always obvious, upon entering the parking garage, whether he was at the office. Maher, a car aficionado, reliably drove a striking set of wheels. A few months before retiring, he showed up to the new Rockville headquarters in a sleek silver Corvette.

Steve Miller, the society's executive director, has been known to give Maher a good-natured ribbing.

"I wouldn't be surprised if Ned has had 17 cars in the 27 years he's been with the ASBMB. He's had anything from a Prius to a Porsche. It's like he's been auditioning for his next career as a car salesman," Miller quipped. "But, in all seriousness, it's been a real pleasure working with Ned, and I will miss him. I recall fondly consulting him when he was redesigning a vacation home on a river. I'm still awaiting my consulting fee. Good times."

Ed Marklin worked with Maher for his entire tenure. He said they first met when Marklin was troubleshooting computer issues for the IT department at the Federation of American Societies for Experimental Biology.

"We struck up a quick kinship for our love of cars. We would always discuss the newest models, styles and performance from various automakers," Marklin said. "Later, when Steve Miller was hired, he would join in our discussions. Steve and I would try and spark Ned's interest to go out and look for a new car. Sometimes it worked, other times it took a little longer for Ned to think about. But, eventually, it would happen. We would drive into the office garage on Monday morning, and there would be a new shiny set of wheels."

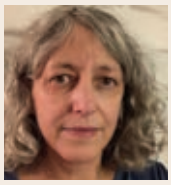
Marklin said Maher always would give his work pals "the grand tour of his new beast."

"I am going to miss seeing his new cars and really miss our daily conversations," he said. "Ned has been a great colleague and a true friend."

New committee members

Public Affairs Advisory Committee

JILL JOHNSON, professor, University of Idaho



Johnson's lab focuses on the role of molecular chaperones in the cell. She currently is studying the role of co-chaperones Hsp40 and Hsp70, which interact with client proteins before Hsp90. She's a member of the Institute for Bioinformatics and Evolutionary Studies at U of I. She earned her Ph.D. at the Mayo Graduate School in 1994.

JEFFREY WILUSZ, professor, Colorado State University

Wilusz is a microbiologist whose lab studies RNA–protein interactions, mechanisms of cellular RNA decay, and the interplay between noncoding RNAs and cellular RNA processes/post-transcriptional control. He is a fellow of the American Association for the Advancement of Science. He earned his Ph.D. at Duke University in 1985.

Membership Committee

CHI FUNG LEE, assistant member, Oklahoma Medical Research Foundation

Lee's lab is interested in metabolic signaling of heart disease. His research program focuses on NAD+ redox balance, consumption and synthesis pathways, and mitochondrial biology. He is a member of the American Heart Association and the American Physiological Society. He earned his Ph.D. at the University of Texas Health Science Center in San Antonio in 2011.

ROSS HARDISON, professor, Pennsylvania State University

Hardison's lab measures transcriptome profiles and uses epigenetic marks (such as transcription factor occupancy and histone modifications) and comparative genomics to predict gene regulatory modules. He is a member of the Journal of Biological Chemistry editorial board. He earned his Ph.D. from the University of Iowa in 1977.

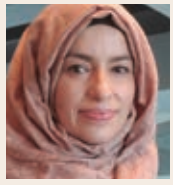
AKPEDJE DOSSOU, Ph.D. candidate, University of North Texas Health Science Center at Fort Worth

Dossou studies tumor-associated macrophages and their targeting via lipoprotein-based nanoparticles in Rafal Fudala's Lab. She's a member of the American Physiology Society, the American Association for the Advancement of Science, and the Society for Experimental Biology and Medicine. She earned her M.S. at UNT Health Science Center and B.S. at UNT.

RACHELL BOOTH, professor, University of Incarnate Word

Booth is a member of the steering committee that rapidly responded to the COVID-19 pandemic by providing members with resources for pivoting to online teaching. She also served as a regional director for Student Chapters from 2012 to 2021. She earned her Ph.D. from the University of Southern Mississippi in 2001.

MONA AL-MUGOTIR, analytical chemist, Glaxo Smith Kline



With a background in both pharmaceutical companies and academic research, Al-Mugotir aspires to contribute to the production of disease diagnostic markers, therapeutic molecules for drug development and understanding new mechanisms of action for existing drugs. She earned her Ph.D. at the University of Nebraska Medical Center in 2018.

Education and Professional Development Committee

NISHA CAVANAUGH, associate director of career development and postdoctoral programs, Sanford Burnham Prebys Medical Discovery Institute

Cavanaugh works to expand career and professional development for biomedical Ph.D. students. She was a member of the National Postdoctoral Association Advocacy Committee for eight years. She earned a Ph.D. from the University of Colorado Boulder in 2008.

THOMAS KISELAK, patent agent, Clark+Elbing LLP

Kiselak helps clients obtain patents related to chemistry and biotechnology, specifically in areas of analytical and organic chemistry, biosurfactants and proteomics. He earned a Ph.D. at the University of North Texas and is a student at the University of New Hampshire Franklin Pierce School of Law.

CHANDRIMA MAJUMDAR, postdoctoral researcher, University of California, Berkeley

A postdoc in Jamie Cate's lab, Majumdar is interested in the synthetic biology of the ribosome, specifically the generation of sequence-defined polymers with nonnatural amino acids. She is a member of the American Association for the Advancement of Science and a fellow of the UC Davis Leaders for the Future. She earned her Ph.D. from the University of California, Davis, in 2020.

REINHART REITHMEIER, professor, University of Toronto

Reithmeier's lab studies the structure and function of membrane proteins, in particular the chloride/bicarbonate anion exchanger AE1, Band 3, a glycoprotein of the erythrocyte membrane responsible for the exchange of chloride and bicarbonate across the plasma membrane, which is necessary for respiration. In 2012, he was elected to the Canadian Academy of Health Sciences. He earned his Ph.D. at the University of British Columbia in 1977.

Minority Affairs Committee

ALLISON C. AUGUSTUS–WALLACE, associate professor, Louisiana State University Health Sciences Center New Orleans

Augustus–Wallace promotes equity and inclusion, to increase the presence of historically excluded groups in medicine and biomedical research, and to promote health equity and improved health outcomes of marginalized groups. She is a member of the scientific research honor society Sigma Xi and the National Association of Diversity Officers in Higher Education. She earned her Ph.D. at LSU Health Sciences Center–New Orleans in 2014.

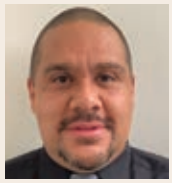
CECILIA GIULIVI, professor, University of California, Davis

Giulivi's lab explores the mechanisms underlying mitochondrial biology in disorders such as autism, schizophrenia, Huntington and fragile X tremor and ataxia syndrome. She is a member of the scientific research honor society Sigma Xi. She earned her Ph.D. at the University of Buenos Aires in 1989.

LEA VACCA MICHEL, associate professor, Rochester Institute of Technology

Michel's research is focused on dual-oriented bacterial lipoproteins and crystallin proteins, which are localized in the eye lens. She received the 2022 ASBMB Early Career Leadership Award. She earned a Ph.D. at the University of Rochester in 2007.

ALBERTO RASCÓN JR., associate professor, San José State University



Rascón studies the expression, characterization and inhibition of mosquito proteases with a goal of limiting the mosquito population and minimizing the spread of mosquito-borne viruses. He earned his Ph.D. at the University of Arizona in 2010.

YUFENG WEI, associate professor, New Jersey City University

Wei's research focuses on interactions between signaling proteins, including in the MAPK pathway, in apoptosis signaling and in the inflammasome. He is a member of the New York Academy of Sciences and Sigma Xi, the scientific research honor society. He earned his Ph.D. at Columbia University in 2002.

Science Outreach and Communication Committee

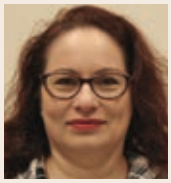
ADRIANA NORRIS, graduate student, Vanderbilt University

Norris is a graduate student at Vanderbilt University, where she studies the role of phospholipid flippases in the development of diabetes and metabolic syndrome in a mouse model. Norris also is an avid science communicator with experience in teaching and tutoring. She earned her bachelor's degree at Armstrong State University in 2018.

MELISSA ROWLAND–GOLDSMITH, associate professor, Chapman University

For the past several years, Rowland–Goldsmith has been teaching the blended ASBMB Art of Science Communication class within her cancer biology course. She is involved in both biology education research as well as working with undergraduate students to utilize molecular biology techniques to study pancreatic cancer inhibition and invasion when treated with various agents. In addition, she is the co-director of her university's Institute for Excellence in Teaching and Learning. She earned her Ph.D. at the University of California, Riverside, in 1997.

MICHELE VITOLO, assistant professor, University of Maryland, Baltimore



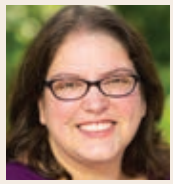
Vitolo studies cell signaling that promotes attachment and invasion in cancer cells, with particular interest in cellular microtentacle formation. She earned her Ph.D. at the University of Maryland Baltimore in 2004.

MICHAEL WOLYNIAK, associate professor, Hampden–Sydney College

Wolyniak's research interests in molecular biology are wide-ranging, but recently he has focused on applying engineering to brewer's yeast to benefit a local microbrewery. As director of undergraduate research, he also conducts pedagogical research. He earned his Ph.D. at Cornell University in 2004.

Student Chapters Committee

CORINA MAEDER, associate professor, Trinity University



Maeder studies protein–protein and protein–RNA interactions in the spliceosome, which governs pre-mRNA splicing. For work on how splicing mutants contribute to the degenerative eye disease retinitis pigmentosa, Maeder recently received a Voelcker Young Investigator Award. She earned her Ph.D. at Johns Hopkins University in 2005.

ERIK YUKL, assistant professor, New Mexico State University

Yukl is interested in the mechanisms by which bacteria acquire transition metals from the environment, and how certain metalloproteins are used as sensors of environmental conditions. He earned his Ph.D. at Oregon Health and Science University in 2009.

Women in Biochemistry and Molecular Biology Committee

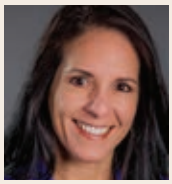
MARIANA BARBOZA GARDNER, associate project scientist, University of California, Davis

Barboza is a glycobiologist. Her research focuses on glycoproteomic studies to elucidate host cell surface glycans on the gut–brain axis and understand their modulation by diet and gut microbes in health and disease processes. She earned her Ph.D. in 2006 at Universidad Nacional de San Martin in Buenos Aires, Argentina.

MEGHNA GUPTA, research specialist, University of California, San Francisco

Gupta studies membrane proteins and transporters using cryo-electron microscopy in Robert Stroud's lab. Her work has expanded to encompass the coronavirus spike protein and other pandemic-related studies. Gupta earned her Ph.D. at Jawaharlal Nehru University in 2016.

KARLETT PARRA, professor and chair, University of New Mexico



Parra studies yeast vacuolar ATPases, investigating their assembly and how they regulate homeostasis, secretion and filamentation in the opportunistic pathogen Candida albicans. She chairs the biochemistry and molecular biology department at the University of New Mexico School of Medicine. Parra earned her Ph.D. at the State University of New York Upstate Medical University in 1998.

Meetings Committee

KIM ORTH, professor, University of Texas Southwestern Medical Center and Howard Hughes Medical Institute

Orth studies bacterial virulence factors to elucidate biochemical mechanisms used by pathogens to manipulate host signaling pathways. She discovered a family of Fic enzymes that mediate AMPylation, a posttranslational modification used by both pathogens and host cells to regulate signaling. She is recipient of the ASBMB Merck Award and a member of the National Academy of Sciences. Orth earned her Ph.D. at UT Southwestern Medical Center in 1993.

MARTHA CYERT, professor and department chair, Stanford University

Cyert uses systems biology techniques to study the calcium-dependent phosphatase calcineurin, which her lab identified as the target of immunosuppressant drugs such as cyclosporine A and FK506. She is a co-organizer of the 2022 ASBMB annual meeting. Cyert earned her Ph.D. at the University of California, San Francisco, in 1988.

AARON HOSKINS, associate professor, University of Wisconsin–Madison

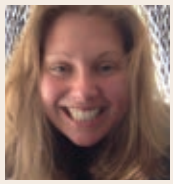
Hoskins studies the enzymes that control pre-mRNA splicing, using single-molecule techniques to see how splice sites are recognized and how events in RNA processing are linked. He is a past participant in the Beckman Young Investigator program. He earned his Ph.D. at the Massachusetts Institute of Technology in 2006.

JARED RUTTER, professor, University of Utah and Howard Hughes Medical Institute

Rutter studies how the mitochondrial proteome controls metabolism, a goal pursued by determining the functions of mitochondrial proteins and systematically identifying allosteric interactions between proteins and metabolites. He is a former ASBMB Council member and plenary lecturer. He earned his Ph.D. at the University of Texas Southwestern Medical Center in 2001.

ASBMB Today Editorial Advisory Board

JEANINE AMACHER, assistant professor, Western Washington University



Amacher studies peptide-binding protein domains and how they recognize their target peptide motifs, focusing human scaffolding domains (e.g., PDZ and SH2) and bacterials sortases, and their interactions with ligands. She earned her Ph.D. from Dartmouth University in 2014. She was a Jane Coffin Childs postdoc at the University of California, Berkeley.

PAUL CRAIG, professor, Rochester Institute of Technology

Craig's research focuses on software development for mass spectrometry and enzymology. He also develops programs for teaching biology and helping students think like scientists. He won the 2018 ASBMB Exemplary Contributions to Education Award. He earned his Ph.D. from the University of Michigan in 1985.

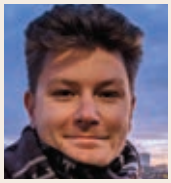
RENÉ FUANTA, assistant professor, East Stroudsburg University of Pennsylvania

Fuanta uses biophysical methods to study enzymes involved in the survival of respiratory pathogens such as Pseudomonas aeruginosa, which eventually could contribute to new antimicrobial molecules, and investigates virulence-related genes. He earned his Ph.D. at Auburn University in 2018.

DANIELLE GUARRACINO, professor, the College of New Jersey

Guarracino's lab works in the field of chemical biology, developing peptides that behave as inhibitors to the von Willebrand factor–collagen interaction that initiates thrombosis. She also studies how peptide sequences affect folding. Guarracino earned her Ph.D. at Yale University in 2008.

KEN HALLENBECK, scientist, Avitide



Hallenbeck is a drug-discovery researcher focused on novel ligand identification. A frequent contributor to ASBMB Today, he serves on the board of directors of the nonprofit ReImagine Science, which aims to find new ways to conduct and share science. Hallenbeck earned his Ph.D. at the University of California, San Francisco, in 2018.

BRIAN O'FLYNN, postdoctoral researcher, St. Jude Children's Research Hospital

O'Flynn is in the lab of Tanja Mittag at St. Jude Children's Research Hospital, where he studies biomolecular phase separation and the role it plays in functional and pathological processes. He uses a combination of cryo-electron microscopy and crystallography to investigate the assembly of multivalent biomolecules. He earned his Ph.D. at the University of South Florida in 2019.

JEN QUICK–CLEVELAND, postdoctoral researcher, University of California, Santa Cruz

Quick–Cleveland's research focuses on RNA splicing in yeast, which she studies using RNA nanopore sequencing, among other techniques. Quick–Cleveland is a Jane Coffin Childs postdoctoral fellow. She earned her Ph.D. in 2017 at the University of California, Los Angeles, where she studied microRNA biogenesis.

BRANDON ROY, Ph.D. student, Cornell University

Roy is a member of the plant pathology and plant microbe biology program at Cornell. His research focuses on viruses that infect grapevines. When not volunteering for the ASBMB, Roy also works with a STEM outreach program and is a church organist. He earned his bachelor's degree at Lebanon Valley College in 2020.

QIOU WEI, associate professor, University of Kentucky

Wei is an associate professor of toxicology and cancer biology at the University of Kentucky. He studies the oxidative stress–induced redox protein sulfiredoxin, which is overexpressed in some types of cancer and promotes metastasis. Wei earned his Ph.D. at the University of South Dakota's Sanford School of Medicine in 2005.

ASBMB

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Researchers make sense of scents

By Leia Dwyer

Almost all organisms, from single-cell bacteria to complex species, can detect chemicals through the pairing of chemical ligands and their receptors. Humans and other vertebrates mostly detect chemicals through our senses of smell and taste. Chemicals that we can sense by smell, called odorants, are ligands that bind to odorant receptors in the body, primarily in the nose.

Gaurav Ahuja's lab at the Indraprastha Institute of Information Technology, Delhi, studies this chemodetection — how it influences complex behavioral outputs and the genetics behind these processes. The lab recently released an artificial intelligence–driven prediction tool for olfactory decoding and authored a paper in the **Journal of Biological Chemistry** detailing the construction of the tool and data behind it.

The researchers named their tool OdoriFy; it is open-source, accessible to other researchers and highly interpretable. An interdisciplinary team of authors spanning computational biology and computer science and several institutes helped on the project. Co-first authors Ria Gupta, a fourth-year undergraduate student who worked on the deep learning behind the model and interpretability, and Aayushi Mittal, a second-year doctoral student who spearheaded data collection and design, share enthusiasm for the tool's potential uses.

OdoriFy's four modules or prediction engines — Odorant Predictor, Odor Finder, Odorant Receptor Finder, and Odorant–Odorant Receptor Pair Analysis — are available through a user-friendly website. Ahuja and team believe the use of cutting-edge neural network architecture, a series of algorithms that make up the artificial intelligence approach, helps distinguish their tool.

The data set behind OdoriFy is one of the largest curated data resources to date. The team manually checked and cross-checked olfactory information of more than 5,000 odorants, 800 nonodorants and 6,000 interaction pairs (between odorant and receptor) — a massive effort to read the scientific literature and document their findings. Mittal said the team "had so many sleepless nights, holding meetings asking ourselves, how can we approach this problem? How can we solve this?"

"There's a concept in machine learning called garbage in–garbage out — good data in, good data out," Ahuja said. Without highly accurate input data, their precisely designed computer model wouldn't be as strong as a predictive tool. As a result, OdoriFy consistently outperforms other models in the olfaction field and scores high across a number of validated metrics for measuring accuracy in prediction.

Scientists understand that humans' ability to distinguish odors is combinatorial. "Nature has developed ways to deal with the fact that we're exposed to billions of chemicals, but we have only a limited genome and therefore a limited number of odorant receptors," Ahuja said. "One receptor can recognize more than one odorant, and one odorant can be recognized by more than one receptor." So, while humans have only about 400 functional genes for odorant receptors, the combinatorial effect gives us the ability to detect many more than 400 odorants.

A tool such as OdoriFy that can predict both odorants and odorant-receptor pairing can help open doors for researchers working across this field of chemodetection and novel applications. Ahuja and team already have been contacted by companies and researchers who have used the tool and are interested in further collaboration. One of the most interesting avenues of pursuit is the application to cancer, as human tumor cells are known to express certain odorant receptors.

"Working on this project made us all realize how important olfaction is and how important our tool is for the public," Gupta said.

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Rethinking how culture medium contributes to cellular function

By Isha Dey

Cell culture medium, as we know, contains a combination of growth factors and other components that help researchers grow cells in the lab. An important constituent in the growth medium is serum, an animal-derived complex of growth factors, amino acids and lipids, which provides nutrition to the growing cells. Researchers lack complete information on serum composition and its lot-to-lot variability but have studied the effects of some growth medium components on cellular metabolism. However, they do not yet understand fully the impact of the medium's lipid content on cell function.

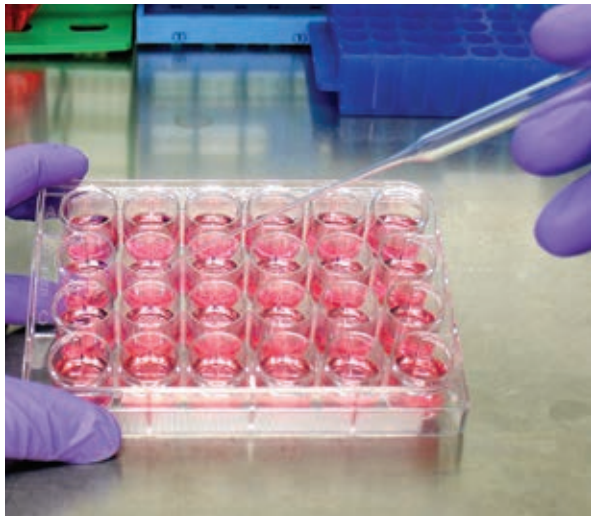
The powerhouse of human cells is mitochondria. An important component that determines mitochondrial function is cardiolipins, or CLs. These phospholipids located on the inner mitochondrial membrane are involved in mitochondrial bioenergetics and maintaining architecture of the mitochondrial membranes as well as in scavenging reactive oxygen species. However, cardiolipin composition is different in different tissues of the body, and because CLs play a central role in mitochondrial function, this means cells in different organs have varied mitochondrial activity.

To better understand the effect of nutrition, especially lipids, on mitochondrial CL composition and function, Markus Keller's lab at the Medical University of Innsbruck in Austria cultured mammalian cells in lipid-free medium and then fed them with various types of lipids. Using mass spectrometry lipidomics and mathematical modeling, the authors were able to quantify the CL composition in the presence of different fatty acids in the growth medium.

Specifically, addition of linoleic acid to the medium altered 76% of the natural CL side chain composition compared to untreated medium. Addition of alpha-linolenic acid and arachidonic acid also altered CL side chain composition significantly. Moreover, linoleic acid treatment increased the activity of the mitochondrial respiratory complex I, which is responsible for generating ATP and thus regulates normal functioning of a cell. The lab's breakthrough findings were published in the **Journal of Lipid Research**.

Gregor Oemer, the first author on the paper, said an initial challenge of this project was finding cells that would grow without lipids, which are usually necessary for cell proliferation. "We got Panserin 401 (a serum-free medium) from a German biotech company and luckily got our HeLa cells to grow in this lipid-free medium," he said.

The work was a collaborative effort. "We were in luck because Innsbruck is the home base for Oroboros, one of the most renowned respirometry companies," Oemer said, "and thanks to Erich Gnaiger, the head, we collaborated for the respirometry assays."



This project was a continuation of Oemer's master's thesis from the Keller lab. "Lipid metabolism is very complex but quite fascinating, and we don't know much about it," he said.

What struck Oemer most was how, by just altering the lipid intake, the researchers were able to influence critical cellular functions. He hopes the work raises awareness that variations in serum in cell culture medium may alter experimental data. This is especially important while studying diseases such as Barth syndrome, a genetic disorder characterized by abnormalities in mitochondrial cardiolipins.

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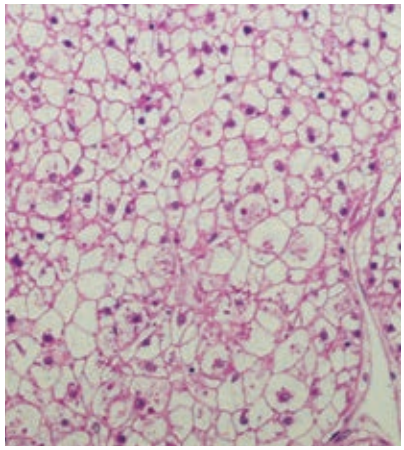
Uncovering the regulatory role of cancer-linked MALAT1 RNAs

By Anna Hu

Scientists have long known that about 99% of all RNAs are noncoding — they do not go through translation to create the dizzying array of proteins that populate our cells. This is an astonishing proportion, and although we now know that these are not "junk" RNA, as they previously were termed, researchers have much to learn about their wide-ranging functions.

In a paper published in the journal **Molecular & Cellular Proteomics**, Hao Wang, Yali Zhang and Xinyu Guan from Tianjin University describe how they and their team uncovered the vast regulatory role of one noncoding RNA in lipid metabolism. Metastasis-associated lung adenocarcinoma transcript 1, or MALAT1, is considered a long noncoding RNA, or lncRNA, because it contains over 200 nucleotides. Found in cancer patients, it is associated with tumor growth and is one of the most well-studied lncRNAs. A growing body of evidence shows elevated lipid metabolism as a driver for tumor progression, so studying the factors that affect this process is increasingly vital.

This is not the lab's first foray into studying MALAT1. In a 2017 study, according to corresponding author Ruibing Chen, they "characterized the proteins bound with MALAT1 using mass spectrometry–based proteomics and found that MALAT1 could interact with many subunits of the spliceosome." While this work



established that MALAT1 could affect gene splicing, it left open the questions of which genes' splicing was affected most and how this changed gene expression.

To clarify this tangle of interactions, the researchers used transcriptomics and proteomics to investigate genes affected by MALAT1 knockdown. Using hepatocellular carcinoma cell lines, they found that downregulating this lncRNA reduced the quantities of proteins in both the fatty acid metabolism pathway and the ubiquitous AMP-activated protein kinase pathway, which regulates cellular energy through glucose uptake. Using bioinformatics tools, they also found evidence that MALAT1 regulation can occur during either pre-mRNA splicing or transcription, depending on the gene. Thus, the team was able concurrently to show a more specific modulatory role for MALAT1 and suggest the cellular mechanism underpinning its effects.

One of the most surprising findings was the broad range of this lncRNA's reach, and Chen emphasized the large number of genes with changed expression levels in MALAT1 knockout cells. "To be specific, the abundance of 2,662 transcripts and 1,149 proteins was changed," she said.

Many of these genes are tied to lipogenesis and contribute to the role of MALAT1 upregulation in tumor growth. This is because rapidly proliferating cancer cells require a large quantity of lipids as membrane components, and lipogenesis provides those raw materials.

In large part, the researchers credit their integrated multiomics approach for the success of this study. This approach represents a new way to "depict the detailed process behind a particular biological phenomenon," Chen said. "You are not looking at one or two genes, but a great many at the same time. And in this way, there's a chance you can actually see the systematic change happen in the cell as well as the interactions between different pathways."

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From the journals

By Isabel Casas, Sarah May & Brian O'Flynn

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

Stabilizing enzymes in the liver

The liver is the organ in charge of breaking down toxic foreign molecules and metabolizing drugs in mammals. The main enzymes involved in these processes are heme-containing cytochrome P450 monooxygenases, or CYP450s. These enzymes accumulate primarily in the liver and have a characteristic catalytic cycle dependent on protein–protein interactions with oxidoreductases. In previous work, Meredith McGuire and a team at Johns Hopkins University had shown that progesterone receptor membrane component 1, or PGRMC1, a heme-binding protein, binds to CYP450s in yeast and mammalian cells and supports their activity. However, the researchers did not yet know the extent of PGRMC1 function in CYP450 biology and whether PGRMC1 is also a heme chaperone.

In a recent article in the **Journal of Biological Chemistry**, the authors write that in studying livers of mice that had the Pgrmc1 gene removed, they found that PGRMC1 binds and stabilizes a broad range of CYP450s in a heme-independent manner and that PGRMC1 supports maintenance of CYP450 protein levels post-transcriptionally. In addition, the mouse livers exhibited reduced CYP450 activity consistent with reduced enzyme levels. The researchers also show that PGRMC1 stabilizes CYP450s and that binding and stabilization do not require PGRMC1 binding to heme. Moreover, PGRMC1-dependent stabilization of CYP450s is physiologically relevant, as Pgrmc1 deletion protected the mice from acetaminophen-induced liver injury.
DOI: 10.1016/j.jbc.2021.101316

Lighting the path to discovery of dark immunopeptides

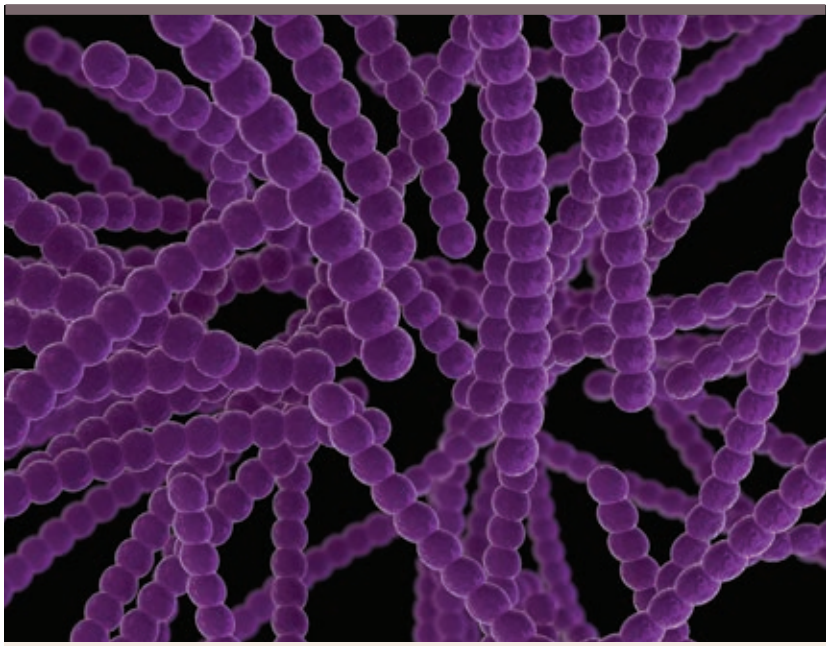
Immune system T cells can recognize and destroy cancer cells. Most cells break down some of their own proteins into short peptides, called immunopeptides, which they present to T cells as if showing an ID. When a cancer cell presents a mutated immunopeptide, T cells recognize it as a fake ID and trigger an immune response to destroy the cancer cell. These mutations could allow scientists to target T cells directly to cancer cells. But researchers have found it challenging to identify the immunopeptides with mutations or other alterations because their sequences do not match the conventional sequences in protein databases. Lacking easy detection, they are known as dark immunopeptides.

In a recent publication in the journal **Molecular & Cellular Proteomics**, Katherine Scull and colleagues at Monash University performed RNA sequencing on the acute myeloid leukemia cell line THP-1 and used those results to create a protein database that includes both conventional and unconventional immunopeptide sequences. By the conventional method, the researchers identified 14,000 immunopeptides in THP-1 cells. Their new method captured over 85% of these immunopeptides and led to the discovery of an additional 1,029 unconventional peptides not found in protein databases. Their workflow may help scientists identify dark immunopeptides in other cancers and develop cancer-specific vaccines.
DOI: 10.1016/j.mcpro.2021.100143

Pinpointing substrate specificity for phospholipase A2s

The phospholipase A_2, or PLA_2, superfamily catalyzes the hydrolysis of the phospholipid sn-2 ester bond with an elegant simplicity that requires extreme specificity. The products of this reaction play vital downstream roles. Free arachidonic acid, for example, is the precursor in the synthesis of the proinflammatory prostaglandins and the leukotrienes. To ensure this specificity is met, expression levels and localization of each PLA_2 group are finely tuned. So too is the substrate specificity.

In a recent publication in the **Journal of Lipid Research**, Daiki Hayashi and a team at the University of California, San Diego, describe their effort to catalog the selectivity of each PLA_2 for omega-3 and omega-6 fatty acids. Using a



This computer-generated 3D image shows Gram-positive streptococci bacteria, which grow in chains.

Flipping the switch for competence

Bacteria can put in place different paths to transfer genetic material. Horizontal gene transfer, moving genetic material between organisms other than from parents to offspring, is essential for bacteria to survive in challenging environments. In pathogenic bacteria, such as streptococci, the ability to take up external DNA — known as competence — allows them to get new genetic material that has been associated with gain of virulence-related mechanisms and multidrug resistance.

In streptococci, competence is tightly regulated by the competence stimulating signaling system, or ComRS, that is activated by the ComR sensor and the SigX-inducing peptide, or XIP, pheromone. A better understanding of how this system is activated provides insights to identify potential targets for drug development and other biomedical purposes, as Laura Ledesma–García of the Louvain Institute of Biomolecular Science and Technology and colleagues describe in a recent article in the **Journal of Biological Chemistry**.

The group proposes a model for ComR activation based on two major conformational changes of the XIP-binding domain. Using a semi-rational mutagenesis approach, they first identified two residues within XIP that increase ComR sensor activation by interacting with two aromatic residues of its XIP-binding pocket. Then, using random and targeted mutagenesis of ComR, they determined that the interplay among these four residues remodels a network of aromatic–aromatic interactions involved in relaxing the sequestration of the DNA-binding domain, flipping the switch on for competence.

DOI: 10.1016/j.jbc.2021.101346

— Isabel Casas

combination of mass spectrometry and molecular dynamics simulations, the researchers presented in detail the substrate specificity for each PLA_2 toward arachidonic acid and the fish oil–derived omega-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid. The MD simulations demonstrated this specificity to be rooted in the geometry of the hydrophobic active site, with encoded selectivity toward chain length and double-bond position.

As the authors state, "This illustrates the enormous power of a hydrophobic site cavity to show the unexpected, exquisite specificity and sensitivity generally attributed to charged and polar sites in proteins."

DOI: 10.1016/j.jlr.2021.100113

Nature to the rescue: Inhibiting SARS-Cov-2 replication

Diterpenoids are an extensive family of natural products produced by plants. Within this family, ent-kauranes are involved in many aspects of plant growth and protection from feeding insects. When ingested by humans, these compounds have anti-inflammatory, hypoglycemic and anti-viral properties.

The SARS-Cov-2 pandemic is driving drug development aimed at identifying new antiviral compounds that target coronaviral proteins. Research performed in previous epidemics identified enzymatic nonstructural proteins, or NSPs, involved in viral replication inside host cells. Nsp9 is a conserved essential replicase, and researchers are looking for compounds that interfere with its activity.

A recent article in the **Journal of Biological Chemistry** describes

how Dene Littler at Monash University and collaborators used a native mass spectrometry–based approach to screen a natural product library for compounds that bind Nsp9. They found that the ent-kaurane oridonin binds to purified SARS-CoV-2 Nsp9 with micromolar affinities. They also determined the crystal structure of the Nsp9–oridonin complex and showed that oridonin binds Nsp9 through a conserved domain.

Oridonin reduces Nsp9's ability to act as a substrate for Nsp12, an essential RNA-dependent RNA polymerase. The authors also show that oridonin has broad antiviral activity, reducing viral titer after infection with either SARS-CoV-2 or, to a lesser extent, MERS-CoV in cellular assays in the lab.
DOI: 10.1016/j.jbc.2021.101362

Exploring the relations between acylations

One type of protein modification, known as acylation, or the addition of an acyl group, can occur at the side chain of lysine residues. Acyl groups come in several varieties, including acetyl and succinyl groups. Acylation can impact a protein's function drastically by regulating its activity, stability and location within the cell. Researchers don't know if different acylations work together to perform their biological roles in gene transcription, metabolism and aging.

Yujiao Yang, Hong Zhang and colleagues at the Chinese Academy of Sciences used immunoaffinity to enrich for proteins with modified lysine and mass spectrometry to quantify

Making heads or tails of flatworm regeneration

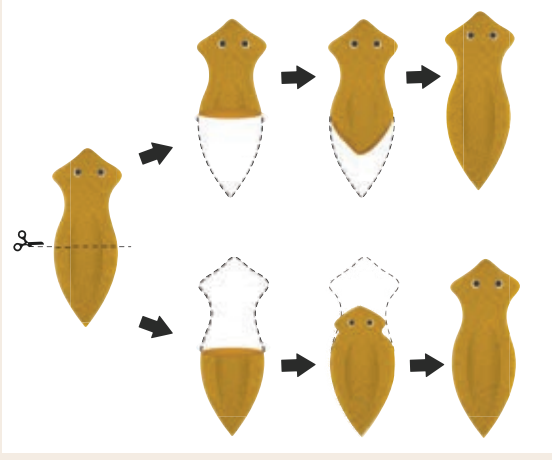
Flatworms have the extraordinary ability to regrow most of their bodies — even a new head and tail — after amputation. Humans can only regenerate certain tissues, mainly the fingertips and liver. If we understood how to turn on regeneration in humans, we potentially could activate it to restore other damaged tissues and organs.

Regeneration only occurs when cells are in the right environment. The extracellular matrix, a scaffold that covers the outside of cells, could lay the foundation for new tissue growth and carry the biological signals that turn on regeneration. But researchers do not know which components of the extracellular matrix enable organisms like the flatworm to regenerate lost or damaged tissue.

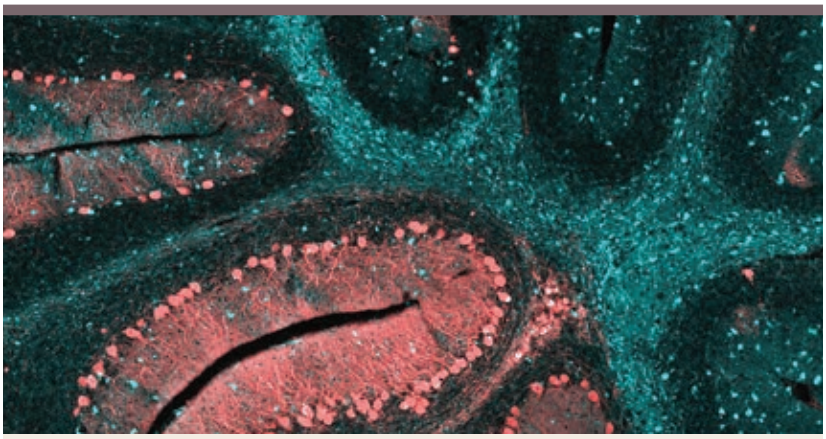
In a recent study published in the journal **Molecular & Cellular Proteomics**, Ekasit Sonpho and colleagues at the Stowers Institute for Medical Research used three techniques to remove the cells of Schmidtea mediterranea, a type of flatworm, leaving behind a purified extracellular matrix. Performing liquid chromatography with tandem mass spectrometry, the researchers identified proteins in the flatworm's extracellular matrix, with each isolation technique enriching for a different set of proteins. After knocking down 39 candidate extracellular matrix proteins in S. mediterranea by RNA interference, one protein — heparan sulfate proteoglycan — emerged as a key factor in tissue regeneration. Its presence enabled flatworms to survive in the early days after tissue injury.

The authors highlight the feasibility of using S. mediterranea as a model system for studying the function of the extracellular matrix, particularly in whole-body regeneration. Compared to other regenerative model organisms, such as axolotls and zebra fish, researchers can use flatworms to more easily identify extracellular matrix proteins and determine their roles in regeneration through loss-of-function screens. These new tools could give us clues to the process of regeneration and its potential applications for human health.
DOI: 10.1016/j.mcpro.2021.100137

— Sarah May



Cut in half, the flatworm Schmidtea mediterranea regenerates into two complete worms.



EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT, NATIONAL INSTITUTES OF HEALTH

Cerebellum of a mouse brain in the late stages of Niemann–Pick type C1 disease. The dense lipid pockets shown in blue are due to reduced cholesterol transport.

Targeting protein folding to combat Niemann–Pick type C1

The glycoprotein Niemann–Pick type C1, or NPC1, functions in intracellular cholesterol transport. Mutation of this protein hinders its folding and trafficking between organelles, which leads to reduced cholesterol transporting and subsequent accumulation. This disorder can have early- or late-onset consequences ranging from death in infancy to adult neurodegeneration. No treatment exists for NPC1 disorder; trials of intrathecal therapies only slow disease progression.

Previous research showed that histone deacetylase, or HDAC, inhibitors offered some correction for the NPC1 mutant in cells. Researchers believed this was caused by changes in molecular chaperone activity, in particular HSP70 and HSP90, in the presence of HDAC inhibitors. In a recent publication in the **Journal of Lipid Research**, Nina Pipalia of Weill Cornell Medical College and a multi-institutional team investigated the effects of HSP90 inhibition on NPC1 mutant fibroblasts.

The investigators confirmed that inhibitors of HSP90 showed potent dose-dependent effects, with one in particular, AUY922, counteracting the NPC1 mutation phenotype after 48 hours at subnanomolar concentrations. This was due to the NPC1 mutant's increased ability to exit the endoplasmic reticulum after folding — hindrance of which is the main phenotype of the disorder. This was coupled with increased ability to localize within late endosomes and lysosomes and perform its function — transport of cholesterol.

But why would chaperone inhibition increase protein folding and trafficking ability? HSP90 inhibition actually resulted in overexpression of HSP70 and HSP40, both of which were shown to play a role in counteracting NPC1 mutant phenotypes. While mouse models will provide the real litmus test, the authors state that "the promising effect of HSP90 inhibition and HSP70 over expression provides a basis for further investigations of protein chaperones in the treatment of NPC1 disease."
DOI: 10.1016/j.jlr.2021.100114

—Brian O'Flynn

global acetylation and succinylation of the bacteria Streptomyces coelicolor. Their publication in the journal **Molecular & Cellular Proteomics** shows that many lysine residues can be both acetylated and succinylated, suggesting that they could compete to modify the same lysine. Of the proteins with lysine acylations, approximately 75% were both acetylated and succinylated, either at the same lysine or different lysine residues. For central metabolism proteins, the percentage was even higher. Knocking out the desuccinylase ScCobB2, which removes succinylation, also affected protein acetylation, suggesting there is crosstalk in regulating lysine acylations. Overall, the authors provide new protein targets for studying lysine acetylation and succinylation in metabolism.
DOI: 10.1016/j.mcpro.2021.100148

High-throughput assay of lipase activity

Measuring the activity of lipases in a research setting often involves cumbersome multistep protocols using radiolabeled substrates and separation of substrates from products. This time-consuming process has hindered thorough investigation of inhibitors of lipases, leading to a lack of clinically approved lipase-targeting drugs with potency and specificity. This is of significant concern because lipases have relevance in numerous metabolic diseases.

In a recent paper in the **Journal of Lipid Research**, Sujith Rajan and colleagues at New York University Long Island School of Medicine describe how they developed a more streamlined method

to determine rates of hydrolysis of triacylglycerols, or TAGs, by lipases. This was validated by testing a panel of lipase inhibitors.

The researchers incorporated a fluorescent nitrobenzoxadiazole moiety onto the TAG substrate to form an NBD-TAG substrate, which they incorporated into liposomes, thus developing a rapid, fluorescence-based assay. This was partnered with the use of Cos-7 cells for enzyme overexpression, due to their low levels of naturally occurring lipases. Finally, incorporation of the phosphatidylinositol into NBD-TAG substrate vesicles was found to greatly increase enzyme activity. This negated the cumbersome step of separating substrate from product to accurately measure activity. Combined, this presents a promising route for future lipase inhibitor discovery studies and opens such studies up to the promise of high-throughput screening.

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Upcoming ASBMB events and deadlines

JANUARY

10	**DEUEL** abstract deadline
24	Marion Sewer scholarship applications accepted
27	ASBMB annual meeting last-chance abstract deadline
31	Honor Society nominations deadline

FEBRUARY

	Black History Month
1	**DEUEL** registration deadline
7	*Periodic Table Day*
7	ASBMB annual meeting early registration deadline
11	*International Day of Women and Girls in Science*
14	Annual meeting outstanding Student Chapters award nomination deadline
14	Regional Meeting award deadline
25	PROLAB application deadline
27	*National Protein Day*
28	*Rare Disease Day*

MARCH

	Women's History Month
	Multiple Sclerosis Awareness Month
	National Kidney Month
1	Undergraduate Research Award deadline
1	Student Chapter Outreach Grant spring deadline
1–4	DEUEL conference on lipids
11	*World Kidney Day*
14–20	*Brain Awareness Week*
18	ASBMB annual meeting advance registration deadline
19	*World Sleep Day*


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The secret history of touch

Stories from the labs that found two groundbreaking receptors

By Laurel Oldach

Most experiments fail.

Only a fraction of scientists' work at the bench makes it into published papers. Often, the bulk of a researcher's efforts is fruitless, producing months' or years' worth of negative data that don't provide new insights, data that answer the motivating question with "We still don't know." Against that backdrop, it is remarkable when a discovery actually materializes.

The 2021 Nobel Prize in physiology or medicine was awarded to David Julius and Ardem Patapoutian for their discoveries of receptors that sense temperature and pressure, work that exemplifies how difficult research can be. Through hundreds of mice, tens of thousands of cells and millions of bacterial colonies, the research groups that made the winning discoveries persisted in asking important questions about how the brain detects its surroundings.

"A lot of what we do is not success. It's failure," Julius said on the day the prize was announced. "I think there's two things that have to keep you going. One is just persistence … and the other is that you have to get enjoyment out of what you do every day."

The scientists in Julius' and Patapoutian's labs who made key discoveries at the bench worked through many technical problems and disappointments in pursuit of the molecules behind sensation.

Here are five stories of their persistence.

Pool DRG-11

Michael Caterina and the capsaicin receptor

Michael Caterina, now a professor at Johns Hopkins, with David Julius during a 2014 award ceremony

Most human senses — sight, scent, taste — involve receptors for a chemical ligand. Temperature sensing involves a response to ambient conditions, with no ligand to be found (see "The last sensory system to fall").

In the 1990s, David Julius unexpectedly found a way in while trying to understand a molecule that was interesting because it was irritating. Julius and his trainees studied capsaicin, a compound from hot peppers, because it caused a sensation of pain. Julius said, "The connection to heat wasn't something that we had preemptively figured out."

Michael Caterina, who conducted many of the key experiments as a postdoc, initially had laid the groundwork to look for a different receptor altogether; Julius had a reputation for discovering new receptors. Caterina had joined the lab hoping to find the protein that recognizes the neurotransmitter gamma aminobutyric acid, better known as GABA. But after he had worked on the project for some time, someone else published the receptor's identity.

"It was devastating," Caterina said. "You open up Nature and see this full article on this beautiful experiment. But the kicker was that because of a peculiarity in the way the GABA-B receptor functions … we never would have gotten it with that assay that we were using."

Still, the assay had to be useful for something.

Being scooped left Caterina with a toolkit for hunting receptors: a fluorescence assay that could detect a cellular calcium influx and a library of millions of genes expressed in the brain.

There's an anecdote about Julius and a moment of inspiration in the hot sauce aisle that has taken on a life of its own. He didn't decide to hunt for the capsaicin receptor while picking up the week's groceries, he said at a press conference — although he said a trip to a supermarket did prod him to think, "'We really have to get this project done.'"

Physiologists had shown that capsaicin could activate pain-sensing neurons in the dorsal root ganglion, or DRG, a relay station for sensory signals on their way from the skin to the brain. DRG neurons are heterogeneous. Some respond to pressure, some to cold, some to heat and some to chemical irritants — such as capsaicin. It stood to reason that there must be a receptor. Could the team use its tools to find it?

"This idea about the capsaicin receptor had been floating around in our lab for a long time, and people had sort of taken stabs at it, but no one had really done it seriously," Julius told ASBMB Today. "Realizing that Mike needed something and that he was incredibly capable, I said, 'Why don't you do this?'"

It was a risky project. As the GABA receptor just had shown, Caterina's approach only could find single-protein receptors. If capsaicin bound to a complex of two or more proteins, he would fail. Additionally, plenty of other labs had failed to identify a capsaicin receptor, to the point that some argued that perhaps it wasn't sensed by a protein at all. "All the obvious things had been tried," said Toby Rosen, then an undergraduate in the lab.

Despite the risks, Caterina decided to take on the project. With help from research scientist Tony Brake (see "A happy accident"), he generated a new coding library with millions of transcripts from DRG neurons and set up a screen for a capsaicin-binding receptor. He transfected pooled subsets of the library into cells loaded with a fluorescent calcium sensor and then added capsaicin, watching for a response.

Everyone from the Julius lab who spoke to ASBMB Today for this story remembers that the 11th pool Caterina tested showed the first flicker of fluorescence. Most volunteered its name: pool DRG-11. Given that there were 120 pools, this was statistically pretty fortunate. Still, the pool included 16,000 genes, any of which might code for the receptor. Caterina subdivided and subdivided again, using bacteria to amplify increasingly narrow subsets of the library. Julius got involved too, helping to pick bacterial colonies on at least one occasion.

"He was just cranking — incredible hours during that period," Rosen said of Caterina. "I want to say 18 to 20 hours a day. It was breathtaking."

With every subdivision, more cells fluoresced in response to capsaicin. "Mike came in one day with this incredible picture: really massively responding HEK293 cells, which looked like a nuclear explosion," Rosen said. "And the controls were just totally untouched."

In just three weeks of long days, Caterina had narrowed the response down to a single gene.

"You spend so much time in research with projects that take a long time and that move slowly," Caterina said, looking back. "When you have these windows of time when things are actually moving more processively, it's really a special thing."

On the day he received the Nobel Prize, Julius recalled this experiment as one of the most beautiful he'd ever been involved in.

The receptor, dubbed transient receptor potential vanilloid 1, or TRPV1 for short, was an ion channel. The team suspected that its response to capsaicin was a side effect and that the protein might have evolved to recognize some stimulus more relevant to cells. What was the receptor really there for?

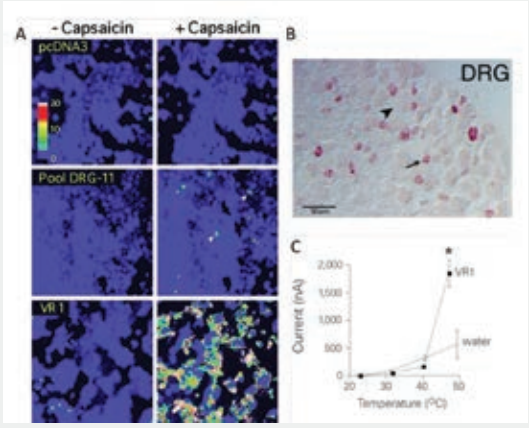
CONTINUED

The last sensory system to fall

At a press conference, a journalist asked David Julius why it had taken so long for the Nobel committee to award a prize based on the neurobiology of touch. After all, they had years before honored discoveries in other sensory organs including how the eye recognizes light; how olfactory receptors match specific odorants; and how G protein–coupled receptors, including those that recognize bitter and sweet tastes, activate cell signaling.

"This has sort of been the last main sensory system to fall to molecular analysis," Julius agreed.

He cited two reasons. One is that, unlike sight, taste and olfaction, the sense of touch is distributed widely across the surface of the body and inside it, making it hard to isolate a cell population involved in sensation. Secondly, that the signal isn't a specific chemical ligand that can be added to a cell culture or crystallized as part of a complex. In contrast, the cues that these particular neurons sense are insubstantial; there is no ligand linked to feelings of pressure or temperature. That was what made the existence of molecules that feel hot and cool so useful to Julius' studies.

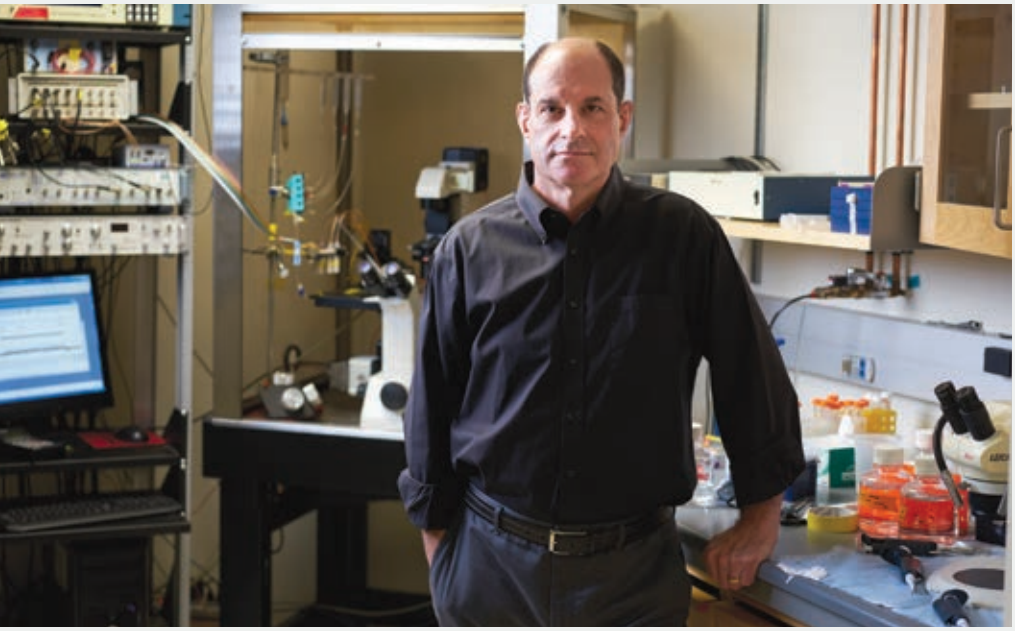


COURTESY OF THE NOBEL FOUNDATION

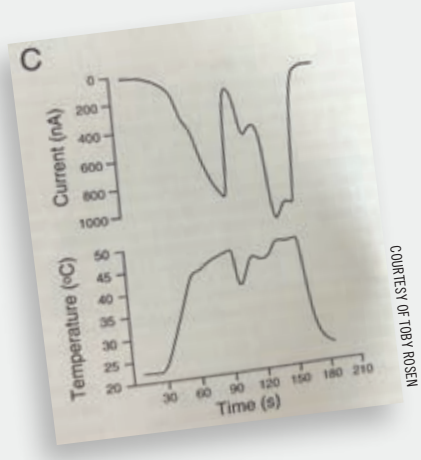
A figure from the 1997 paper that described TRPV1 shows (panel A) the gradual appearance of cells that responded to capsaicin as the lab narrowed down the TRP channel's identity; (panel B) the presence of TRPV1-expressing cell bodies in the dorsal root ganglion; and (C) the impact of TRP expression in an oocyte on current across its membrane as temperature increased.

The wiggle–waggle experiment

Makoto Tominaga, Toby Rosen and TRPV1 heat sensation



David Julius in front of an electrophysiology rig in his lab after being awarded the Breakthrough Prize in 2016.



COURTESY OF TOBY ROSEN

A photo of a figure from a paper shows the sensitivity of the TRP channel to temperature. A high current (top panel) indicates that the channel is open. As temperature increases (bottom panel), so does current, when temperature is turned back down, current drops off. The lab concluded that TRPV1 has a threshold temperature for activation and opening.

Julius' lab had found the receptor that binds to capsaicin, and they doubted that was all it did. But for technical reasons, the assay Caterina had used to identify the channel, TRPV1, was not well suited to finding other stimuli.

"That's when this dual approach of using patch clamp electrophysiology and oocyte two-electrode voltage clamp (recording) became really helpful," Caterina said. "Makoto and Toby were able to show definitively, and more convincingly, that this was a heat-activated channel."

Makoto Tominaga, an electrophysiologist, was already an assistant professor in Japan when he joined the Julius lab in San Francisco to learn molecular cloning. While Caterina had been working to discover new ion channels, Tominaga had been building an instrument for patch clamp electrophysiological recording, often called a rig, that would let the lab listen in on electrical impulses from individual channels (see "How can you tell if a channel is open?"), which he used to confirm that TRPV1 opened a cation channel in response to capsaicin.

The lab suspected, based on noisy preliminary data and on knowing that TRPV1 governed a response to pain, that the channel might also open in response to heat.

The experiments were difficult to perform. Adding heat introduced problems with the microscope: It changed the volume of liquids, including the oil between the microscope lens and the sample, causing cells to heave out of focus. Temperature-induced shifts in position also sometimes broke the fine stretched-glass electrodes that Tominaga used to isolate a single patch of membrane. In addition, before fluorescent proteins were widely available, it was hard to tell which cells had been transfected, so he had to work through many cells to find the few that responded to capsaicin.

As with the calcium imaging, the difficult experiments paid off in the end. Tominaga found that heating a cell would open the channel, letting cations flow into the cell.

"The most exciting time in my life was when I saw the heat-evoked activation of the ion channel," Tominaga said. At the time, he added, "there was no such concept" as a channel opened by temperature. "I was really, really surprised and

really excited to see that."

He wasn't alone in his excitement. Rosen said, "Once we saw the heat data, it became clear, like holy cow, this is why hot peppers are hot."

Having shown that changing temperatures could open the channel, the lab wanted to learn more about how it detected shifting temperature, whether the cation influx was fast or slow, changing stepwise or all at once as the media heated up. But the cell heating equipment they used relied on what Rosen called a "toaster oven–type technology." It tended to switch on and off, oscillating through a range of a few degrees instead of maintaining one temperature — which made it very difficult to be certain what, precisely, the channel was responding to.

Rosen was the only undergraduate Julius had ever hired. As the youngest and least experienced member of a lab full of postdocs, he found that their jargon-dense molecular discussions sometimes went over his head.

"After four years at Berkeley, I could just barely understand these guys," he said. But having worked as a sound engineer at concerts throughout high school and college, he was by far the lab member most comfortable with building complex electrical systems.

Using parts he ordered from an electronics catalog, Rosen developed a device that could control and record the temperature of the cell media with much greater precision. Using it, he showed that in frog eggs expressing many TRPV1 channels, increasing the temperature gave a stronger cation current; decreasing the temperature did the reverse.

One memorable assay, which Caterina playfully called the "wiggle–waggle experiment," showed just how temperature-sensitive the channel was. When Rosen warmed a frog oocyte expressing TRPV1 past 43 degrees Celsius, he saw a quick increase in current as the many channels in the oocyte's membrane shifted from closed to open. When he turned the heat back down to just below the threshold, the channels closed, and the current ceased. Up, down: The ion flow, which reflected the behavior of many TRPV1 channels added together, increased dramatically above a characteristic temperature and dropped off below that temperature. Within a range near the threshold, where many ion channels opened or closed at once, the current and temperature graphs formed mirror images.

"Even the small reduction of temperature caused a huge reduction of current," Tominaga said. "This experiment clearly suggests this channel has a thermospecific threshold for activation."

As it happened, that threshold temperature was also very close to the temperature at which humans begin to feel heat as painful. But the threshold was not fixed immutably. TRPV1, the lab found, can respond to numerous stimuli, often in an additive way. For example, acidity can lower its opening temperature, suggesting a partial explanation for why damaged tissue can feel pain at normally harmless temperatures.

David McKemy, who joined the lab as a postdoc a few years after TRPV1 was found, recalled that after presenting on the lab's investigation into TRPV1 heat sensing, Julius often was asked, "What about cold?"

After all, temperature sensing is not binary. If we can feel other temperatures, did that hint at other TRPs?

CONTINUED

How to tell if a channel is open

The TRP and Piezo channels have something in common: They are cation channels that allow positively charged ions such as sodium and calcium to cross the plasma membrane.

Neurons maintain an ion imbalance that gives them a negative charge compared with the environment. As a result, when a TRP or Piezo channel opens, sodium and calcium flow into the cell, reducing the negative charge.

The studies that led to this year's Nobel Prize used two methods to determine whether these channels were open.

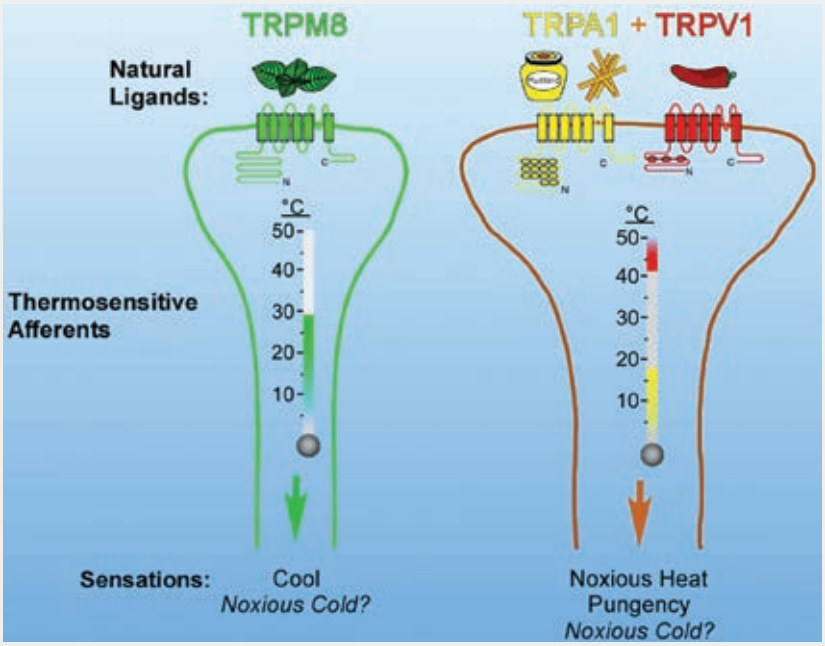
Calcium imaging: Because mammalian cells keep calcium concentration very, very low compared with the outside of the cell, a spike in intracellular calcium is a sure sign that a calcium channel has opened. Researchers can use indicators that fluoresce when bound to calcium to check for influx through channels in the plasma membrane or release of internal calcium stores. Caterina and McKemy used this approach to narrow a list of candidates to individual genes in capsaicin and menthol.

Whole-cell electrophysiology: To detect ion flow through a channel, an experimentalist uses an extraordinarily fine electrode, usually made from a stretched glass micropipette, to poke through a cell membrane and then record changes in current at a set voltage.

Patch clamp electrophysiology: A wider pipette is used to suction into a cell's membrane, separating one section of the membrane from the rest. The researcher can record from the whole cell or detect individual channel opening events as tiny changes in current. This technique is useful for isolating channels and seeing how they respond to stimuli.

Another 5,000 colonies

David McKemy and the cold receptor



DAVID MCKEMY/WIKIMEDIA

A figure that Dave McKemy published in 2005 shows how the channel TRPM8, which he discovered, recognizes cool temperatures and menthol (left). It also shows a single neuron expressing two TRP channels with different sensitivities, raising questions about how the brain interprets a signal from such a cell.

Since capsaicin, a molecule the body registers as hot, was sensed by a protein that also responds to high temperatures, it followed that the mint compound menthol, which feels cool, might bind to a cold-sensing protein.

When Julius asked postdoc David McKemy whether he would be interested in taking on a hunt for the menthol receptor, even though he knew it would be competitive, McKemy was game. "It was a risky project, but that's what had been successful in the Julius lab," he explained.

Conceptually, McKemy's project was very similar to what Caterina had done a few years prior. However, based on intuitions from years of thinking about molecules, McKemy said, "Everyone really thought that cold was inhibiting things. Cold wasn't going to actually activate something."

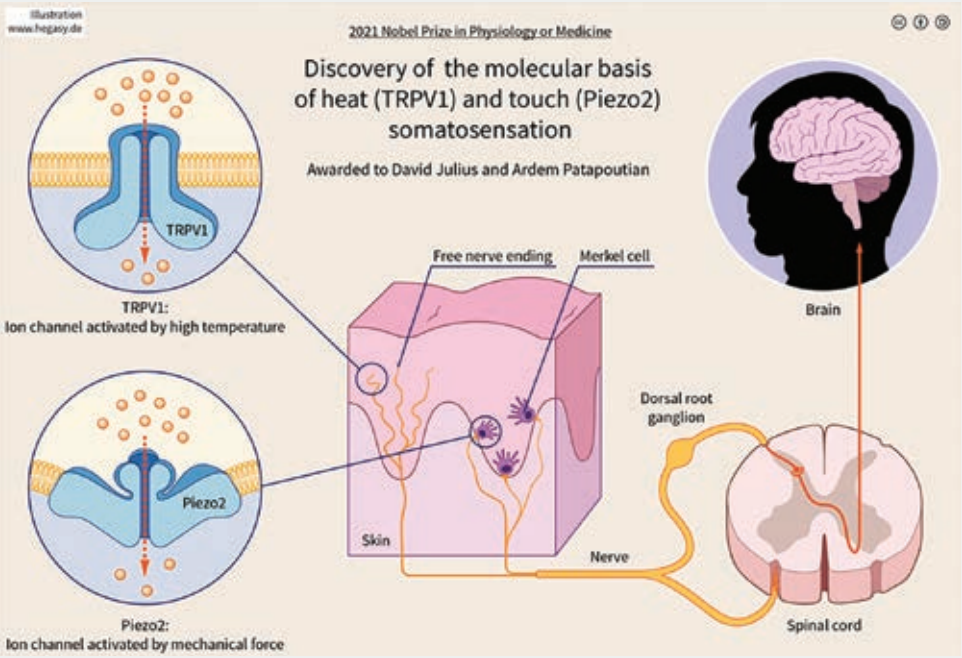
At first, it seemed as if everyone might be right. After months of screening in a DRG library, the menthol receptor did not materialize.

"I remember Dave McKemy picking colonies and then getting frustrated," Julius recalled. "I said, 'OK, let's get your pools out of the autoclave bag … and let's go back and pick another 5,000 colonies.' This is the nature of doing bench work. We all go through those periods when stuff's not working, and that's when you have to work hardest, I guess."

Julius said he helps trainees cope with the long slog through a combination of reminding them why the work was worth doing in the first place and finding practical ways to get past the failed experiments (see "Motivation to persist").

"When I was a student, when things weren't working, I would get re-energized to go back into lab and try something if I could think of one reason why something may not work," Julius said, "or if I could think of another way to do something and give it a shot."

In McKemy's case, that different approach was to use a different set of neurons. Neurons from the DRG respond to heterogeneous stimuli. There are many fewer that act in response to menthol than to capsaicin. So McKemy looked instead



COURTESY OF THE NOBEL FOUNDATION

A schematic from the Nobel committee illustrates the anatomy of heat and touch sensation. TRPV1 is expressed in heat-sensitive neurons, and Piezo2 in pressure-sensitive Merkel cells that synapse with neurons. Both types of neuron transmit signals from the skin through the dorsal root ganglion, or DRG, to the spinal cord. From there, the sensory signals are passed on to the brain.

at genes expressed in a more cold-sensitive group of neurons, those that innervate the head, which are called trigeminal. McKemy made another cDNA library and started again. In that library, at last, he found an ion channel that responded to menthol — and also cold.

"That paper was, I think, two and a half years of research," McKemy said. "And I think over two years of that is two sentences in the paper."

By the time he found the menthol receptor, McKemy knew that he had to work fast: Others were searching for it too. Caterina, who had discovered the TRPV1 receptor and who by this time had started his own laboratory, said, "There is such a thing as that window of time when the next question is just sitting there and waiting to be asked. … It can be a bit of a race."

Caterina's group was part of the race for the menthol receptor. So was Ardem Patapoutian's lab, which published just a day after McKemy's paper came out, identifying the same receptor with an opposite approach. Instead of screening for a ligand-binding activity and then sequencing the protein responsible for it, they used bioinformatics techniques to search out new TRP channels and then investigated what those proteins might detect.

McKemy said, "The fact that both labs found the same thing using two independent methods? You're pretty confident everything is right when that happens.

"This is a field of a lot of failure. There are the things that work out, and when they work, it's great. But there's a lot of things that go into getting there, the controls and so forth, before you actually get to the big result."

CONTINUED

A happy accident

Laureates were once trainees themselves. When David Julius was a second-year graduate student at the University of California, Berkeley, his first mentor left the university, shutting down her lab.

"That's how I first initially met him; he was an escapee and desperate, a waif and a stray, looking for a congenial home," Jeremy Thorner, an emeritus professor at Berkeley and Julius' co-mentor, recalled drolly. "It was to my very great advantage that he decided that I was someone he could work with and learn from."

Co-mentored by Thorner and fellow Berkeley professor Randy Schekman, working on how haploid yeast can have and communicate a mating type, Julius identified a protease involved in yeast hormone maturation that proved to have homologs in human cells that regulate the production of insulin and other hormones.

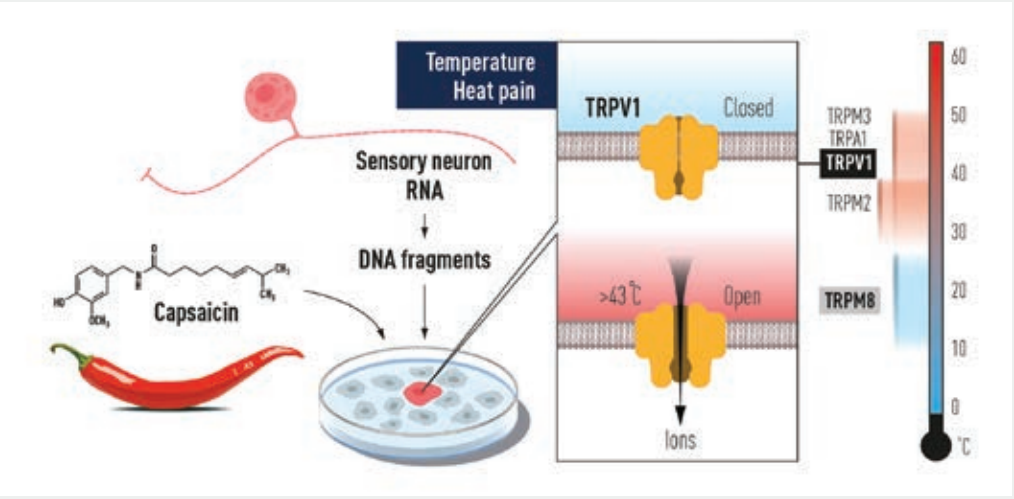
"I was very fortunate actually, in the end, that that whole thing happened," Julius said. He recalls himself as naive and then lucky; the collaboration, put together for administrative reasons, turned out to give him excellent guidance for the project he wanted to work on.

In Thorner's lab, Julius also met Tony Brake, a postdoc who took a job in industry but later returned to academia as a research scientist in Julius' lab.

"A lot of the early cloning work from David's lab came from putting the band back together," Thorner said. As a mentor, he added, "It's all very satisfying."

‘He struck gold’

Bertrand Coste and the pressure receptor



COURTESY OF THE NOBEL FOUNDATION

A schematic shows how Bertrand Coste used patch-clamp electrophysiology to discover piezo1, applying a mechanical force to a cell while also measuring current (top line). Later experiments showed that the protein is a channel that opens in response to mechanical forces against a nearby membrane.

In the mid-2000s, Ardem Patapoutian, known for his studies of TRP channels, wanted to transition into studying mechanotransduction. Patapoutian did not have time for an interview for this story, but in an email, wrote, “After studying temperature sensation for 10 years, it was a natural transition to ask how mechanical force is sensed.”

In some ways, it was a risky question. Sanjeev Ranade, who joined Patapoutian’s lab as a graduate student to study thermosensation, said, “Many labs had been looking for the identity of the gene or genes that allow us to sense touch. Many labs were not successful in finding these genes.”

So when postdoc Bertrand Coste joined the lab to search for the protein that lets human neurons sense pressure, Ranade said, “It was one of those ‘I can’t believe you’re doing this’ kind of projects.”

Like Tominaga in Julius’ lab, Coste was an experienced electrophysiologist who came to a new lab in California with a reputation for receptor hunting and immediately began to build a new electrophysiology rig. He had studied mechanosensory neurons as a graduate student and was skilled at recording from a neuron with an electrode while gently prodding it with a tiny glass probe — a technique that few others in the world used.

“Recording these mechanically activated currents naturally pushed me to the question of what are the ion channels that are involved in this activity,” Coste said. Patapoutian’s lab, which lately had cloned TRPA1 and TRPM8, struck him as the ideal environment to ask the question.

Coste planned to sift through the DRG to find neurons that respond to pressure, extract their RNA and screen for the genes governing the sensation. But pilot experiments made it clear that the strategy was impractical. So he took a different approach: He tested as many cell lines as he could, looking for one that would respond to pressure by depolarizing. “With immortalized cell lines you have endless materials,” he said. “It’s easy to use, and every cell is a clone of the other cells.”

Coste found a neuroblastoma line that fit the bill and winnowed its list of highly expressed genes to the most interesting candidates: transmembrane proteins with unknown function that resembled ion channels.

That left a list of dozens of genes. Coste began to use siRNA to knock them down one at a time and then prodded the altered cells, watching for one that would fail to respond

to mechanical stimulation. Electrophysiology is highly reliable but also very slow. He averaged two candidate genes a week, and, for a year or more, every candidate he tested had no effect on the cells' response. Not making progress is difficult (see "Motivation to persist"). A few months in, after many trials and no success, Coste said, "My mood was declining very fast."

"We are scientists. We like to think, to problem solve," he said. While planning the screen and working around the technical issues, he'd had a chance to solve problems. "But the screen itself was very repetitive." Coste brought the problem to Patapoutian: He was excited about the possible results, but the mindless grind of doing the same experiment over and over with no result was wearing him down. Patapoutian, according to Coste, was understanding; he assigned a technician to help and suggested a more tractable side project. "I was relieved of doing every day the same thing, every day having negative results," Coste said.

Finally, after ruling out 71 candidate genes, Coste found an siRNA that blunted the cell's response to mechanical stimulation. Ranade said, "They could have easily quit at 71, and said, 'OK, it's been a year, we have nothing.' And yet, they found it at 72."

The gene was mysterious, but large, with an estimated 24 to 36 transmembrane domains. Besides controlling the neuroblastoma's mechanical response, when cloned into mechanically inert cells, it made them sensitive. The team dubbed it Piezo, Greek for pressure, and soon found that mice have two Piezo proteins.

"After one year of screening," Coste said, "every experiment you do is telling you something interesting on the activity of this channel."

Coste and many colleagues in the Patapoutian lab would show that Piezo1 and Piezo2 play integral roles in mammals' sense of touch and many other physiological functions. Even before that, Ranade said, it was clear that the finding was important. "Every single one of us in the lab, when Bertrand found Piezos, we all knew … that he struck gold."

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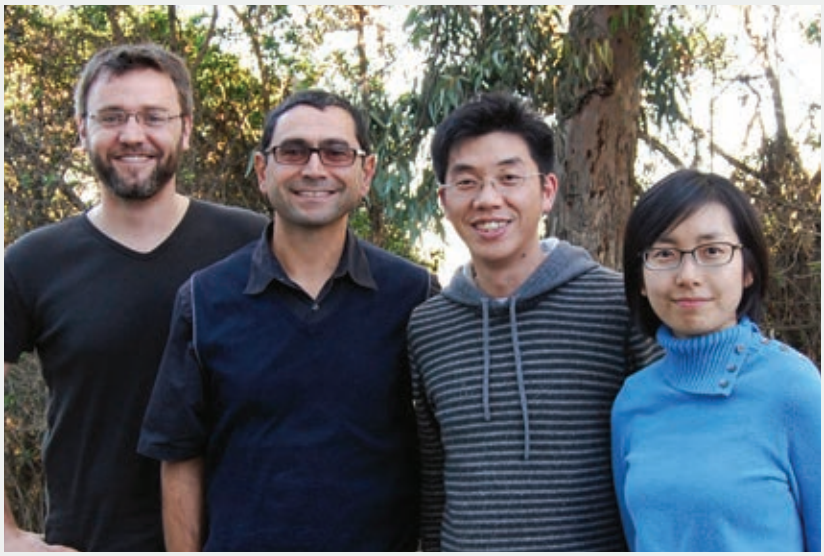


COURTESY OF THE NOBEL FOUNDATION

From left, Bertrand Coste, Ardem Patapoutian, Bailong Xiao and Seung Eun Kim after Coste and Xiao's paper and Kim's paper were published together in Nature in 2012.

Motivation to persist

What keeps researchers going through failure after failure? ASBMB Today asked psychologist Ayelet Fishbach, who studies motivation, work and learning from failure.

Fishbach and colleagues recently published a study investigating work-related one-time failures. After taking a two-option quiz, Fishbach and colleagues found, participants who had received negative feedback performed worse on a follow-up quiz than those who had received positive feedback.

Although the study investigated one-time failure to guess an insignificant piece of information rather than the longer process of research, Fishbach said that its conclusions reflect her experience as a researcher and mentor.

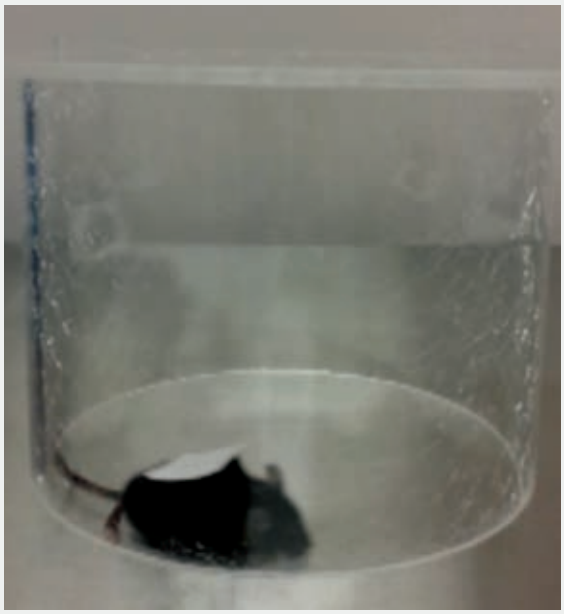
"There are two categories of problems with learning from failure," she said. Cognitively, it can be hard to learn from the unexpected and more difficult to seek out the reasons that a hypothesis missed the mark than to accept that it was correct. "Getting people to pay attention to what didn't work is notoriously hard," she said.

The second category is emotional. It is easier to ignore a failure than to engage with it. And sometimes people with little expertise in a field learn the wrong lesson from failure, concluding that they are unable to execute the task at hand. Fishbach added, "Doing something with no sense of progress is psychologically hard. You can tell yourself that one day it will pay off, but it's not today or yesterday or tomorrow. And people give up."

Much like David Julius, Fischbach said that social support, encouraging words and troubleshooting help from others can keep people motivated. But, Julius pointed out, "It's not just me. They have to have their own gyroscope." He added that there have been times when he has doubted the future of a project and has gotten inspiration from persistent trainees.

The 'kick-me' mouse

Seung Hyun Woo, Sanjeev Ranade and Piezo2 in the sense of touch



COURTESY OF SANJEEV RANADE

A wild-type lab mouse will feel a piece of lab tape stuck to its back, and will make an effort to remove the tape. A mouse with Piezo2 knocked out in its sensory neurons and Merkel cells, such as the one in this still from a video Sanjeev Ranade recorded in the lab, will continue exploring its environment as if there were no tape there at all.

Bertrand Coste had identified two pressure-sensitive Piezo proteins that can make a cell sensitive to pressure. They were expressed in the sensory neurons of the dorsal root ganglion, and using RNA interference to reduce Piezo2 in those cells seemed to compromise pressure sensing. The Patapoutian lab was curious about how the two proteins worked together in the complex environment of a whole mouse.

Seung Hyun Woo, a postdoc in the lab, investigated the expression of Piezo1 in the most common skin cell. "Piezo1 is in keratinocytes. It's a huge population, and piezo1 was highly enriched," she said. "So we all thought, 'OK, it's piezo1 that's doing the touch sensing, along with piezo2 in neurons.'"

But a control experiment that she ran to save time showed that that hypothesis might be incorrect. Woo lived halfway between San Diego and Los Angeles and commuted a punishing 85 miles to the lab. "I think that's why I was so successful," she said. "I really had to get stuff done in time so that I could go back home. So I really managed my time efficiently."

Woo had earned her Ph.D. in a dermatology lab, studying touch-sensitive Merkel cells, which are scattered in small numbers through the deepest layer of the skin. She knew that Merkel cells, which are shaped like little balloons, make connections with sensory neurons, so she was curious about their Piezo1 expression. But for efficiency's sake, she checked both Piezo1 and Piezo2 at the same time — and found that Merkel cells expressed an enormous amount of Piezo2.

"Because we were so focused on piezo1, we didn't really think about piezo2 being in the skin cells," she said. "We were all blown away."

The observation led the lab to focus on the role of Piezo2 in pressure sensing. The trouble was that it proved to be very difficult to remove the protein from mice.

Sanjeev Ranade had begun to work on the newly discovered Piezo channels because his first project, investigating crosstalk between TRP receptors, hadn't panned out. He had tried to breed genetically complex mice that expressed some TRPs but not others in certain tissues, and he had run into numerous challenges.

"I basically was rounding out my fifth year (of graduate school), around Christmas time, and I looked up and realized that I had no real viable path to a thesis," Ranade said. "But I had gained all of this experience and knowledge of the pitfalls with making transgenic mouse lines ... and that made me ideally positioned to generate the constitutive and conditional knockout mouse models for piezo1 and 2."

Generating both mice — especially the Piezo2 knockout — took further years of effort. Complete removal of the gene kills mice as embryos. Mice lacking Piezo2 only in their sensory neurons die soon after birth. And removing the gene from only certain tissues in adults was challenging for the same technical reasons that removing TRPs had been. Eventually, Ranade said, it was time to finish

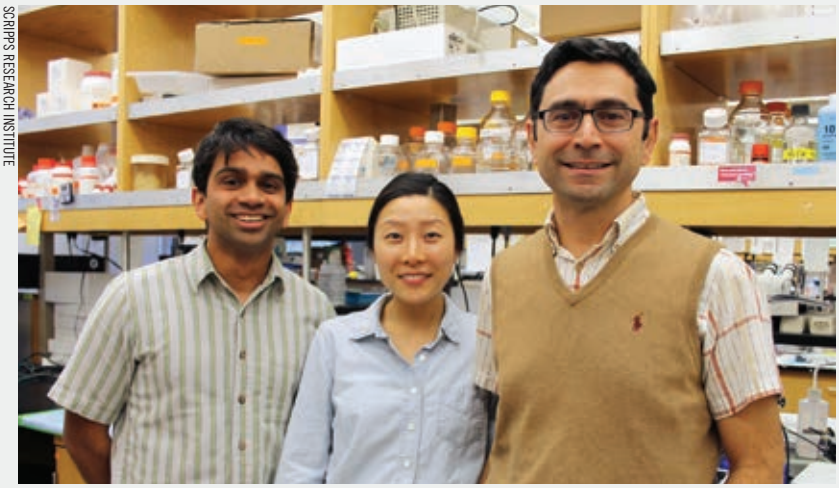
and move on. But he hated to leave without finding out how a mouse lacking Piezo2 in its sensory neurons would behave. As he wrote up his thesis, he tried one more strategy to breed a drug-inducible knockout. "That was my last shot."

He remembers clearly checking the day after his thesis defense to see how a group of mice was faring. "I defended on a Thursday," he said. "The next morning, I came into lab, and I went upstairs from the vivarium to tell Ardem, 'Hey. I think we got something.'"

Patapoutian went down to the mouse facility with Ranade and another postdoc, Stuart Cahalan, to see for himself. There were four mice in the cage; Ranade had induced Piezo2 knockout in sensory neurons in just two. "I asked them to tell me which ones they thought were the test. And Stuart just laughed and said, 'that one and that one.'"

Cahalan had guessed right. Mice without Piezo2 in their sensory neurons walk with an odd, shambling gait. Later, Woo would show that they are unable to feel the position of their limbs.

"There were so many technical challenges, and so many things that went wrong, that actually getting the mouse felt like climbing a huge mountain," Ranade said. "But then, once you have the mouse, it's simply a tool; you still have to do the actual scientific experiment. So you climb one mountain, you look up, and you realize there's an even bigger one."



SCRIPPS RESEARCH INSTITUTE

Ardem Patapoutian, Sanjeev Ranade and Seung Hyun Woo when their paper identifying Piezo2 as the main mechanosensor was published in 2014.

Using mice lacking Piezo2 in both Merkel cells and neurons, the lab found that the animals had no problem detecting noxious heat or jabbing touch. But they failed to feel gentle stimuli like the soft swipe of a cotton swab over a paw or a piece of lab tape applied to a furry back. An ordinary mouse will make an effort to remove a piece of tape; the knockout mice, Ranade and technician Matt Petrus showed, blithely continue to explore their enclosure, paying it no attention. At one conference, Ranade said, "I presented these results and some of the trainees jokingly referred to it as the 'kick-me' mouse."

After following up on the accidental observation, the lab concluded that Piezo2 in sensory neurons and Merkel cells is the main protein in control of a mouse's sense of innocuous touch.

EPILOGUE | The other side of the rainbow

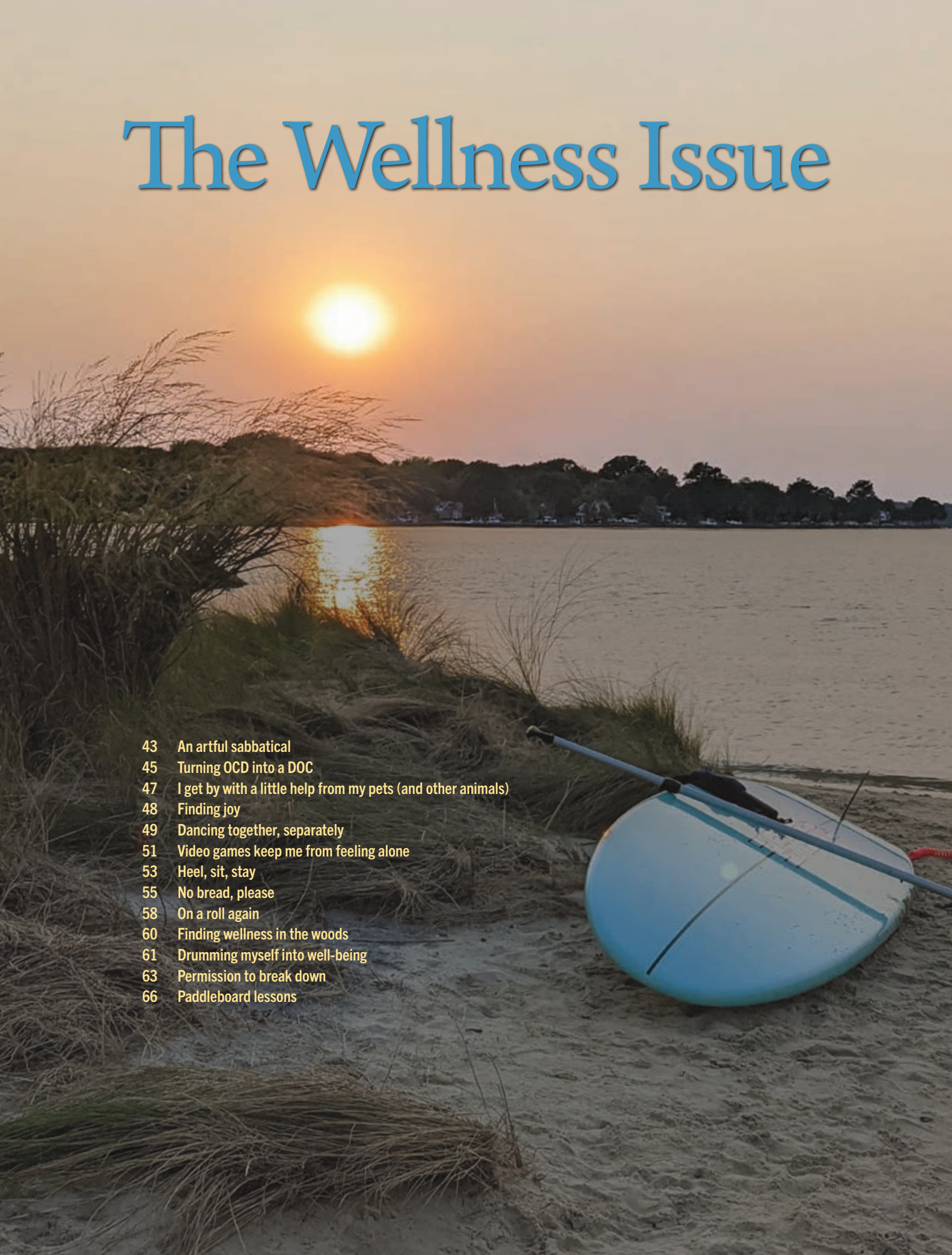
The work behind the 2021 Nobel Prize was slow and difficult, demanding a lot of the researchers at the bench — including many whose names do not appear in this story. According to Rosen, now an effects artist at the animation studio DreamWorks, seeing those discoveries recognized has been deeply gratifying.

"I burned the candle for a long time on both ends," Rosen said. "I did a lot of work — and it matters, you know? Twenty-five years later, it comes back."

Meanwhile, the long, slow slog continues. There are still plenty of questions about how thermo- and mechanosensation work. The stimuli that activate several TRP channels remain controversial. While high-resolution structures of TRPV1 show in great detail how the channel opens when ions or ligands bind, it remains a mystery just how a specific temperature can open the channel so acutely. The structures of Piezo channels also have been published, but, according to Coste, researchers still are hunting for the genes that govern residual pressure-activated currents in cells that lack Piezo1 and 2. Elsewhere, neuroscientists are trying to find out what it means when a neuron expresses both heat- and cold-sensitive TRP channels.

Thinking back on mentoring his students through tough patches, Julius said, "I have a few things like that now in my lab, where people are trying to get through to the other side of the rainbow."

The Wellness Issue



An artful sabbatical

By Pam Mertz

Newly thrown pot

I was on sabbatical for the 2020-2021 academic year, and one of my goals was to include more art in my life. My 12-year-old son has attended art camps and taken many lessons, and I always wished I could take classes with him, but during a typical academic year, it's hard to find time to focus on art.

More than a dozen years ago, I signed up for my first ceramics class on a whim at a time when I was sad about my mother's recent death as well as other personal issues. It turned out to be a painting class; the ceramics were already made, and we just decorated them. It was fun and relaxing, but I really wanted to get my hands on the clay itself, not just a premade bowl or dish.

I discovered an art studio closer to my house and took a few pottery classes, but life got fuller with the birth of my son, and I stopped. A few years ago, I started taking classes off and on again. During my sabbatical, I decided to take classes consistently and work on improving. Like so much in life, pottery takes a lot of practice to get better.

Pottery is one of the few things I can do to let go of external stressors or problems I am trying to solve — and the pandemic sure brought extra worries. I sometimes take yoga classes to stretch and help with stress, but I struggle to meditate during Savasana; I'm already thinking about the next few things I need to do when it's time to get up off the mat. I am sure there is an art to relaxing during Corpse Pose, but I haven't mastered it, so I prefer to relax by focusing on creating something. With pottery, I am able to focus on the task at hand. And working with clay, especially the glazes, is all about experimentation, which parallels my scientific interests.

During my sabbatical year with art, I took a number of pottery classes (both wheel and hand building). When the local art studio closed due to the pandemic, my teacher offered classes at his home studio to keep us engaged. (We did this safely with masks, distancing, and small classes.) The hand-building classes opened up more levels of creativity for me than wheel work. For example, I made a vase with square corners and a few charcuterie platters. But I also got better at the wheel and felt that some of my pieces were good enough to give as gifts to friends and family members.

Other artists visited my teacher's studio to offer specialized pottery classes on different techniques or specific projects — from hand building a delicate porcelain vase to making a decorative tile with a relief sculpted bird as well as fun seasonal projects

like pumpkins in October. I learned about surface treatments of clay such as slip trailing, the application of watered down clay, often containing colorant, onto leather-hard clay to add dimension after firing, and sgraffito, a form of decoration that involves scratching a design onto a dark coated surface. I really enjoyed sgraffito, even though it takes planning and lots of patience to do well. Besides getting out of the house, I enjoyed meeting new people and seeing what others in my classes were creating.

I also took free online classes in drawing, watercolor and acrylic painting through my local library and an art studio. I discovered that I liked watercolor much better than acrylic painting; I enjoy the fluidity and use of water to dilute and blend colors, and the final product appeals more to me. I bought myself a good set of watercolor pigments and a few high-quality brushes for a Christmas present.

To end my sabbatical year, I did a raku workshop with my son just before the new academic year started; this was something I had wanted to try for a long time. Raku firing is a reductive process; pieces are taken out of a kiln when they are red hot and placed in closed containers with sawdust to starve them of oxygen. People usually do this outdoors in kilns that might be just glorified garbage cans. This type of firing involves so many variables that you really don't know what you will get until you cool the pieces with water and wipe off some of the black from the firing. My son and I created some very colorful fish and small cups. It seemed somehow fitting to end the year with a lot of fire and smoke and the excitement of not having a clue how things would turn out.

COURTESY OF PAM MERTZ

Finished pieces from raku firing.

A raku piece is fired in an outdoor kiln.

COURTESY OF PAM MERTZ

I am back on campus with a full teaching load and struggling to find time to keep up with grading, course preparation, the laundry and grocery shopping. But I hope to continue to create art in the future; the stressors never go away, but keeping them at bay and manageable is a lifelong skill. Plus, I feel joy when I look at something and think, "Wow, I actually created that."

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Turning OCD into a DOC

Pursuing science with obsessive compulsive disorder

By Frances Smith

I was diagnosed with obsessive-compulsive disorder in graduate school. The psychiatrist was dumbfounded. "We usually diagnose people after seeing them for six months," he said, "but I don't think that will be necessary for you."

It was my first time seeing a therapist, and I was 23 years old. I thought I had my whole life together, and then this diagnosis came crashing through.

Obsessive-compulsive disorder may not be what you think it is — I've met tons of people who assume it's a need for organization and order. But that's not necessarily true or may only be partially true. My OCD is truly what it sounds like: having compulsions about tasks that my mind obsesses over and that I must complete for reassurance.

And I also catastrophize; that is, I obsess over the worst possible outcome of some miniscule mistake — real or perceived. For instance, several years ago I lived in an apartment for a year without ever having a carbon monoxide detector. I didn't know it was missing. And yet once I became aware of this, I couldn't stop panicking that I might silently poison an entire apartment complex full of people and pets. This never could be considered my fault; my state requires that rental property owners install CO detectors, so it really came down on my landlords.

In coming to terms with this situation, I had to ask why I was pushing the blame on myself. This is the core of how OCD manifests for me, and I had to learn how to identify those feelings of unnecessary guilt that my OCD had installed in my brain.

Some people obsess over making sure the curling iron is off, triple checking that the front door is locked and checking that a candle is blown out about a dozen times before going to bed.

Those examples are almost too easy to list — they're the three things I check each day. Even if I haven't burned a candle in months.

In the lab, it's more of the same. I place my hand over a Bunsen burner to make sure it's off several times throughout the day. I check to make sure all freezers and refrigerators are completely closed. And of course, I've had to return to the building late at night to make sure I'd locked all the doors (spoiler alert — I had).

Getting the OCD diagnosis nearly shattered my career plan; I wondered if I was even hirable with this hypersensitivity to imperfections. When I think of a scientist, it's a person with unruly hair (a complete fire hazard), papers spilling out of folders, stains on their lab coat and some neon green liquid boiling out of a beaker somewhere. I've met many scientists who really have this so-what mentality when it comes to mistakes. I wondered to myself how I could fit into this go-with-the-flow environment when I am so not that.

Before I saw the psychiatrist, I thought that I was just a hyperconscientious person, but for some reason, my diagnosis tarnished who I thought

I began to see that my peers didn't care about my mistakes as much as I did. Scientists are just people. And if OCD affects 2% of the population worldwide, some of those people have to be scientists too.

I could be. I worried that other scientists would find me unfit for the job — who wants a neat freak in charge of the whole operation? So I tried to squeeze myself into the so-what image for a while. It was easy to mask myself as calm, cool and collected on the outside. Or at least I thought so. It all came crashing down soon after my diagnosis.

One day, when I'd been in my grad school lab only about three months, I was adjusting the pH on a buffer before heading out to attend a colleague's preliminary exam talk. As I put away the bottle of 1N NaOH — a plastic bottle that was likely older than myself — my thumb went right through the material. Base splashed in every direction in a two-foot radius, and it probably would have been more if I hadn't been a good enough scientist that day to lower the fume hood sash to an appropriate level. My lab mates gathered to help me clean it up. They still were neutralizing the floor with boric acid as I left to attend the preliminary exam, apologizing profusely. One of my colleagues said, "It would benefit you more to go to the talk than to clean up the garbage."

After attending the talk, I stopped in at my mentor's office and sheepishly told him about the spill. He burst out laughing. He said his lab had moved to three different buildings, and within the first year at each location, a student had something explode. At least I'm not the person who got agar on the ceiling.

I began to see that my peers didn't care about my mistakes as much as I did. Scientists are just people. And if OCD affects 2% of the population worldwide, some of those people have to be scientists too.

I started seeing a therapist who introduced me to cognitive behavioral therapy, a technique that is used to alleviate harmful thinking patterns in a number of mental health conditions. The core of CBT is learning how to understand your own thought process. One of my favorite techniques is called "leaves on a stream": I close my eyes and picture a scene of a flowing stream. Above it stands a tree adorned with leaves, and each falling leaf has my current thought written on it. Following that leaf as it falls and then wafts down the stream and out of sight, I experience the generation and alleviation of a thought. My thoughts, no matter how good or bad, significant or insignificant, are temporary. And this technique establishes my power over my thoughts; any thought I make, I can get rid of too.

With this technique in my back pocket, I now manage my OCD by knowing that I am in control of my thoughts, and it's no longer the other way around. Coping with OCD has been a long and imperfect process, but I no longer question whether I fit the description of an occupation, and I certainly don't try to fit into any preconceived mold.

I also should say that OCD is genetic, so I should have known it would come for me. To avoid the panicked question "Did I leave the iron on?" whenever she leaves the house, my grandmother unplugs that appliance and takes it down a flight of stairs to the kitchen counter, where it waits, unplugged, for her return.

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I get by with a little help from my pets (and other animals)

By Jessica Desamero

First thing in the morning, I let my dog Muffin and my cat Mochi outside and into the backyard. They wander about and do their business. Often, Muffin looks up the tall tree for squirrels and gets excited when she sees one. Eventually, I say, "Look, Muffin, there's Mochi!" and she runs to my cat. They run after each other back and forth across the yard. My dog wags her tail, and my cat gets vocal. It is a nice start to the day.

Over the seasons, I see them do funny things outside. In the spring, when the bushes are full of leaves, Mochi jumps into a bush to hide and then jumps out and surprises Muffin. In late fall, when the leaves have all fallen, Mochi sometimes runs across the yard and straight up the tree and then comes back down quickly. It's fun to see how high he can go. He also leaps into leafless bushes, closes his eyes, and rubs his face among the twigs. While he does this, Muffin just stares in confusion, which adds to the silliness. I love it when they play in the snow in the winter. They can't stay long because it's cold, but in the short time they're allowed out, they love it and make the most of it.

Watching my pets play and get into their backyard antics brings joy to my mornings. I used to check my email or social media first thing in the morning. For the sake of my mental health, I started to avoid my phone and instead went straight to taking my pets out. This helps me have calmer mornings.

JESSICA DESAMERO

Muffin the dog and Mochi the cat frolic in the author's backyard.

My pets also help with my headaches and stress. Since the pandemic began, I have been and continue to be more prone to chronic headaches. And these days, my stress levels are high from trying to balance teaching, research, thesis writing and science writing. I feel a general anxiety and sadness from still being in a pandemic. But my pets make me feel a little better.

Watching them play makes me happy and calms me down when I feel overwhelmed. What brings me extra comfort is petting them. My dog likes when I rub her belly; my cat purrs loudly when I stroke him. I sometimes hug Muffin. She can sense when I'm sad, and she gets sad too. She looks at me, comes closer to me and licks me to try to make me feel better. I admire her empathy.

On the weekends, especially when I'm feeling down but don't want to associate with anyone human, I take Muffin to the park to walk her. The ambience of being outdoors with only my dog helps clear my head. In those times, my dog is all the company I need.

During our morning playdates and walks at various parks, I started noticing the behavior of other animals. From discovering the sound that a squirrel makes, hearing all the distinct bird songs and seeing a woodpecker pecking at a tree live for the first time to anticipating the hatching of a swan's eggs and awaiting the baby chick family, it was all so exciting. I already loved animals, but I've grown to appreciate them even more.

My cat and dog have helped me so much throughout this pandemic in many ways. They may need me, but I also need them, and I don't know what I would do without them.

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Finding joy

By Paul A. Craig

We had a trying summer. My wife broke her ankle early on, and I broke my wrist 10 weeks later. It was pretty discouraging for both of us. We are afraid of becoming old and feeble — I'm 64, though my wife is much younger. After weeks of ups and downs and friends and family helping us, things turned around.

Our son and his wife used Marie Kondo's books ("Spark Joy" and "The Life-Changing Magic of Tidying Up") to improve their family life in a small apartment in a big city. As they cleaned out their closets and shelves, they kept asking the question, "Does this bring me joy?"

This caused me to explore my life and think about simple things that bring me joy and then to do those things. Here is a list with a brief description of a few of those things.

Sunflowers in my garden
Marigolds around the edges
Sourdough starter from a friend
A knowing look from my wife
Monarchs emerging from cocoons
A walk with an old friend
The quiet of the evening
I love to find the joy

Monarch butterflies. My wife's friend brought over some monarch butterfly caterpillars and milkweed in a jar. Over the next week, we saw three caterpillars make their cocoons. One by one, they emerged and flew away. It was simply wonderful. When the butterflies started to emerge, we dropped everything and watched them until they flew away. Before we received the caterpillars, I would have dismissed this as a science project for elementary school children. And I would have been very wrong.

Sourdough bread. A colleague in a Slack group mentioned that she had sourdough starter to spare, so I asked for some. She sent me the starter, instructions and a loaf of bread (delicious). I started making sourdough bread in June and am loving it. The fermentation process is great. Plus, the recipe is in grams, not cups, so I ordered a scale and it's like being in the lab. By late September, I'd made seven or eight loaves. I'm not sure which is better — the smell as it rises, the smell of baking or the taste of the bread.

Yogurt. I visited another one of our sons earlier this summer, and we ate fruit mixed with yogurt that he prepared in his Instant Pot. So I ordered an Instant Pot during Prime Days on Amazon and started making yogurt in July. At first, I did almost everything wrong, and I still got some decent yogurt. Things are going better now, and we eat our homegrown yogurt all the time.

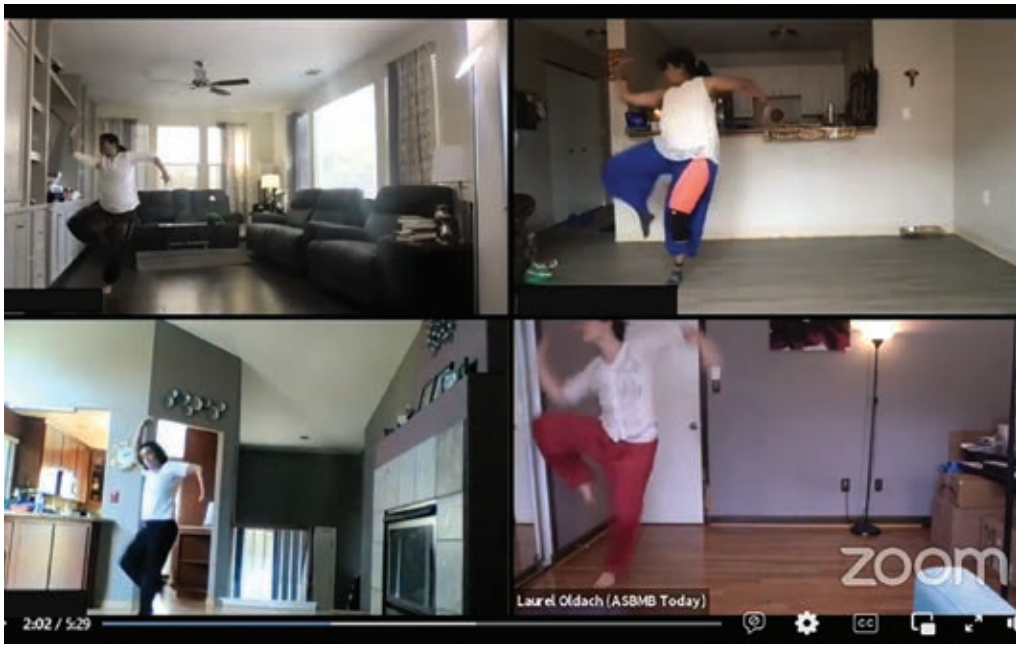
Sunflowers and marigolds. We did not get our vegetable garden planted in time for the short growing season in upstate New York, so I rototilled the garden and planted some sunflower seeds in the middle and marigold seeds all around the edges. It was simply beautiful. I would stop and look for a while every time I went out to get the mail and often when I came home from work. The bees and butterflies did their job, so when the seeds were mature, small birds would land for a meal. I love to see the goldfinches land on the flowers.

I am grateful for the joy of simple things.

Paul A. Craig (paul.craig@rit.edu) is a professor at the Rochester Institute of Technology, where he teaches general chemistry and biochemistry, and he is PI of the Biochemistry Authentic Scientific Inquiry Lab, a team of faculty from more than 10 campuses. Follow him on Twitter: @pac8612.

Dancing together, separately

By Laurel Oldach



LAUREL OLDACH

The author (lower right) and other students attend a Zoom dance class from their homes.

When the pandemic struck, I watched Bollywood dance videos until YouTube's algorithm served me nothing else.

I've always felt a little uneasy about how much I love Indian movies; part of me worries about cultural appropriation. But 2020 brought bigger things to worry about. I became an adherent of muddling through, and when I wasn't following the COVID news, that meant hours of catchy music, beautiful lead actors and crowds of backup dancers on sun-drenched sets. That gave way to dance covers by fans — some even more beautifully choreographed than the originals.

Eventually, somewhere deep in an escapist dance rabbit hole, I found that a dance company whose work I admired was offering online classes. I signed up and, with some trepidation, logged onto Zoom for the first lesson.

A dance class is a lot like any other Zoom meeting, only everyone can see you're wearing leggings. Other students appeared one by one in their living rooms and garages. The instructor gave us a quick explanation of first and second position and a few simple gestures and then began to demonstrate choreography for us to follow.

At first, I found it hard to remember where to put my hands, feet, hips, shoulders, elbows, knees, gaze and momentum — and where they all needed to go next, and after that. Later, I learned that a small literature in psychology is dedicated to understanding how professional dancers learn and retain complex movement sequences. Picking up two or three measures of choreography would take me a whole hour. Still, after class was over, everything felt lighter.

Physical activity is good for mood — but it wasn't just the exercise. When I was a graduate student, I worked in a neuroscience lab that focused on brain-derived neurotrophic factor, a signaling protein released in response to exercise and novelty. My colleagues would give mice a wheel or add a colorful landscape of beads and upturned egg cartons to their cages and chart their increasing synaptic plasticity. While dancing, I often thought about the alchemy that a combination of spatial learning, physical activity and a constant infusion of novelty can work.

Time fell into a rhythm. The year dragged on, missing almost all of its normal milestones, but every month, I knew I'd have a new dance routine in a different style to learn. (Bollywood dance is less a formal style than a fusion of Indian classical and folk dance forms with other performance styles such as jazz, hip-hop and contemporary.)

My fiancé got used to hearing the same 90-second audio clip again and again, an hour at a time, for weeks. He picked up on the self-consciously cheesy English lyrics peppered into one mostly Hindi song, and for a while would startle me by belting out, "Baby, you're my top tucker!" at odd moments.

I began to learn choreography

more quickly and enrolled in more difficult classes. In the spare bedroom that doubled as my office and my studio, I learned to do a coupe turn and a barrel roll. When COVID-19 case counts surged, focusing on choreography instead of worrying about the future helped me fall asleep.

Each four-week class session ended with a piece that the class would perform together via livestream. Watching those videos, I see the camera lag indicating the distances between us but also a surprising sense of community. My fellow students and I would record a weekly practice video and share it for feedback from the teacher and one another. We were dancing together, separately.

Early in the summer of 2021, the troupe began to talk about winding down its virtual classes, getting people back into the studio in person. This good news came with a little bit of a pang: The school is based in California, and I live in Maryland. While the delta variant prolonged the virtual classes through the fall, they were over by the end of October; to mark the occasion, the teacher played an Adele song while leading warmup.

It took me time to get over the sadness and start looking for classes closer to me. But I look forward to dancing somewhere outside my apartment, with someone I don't see only through a screen.

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Video games keep me from feeling alone

By Alison "Allie" Smith

The morning of my preliminary examination, I was so tired. I hadn't slept through the night in about a week. The bags under my eyes were bigger than the suitcases I wanted to pack for a trip to get away.

As I sipped my coffee, I felt my kidneys scream at me; they hadn't seen much more than coffee and the occasional sip of water in a few days. I was exhausted, and my brain couldn't fit one more piece of information into it without the risk of every other piece of information tumbling out.

My preliminary examination — the hurdle to advance to Ph.D. candidate — involved a seven-page National Institutes of Health–style grant proposal on my project and an oral defense of said project in front of my thesis committee. Normally, the oral defense is done in person, but due to COVID-19, my preliminary examination was held over Zoom.

I sat down at my kitchen table that morning, laptop in front of me, and clicked on the Zoom application. As soon as the app opened, it crashed — over and over again. I frantically opened Twitter and saw the banner "Zoom global shutdown."

Tears started pouring out of my eyes as all the emotions I had been shoving down during my weeks of nonstop preparation erupted like a long-dormant volcano. One of my committee members saw the Twitter notification and wrote, "We should reschedule."

ALISON SMITH

The author (right) and girlfriend Megan have a virtual date night on Animal Crossing.

I felt like I was going to barf. I could not possibly push off this exam any longer. My poor kidneys and brain needed a break.

A moment later, another committee member swooped in to save the day wearing a Google Hangout cape. She already had created a room and invited us all to it. I felt better; the only thing I knew I could not do was postpone this exam. I needed it to be done.

The oral defense went by so quickly it was basically over as soon as it began. We chatted about science, 90 minutes flew by, and before I knew it, I was asked to leave the meeting so the committee could decide if I passed.

I called my friend Allie, who is also in my graduate program, to tell her I thought it went OK. As soon as the call connected and I got three syllables out of my mouth, the committee requested I rejoin the meeting. I had passed — and with flying colors, no less.

The mental Tetris I played to cram every piece of information from every historical paper paid off. The hours I spent mapping out every experiment I proposed and how any result could change the direction of the project paid off. As soon as I jumped

COURTESY OF ALEX SCHIEFER

A screen shot of Among Us with the Hop Pen on Alex (Xandy) Schiefer's Twitch Stream.

off the call, I heard a knock at my door. My girlfriend was standing on the other side, holding a bag of my favorite comfort items from Target so we could celebrate regardless of the outcome. Spilling out of the bag were an extra-large package of Sour Patch Kids, a candle, a new stress ball and some Pokémon cards.

I passed my preliminary examination, but I struggled immensely in the buildup to that day. I felt underprepared, overstressed and disconnected from graduate school and my department. A handful of people including my wonderful advisor, Justin Kumar, kept telling me that I'd be OK, that I was prepared and that I would pass. But I struggled to believe them, because I couldn't believe the expectations for me would be the same as they were before COVID-19. We were stuck in our houses without seeing friends, families or even our lab benches for at least six months. How could expectations possibly be the same? And how could I possibly perform like the students before me who went through this examination without the looming threat of a global pandemic?

I spent many anxious hours asking myself how I could convince myself, and therefore my thesis committee, that I was worthy of passing the examination when I hadn't been able to work for almost six months. How could I convince my committee that I was worthy of becoming a Ph.D. candidate when I had been stuck in my apartment, alone, doom-spiraling on all the reasons I might not belong in graduate school?

If you have read to this point, you are probably wondering, What does this have to do with video games? I know. I know. So now let me tell you.

Being locked in a small apartment with the threat of preliminary exams hanging over my head made me feel more alone than ever — so I needed to find new ways to connect with other people. One way I did that was through video games.

When we couldn't be physically next to one another on the couch watching our favorite TV show, we watched it together on Netflix Party (now Teleparty). When we couldn't go on vacation, we visited each other's Animal Crossing islands. When we couldn't come to terms with our own imposter syndrome, we tried to be the best imposter humanly possible in Among Us.

While playing video games, we could spend an hour or two (or seven) immersed in a universe that was not our own. We didn't have to worry about preliminary examinations, because in that world they did not exist. Instead, we could be concerned solely about paying our incredibly expensive virtual mortgage to Tom Nook.

Being a graduate student this past year has had its challenges — from not being able to be with friends and family (I haven't seen my family since December 2019) to continued high laboratory work demands and graduate school expectations. When my depression started to creep back in from being alone and overwhelmed, video games offered a peaceful solace.

Whether I was playing alone, online with friends in my new favorite Twitch community or over Zoom, for those minutes or hours, I was not alone. I had my villagers on my island, my crewmates in Among Us, my friends laughing at whatever nonsense Quiplash had to offer, and the other members of the HogPen from Alex (Xandy) Schiefer's (co-host of the brilliantly hilarious podcasts "Beach Too Sandy, Water Too Wet" and "Human Seeking Human") Twitch stream to keep me company.

For many of us, the friends who were already there or were made during this time are friends who will last a lifetime; they showed us that during the darkest of times, they would not leave and we would never be alone.

If I spent even one single minute with you this past year on Zoom, on Twitch or playing any video game to seek solace from our day-to-day lives, I want to say thank you. With you, I got through my preliminary examination.

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Heel, sit, stay

Adventures in competitive dog obedience

By Susan J. Baserga

STEVE SURFMAN PHOTOGRAPHY

Susan Baserga and Webster train for rally obedience.

I decided to increase my commitment to competitive dog obedience training in the middle of the COVID-19 pandemic. My life as a biological scientist had been upended by the virus. The pace of work in the laboratory had slowed due to physical distancing protocols; I wasn't even supposed to be there. Why not take this opportunity to intensify my dog training?

I train Webster, my 4-year-old orange roan English cocker spaniel. As you might suspect, he was named by his breeders at Ashbrook English Cockers after Webster's Dictionary. The pups in each litter all have names starting with the same letter, and he was in the "W" litter. His name is all the more fitting because Noah Webster was a Yalie (class of 1778), and I am a professor at Yale. Webster (the dog) is athletic, food motivated and very attached to me. Thus, he is a delight to train.

I've owned many dogs, but I'm a newbie to any kind of dog showing. In December 2020, by chance, I saw that a competitive dog obedience class taught by Joyce O'Connell at Tails-U-Win had an opening, and I jumped at it. Tails is a large, well-equipped dog training center in Manchester, Connecticut. I knew Joyce was an accomplished obedience trainer of border collies (the geniuses of the dog world). Joyce's dogs attain Obedience Trial Championship titles, known as OTCHs, which are considered to be Ph.D.s for dogs.

On my first day, I immediately felt that I belonged there; I was welcomed both by Joyce and by my classmates, almost all of whom had very deep dog showing experience. I had lost my scientific peers to Zoom but had gained classmates who aim to show their dogs in obedience — all kinds of dogs, including other sporting breeds and some mixed breeds as well as one dog who is deaf. Of course, the humans in our weekly classes followed all masking and social distancing requirements.

Between classes, Webster and I worked daily for short periods on skills such as heeling on and off leash, coming when called (the recall), and a one-minute stay with Webster both sitting and lying down, which is tricky with distractions. We continue to work on

ALL: STEVE SURMAN PHOTOGRAPHY

Webster practices his agility and flyball skills

higher-level skills such as fetching a dumbbell on the flat and over a jump. Picking up a wooden dumbbell was a particular challenge for Webster, and we struggled with it. He did not want to hold the dumbbell in his mouth at all, let alone run out, pick it up and run back with it. Just when I was ready to quit, he started to pick the dumbbell up off the ground. I started to cry, relieved of my frustration and so proud of him for learning this difficult skill and for trusting me. Now he loves his dumbbell and wags his tail and jumps up when I bring it out for training.

In July, Webster got his American Kennel Club Companion Dog obedience title in three trials (he won a second and two firsts). We won the title at the Eastern States Exposition Grounds in Springfield, Massachusetts, during a very large and noisy dog show. There were copious distractions. The place was filled with lots of other dogs and people; Champagne corks popped and hands clapped at just the wrong moments during the sits and stays. I was so proud that Webster trusted me enough to maintain his composure in the ring despite the chaos around us. Of course, afterward, he got lots of treats.

The COVID-19 pandemic has given Webster and me the opportunity to grow as a team in competitive dog obedience. While I am pleased with our accomplishments, working with a partner who has four legs and a waggy tail and routinely keeps his nose to the ground is teaching me humility. It's completely different from working in the lab — except that I've found positive reinforcement drives success in both settings.

ASHBEY PHOTOGRAPHY

Susan Baserga and Webster pose after receiving the Companion Dog obedience title in July.

There's a bond between humans and dogs that I feel acutely when I am working to help Webster learn obedience skills, a bond that goes back tens of thousands of years to the first domesticated canine. It has connected me to a new community during a worldwide pandemic — and to all the people who have loved their dogs throughout time.

(With thanks to Robi Tatkin at ABC Obedience for getting me started in dog obedience.)

Susan J. Baserga
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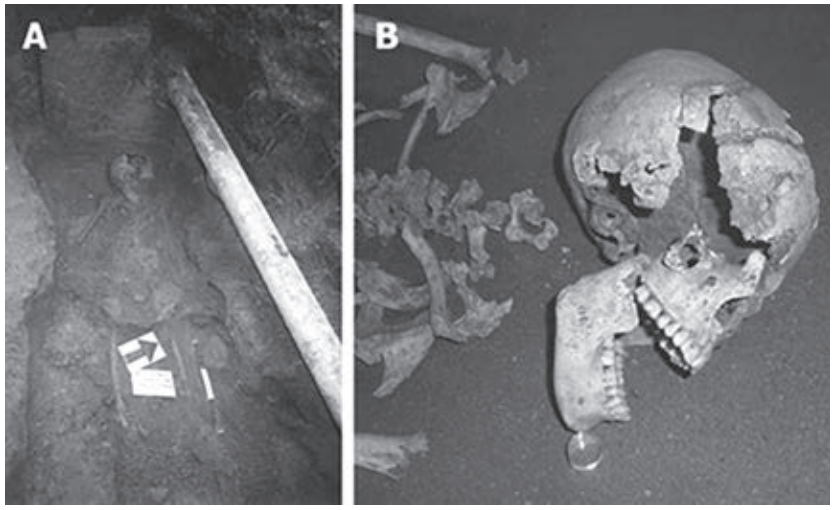
No bread, please

The only treatment for celiac disease is to avoid eating any gluten

By Elizabeth Stivison



GASBARRINI ET AL./WORLD JOURNAL OF GASTROENTEROLOGY

In 2008, researchers uncovered the remains of a young woman from the first century at an archaeological site in Italy. She had telltale signs of celiac disease.

In 2010, scientists discovered a skeleton at an archaeological site in the ancient village of Cosa in Tuscany, Italy. It was a teenage girl from the first century who appears to have died from malnutrition. She was only 4 feet, 7 inches tall and had osteoporosis in all her bones, signs of severe anemia in her bone marrow, and tooth enamel hypoplasia. We don't know her name, but I'll call her Eleanor after my Italian grandmother.

Eleanor was the only skeleton from that time and place with those signs of malnutrition, and there doesn't seem to have been a food shortage. In fact, that part of Italy was a big producer of wheat at the time. While successful wheat production was probably great for the rest of her town, it may have been what killed her. Eleanor may be one of the earliest known cases of celiac disease.

Celiac is an autoimmune disease triggered by ingesting gluten, a protein found in wheat, rye and barley. T cells in people with celiac mistakenly recognize peptides from gluten as a pathogen and become activated. People with celiac develop antibodies against many things, including gluten peptides and the enzyme that deamidates gluten in the digestive tract, transglutaminase. The disease is caused by both environmental and genetic factors; most celiac patients have the HLA haplotype DQ2 on their antigen-presenting cells. Scientists found that Eleanor had this haplotype too when they sequenced her DNA.

In celiac, the immune reaction triggered by gluten ends up destroying the lining of the small intestine. Chronic inflammation along with the loss of the ability to absorb food can lead to nutrient deficiencies, failure to thrive in babies, dehydration, osteoporosis, anemia, increased risk of cancers and other autoimmune diseases and, if left untreated, death. Celiac also can cause neurological and skin symptoms including ataxia, pain, depression, brain fog, neuropathy, rashes and extreme fatigue. The treatment is avoiding gluten in the diet entirely.

While there's direct evidence of nutrient deficiencies in Eleanor's skeleton, we only can guess what other symptoms she faced that weren't preserved in her bones.

I was diagnosed with celiac too, a little over two years ago, but my life trajectory looks pretty different. Much of this is because of the work of countless scientists over the years.

In 1887, English pediatrician Samuel Gee described the symptoms of celiac and suggested it might be treated by diet. Over the next few decades, doctors proposed various diets, getting closer and closer to the real cause, and in 1950, William Dicke, a Dutch scientist, proposed a diet excluding wheat and rye. Dicke and two colleagues then identified gluten as the component of the grains that was harmful. And we were off and running.

Nowadays, a person can be diagnosed with a blood draw to look for the hallmark antibodies and an endoscopy and biopsy to look for intestinal damage. When those both came back positive for me, my doctor said, "Well, good news and bad news. Bad news: You have celiac disease and you can never eat gluten again. But good news: You'll feel a lot better

really soon."

I was pretty shocked. I expected the test results to come back negative and for the doctor to have no real answer for why I felt so bad. Instead I got this gift and this curse. I could feel better. But it would be really difficult to do.

I used to love eating. I would eat anything and everything. "Want to get dinner?" was probably the best thing you could say to me, aside from maybe "Paul McCartney is downstairs. He wants to say hi." I baked a lot, made surprisingly good sourdough bread and, according to my old roommate, the best banana bread.

I also loved to travel, mostly because I got to eat all kinds of stuff I'd never seen before. A good chunk of my time traveling was spent in restaurants or at stands on the street selling I-dunno-what, pointing to what I wanted to buy and excitedly tasting whatever the heck I'd just bought.

All that freedom was gone in an instant, and I suddenly had become a very high maintenance person. Now the thought of going to a restaurant or eating anything outside my own home is mildly terrifying. For the whole first year, I had a recurring dream that I'd forget I couldn't eat gluten and accidentally eat something normal like a goldfish cracker and get sick.

I learned to read every ingredient on labels and scan for less obvious things like soy sauce (usually fermented with wheat) or malt flavoring (usually made with barley), which sneaks into foods like Rice Krispies and Lindt chocolate.

But avoiding food made with gluten was the easy part. The real challenge is that the immune system is super sensitive. It's designed to seek out the tiniest amount of pathogen — a few bacteria, for example — and kill it before it kills us. That means avoiding gluten requires avoiding just about every molecule of it. Some research suggests that as little as 2 milligrams of gluten is enough to trigger a reaction that can last for days with stomach pain, digestive issues, body aches, headaches and fatigue. And 2 milligrams of gluten is about one one-thousandth of a slice of bread — one crumb left on a stick of butter from someone reusing a knife. Then there's the mystery of food processed on shared equipment in a factory. I stick to certified gluten-free food when I can, meaning it contains less than 20 parts per million gluten.

I now go to potlucks, cookouts, friends' houses, and most social and work events just to see the people. The first time I didn't eat the pizza or drink the beer, I felt like a moron. I didn't know where to look or where to put my hands. But I do still enjoy hanging out with friends and co-workers, even if everyone else is eating and I'm not. Would I prefer well-labeled and uncontaminated gluten-free options at social events? Of course. Giving me certified gluten-free food is a very easy way to become my friend.

That might have been true for Eleanor too. We don't know what people in her time knew about celiac, but the isotopes in her bones show that she may have been altering her diet to alleviate her symptoms, eating more fish and meat than an average person in her town. Maybe she'd figured something out and was trying to help herself. I wish I could bring her some gluten-free snacks, hang out, share what we know now about celiac and tell her that she could be OK.

I wonder if anyone tried to help Eleanor get well. I think about what the years leading up to my diagnosis felt like. My skin hurt, my head hurt, my muscles hurt, I was constantly sick and constantly tired and could not figure out why. Nothing I did helped. I guess she felt like that her whole short life.

And hundreds, maybe thousands, of people go to work every day, pipetting,

trying to keep their cells uncontaminated and troubleshooting their assays, all to find ways to help me get well.

This is by far the best time in history to be diagnosed with this disease. Celiac specialists are at most major hospitals, and no fewer than 13 drugs are in clinical trials. These drugs, building on decades of research, aim to break down gluten in the gut, tighten the tight junctions between endothelial cells or block points in the immune response; some even attempt to induce immune tolerance to gluten. My doctor told me I might be able to participate in one of two clinical trials; there's so much research I have to choose which one.

But there's still work to do. There are no drug treatments, and most of the drugs in the pipeline are to be taken with a gluten-free diet to minimize symptoms that still persist (there are many) or to minimize the effects of miniscule quantities of accidental gluten exposure. If they get approved, I'd certainly take them in an instant. But celiacs probably will be relying on a gluten-free diet for a while longer.

I still call out sick from work frequently due to persistent symptoms. In fact, I wrote part of this article from my bed during a sick day. Celiac message boards and Facebook groups always have posts seeking advice for what to do when you're out of sick leave but can't go in because you're sick. I'm lucky to have a kind boss, and I work in a lab that lets me have flexible hours. But we need a treatment besides gluten-free food to help people live their lives.

There's societal work to be done too. Gluten-free food is easier to find than ever, and the Americans with Disabilities Act offers some protections, but food pantries rely on donations; gluten-free food might not be available for someone who's hungry and also celiac. Similarly, nursing homes are required to provide doctor-prescribed diets including gluten free, but assisted living and other senior communities are not. A little digging turns up stories of schools, prisons and even hospitals being ill-equipped to provide gluten-free food. Planes and hotels are another challenge. More relevant to the life of scientists is a lack of guaranteed gluten-free food at science conferences and events. And certified gluten-free foods cost more.

We've come a long way. Thanks to scientists and activists, my life is immeasurably easier than that of generations before me. And we still have a long way to go.

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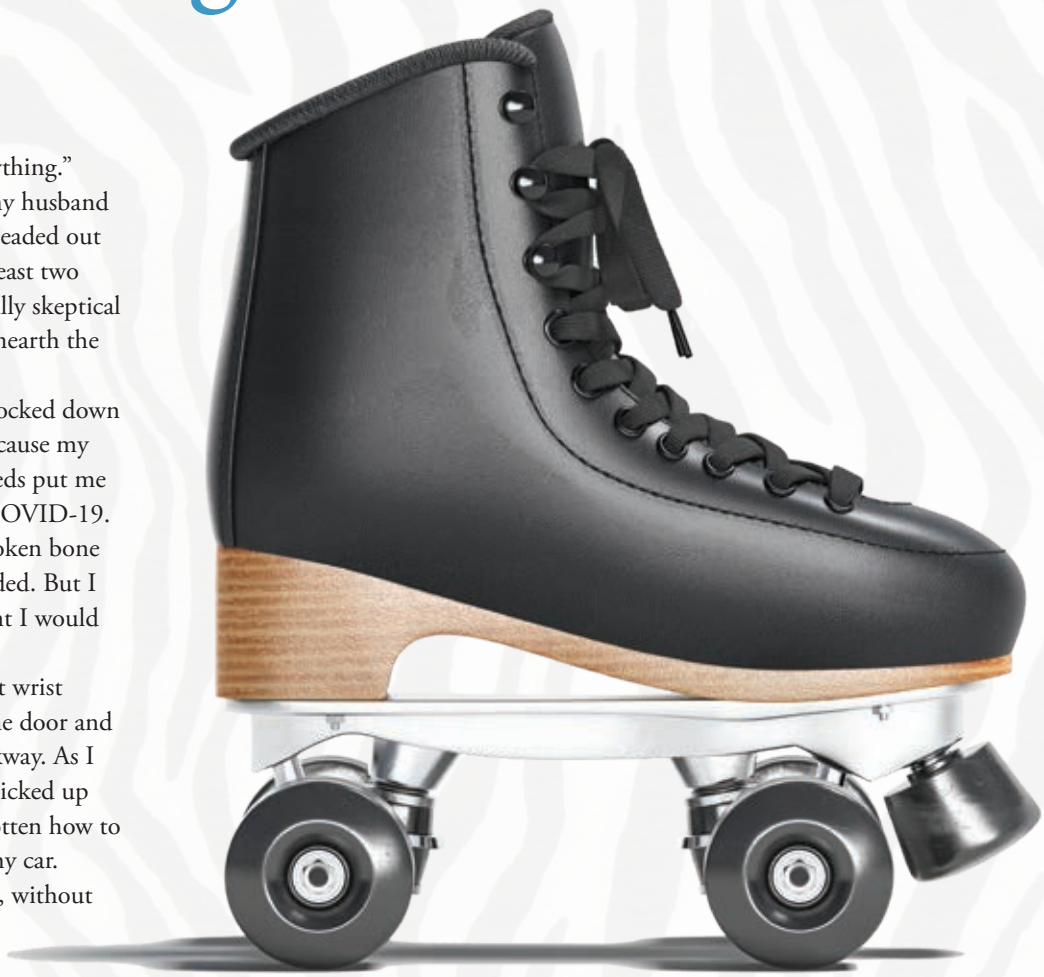
On a roll again

By Angela Hopp



"Don't break anything." That's what my husband told me as I headed out for my first skate in at least two decades. He was rightfully skeptical about my decision to unearth the dusty Rollerblades.

We'd stayed strictly locked down for more than a year because my immunosuppression meds put me at high risk for severe COVID-19. A hospital visit for a broken bone was the last thing I needed. But I was reasonably confident I would not get hurt that badly.

I fastened my ancient wrist guards, stumbled out the door and wobbled down the walkway. As I neared the sidewalk, I picked up speed and, having forgotten how to brake, I smashed into my car.

"I'll be fine!" I yelled, without looking back.

Lacing up

Like a lot of grade schoolers of the '80s, I spent a great deal of time in roller skates. Our next-door neighbors had a double-wide driveway, and the added-on lane was super smooth, perfect for practicing my zigzags while listening to Billy Joel's "New York State of Mind" on my Walkman knockoff.

I was the oldest and only girl on the block, and the boys nicknamed me Judge Wapner after the guy on "The People's Court," likely because I mediated their disagreements about who hit whom first. I didn't look the part of a jurist with my Jams shorts and gapped teeth, but like Wapner, I was opinionated, and in my opinion, I was the best skater on the block.

By middle school, the roller rink was the happening place for richer girls' birthday parties. I was glad to have my own pair of skates, but I never had cash for the snack bar. I didn't understand the crouched speed skaters and didn't have the guts to try to land tricks, but I did once couples skate (no hand holding) to "Red, Red Wine" with a boy I never saw again.

In high school, I got a set of inline skates second- or thirdhand. By then, skating birthday parties had fallen out of fashion; people were trying to get into clubs and going to shows. Nerdy and uncool, I learned to blade on the smooth side of the driveway next door when I wasn't reading fashion magazines or books recommended by Stephen King in "Danse Macabre."

I took the Rollerblades with me to college. I'd gotten my gapped teeth fixed that summer, had acquired glasses that I thought made me look smart, and had traded my grunge staples for crop tops and Lycra. I skated the hell out of that

campus. I felt strong and free, full of potential.

During Labor Day weekend my freshman year, while skating near the dorm, I had my first conversation with Michael, the young man who'd later become my husband. We were both sweaty. He was covered in mosquito bites. It was Houston, after all.

Downhill fast

Fast forward 20 years, and I got sick. My immune system turned on one day and then refused to shut off. It thought my muscles were the enemy.

The pain became so severe and I got so weak that Michael had to help me get out of bed and get dressed. He had to carry stuff for me and open just about every container in the house. We had discussions about what to do if I no longer could get up our townhouse's stairs or if I'd eventually need a wheelchair.

It took more than a year, but I finally got on a monoclonal antibody that did the trick. It took even longer to regain most of my strength. And then came COVID-19, and so began our intensive cocooning.

On daily work calls, my colleagues shared how they were entertaining themselves while staying distanced. A colleague mentioned she'd ordered some roller skates. I looked them up and became intensely jealous. Despite the fact that I absolutely could afford a pair, I couldn't bring myself to drop several hundred bucks. Instead, I pulled out my dusty Rollerblades.

Freewheeling

Once I made it to the street, muscle memory kicked in. I was no good, but I was rolling. It felt amazing. I beamed into the wind.

My street is a court, basically a big circle with some moderate ups and downs. On my first down, I freaked out and threw myself into the grass. I figured it was a better option than crashing into the asphalt. I wasn't hurt, thanks to those wrist guards.

I went out every day after work and skated until dark, and I got better quickly. Mindful of careless drivers, I was not comfortable listening to music because I knew I wasn't steady enough to react quickly if a car came along, so I went without tunes.

One day I wore my "Wear a mask" shirt. As I came over a hill, I saw a man at his car. I was about to skate past him when it dawned on me that I'd left the house without my mask. He probably couldn't have read my shirt, but I was so overcome by my own hypocrisy that I yelled my confession at him: "My shirt says to wear a mask, but I forgot mine. I'm going to get it!"

And that is when I hurt myself the first time. I tumbled forward and mostly caught myself. I ended up with just a skinned knee and a couple of bruises. I decided I should invest in some kneepads and a helmet.

As the summer got hotter, I thought I was ready to leave my circle. I was wrong. I still wasn't great at braking and had to grab at ivy on the neighborhood sound wall to slow down. I turned right back around and returned to the safety of my circle.

New laces

I eventually managed to convince my broken brain that it was OK to spend money on a new pair of roller skates. I even ordered zebra print laces for them. (The zebra is the official symbol for rare diseases. Med students are taught: "When you hear the sound of hooves, think horses, not zebras." But zebras exist too.)

Around that time, I decided I could drive to an empty (and flat) parking lot and finally get to listen to music while skating.

That was when I really hurt myself.

I was listening to Tracy Chapman, very likely singing along, and I fell flat on my rear. I'm lucky I didn't fracture my tailbone or hip, given that long-term steroid use gave me osteopenia. I was sidelined several weeks by my injury and during that time invested in yet more padding.

I'll be honest: I haven't skated a ton since that bad fall. My third COVID-19 shot in September finally made it safe for me to return to work, and it's dark now long before I get home.

But I'm not giving up. And now that I have almost as much gear as a football player, I'm probably not going to break anything.

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Finding wellness in the woods

By Heather Bisbee

HEATHER BISBEE

The author has enjoyed getting lost in the woods of western Massachusetts.

When I moved from the Arizona desert to the woods of western Massachusetts in pursuit of a Ph.D., the change in scenery was initially overwhelming. As I walked home that first evening through my forested neighborhood, I couldn't help but picture countless horror movie scenarios. The vast trees and darkness felt suffocating. Soon afterward, classes began, and I dove headfirst into my research. As the lab became my primary home, my wooded neighborhood became a forgotten part of the scenery.

With the onset of the pandemic, I suddenly found myself in my house, staring out each morning into the trees. The drastic shift to Zoom meetings, presidential press conferences, family emergencies and sheer confusion created a mental health crisis that felt both global and personal. I found comfort in the simple scenery beyond my window, and I eventually ventured out.

What began as an avoidance of cabin fever quickly evolved — from brief jaunts during lunch breaks to longer weekend adventures on more distant trails. The vast network of paths running right behind my own home astonished me. I often got lost that summer, and somehow getting lost was the best part of the journey.

I wouldn't consider myself a particularly avid hiker, and I certainly couldn't keep up on an extended backpacking trip. Even so, I continue to find solace in the backyard woods of my own neighborhood. Whether I've had a long week at the lab bench or cooped up at a desk, the lure of the woods invites exploration.

My slow, rhythmic walking pace may not win any medals for speed, but it is an act of meditative awareness. This is far more effective for me than any guided meditation, as I allow my mind to wander with my feet. And when I allow myself to get too lost, at least I know I'm never too far from home.

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Drumming myself into well-being

By Jelena Lucin

Djambe/djembe/jembe (noun): A rope-tuned, skin-covered, goblet-shaped hand drum carved from a single piece of African hardwood, originating in West Africa.

The sounds of West African instruments blast through the parking lot, and vibrations pulsate in my ear as I approach an open door. I hesitate, thinking, Do I belong here? The roaring beats tell me it's an all or nothing decision.

I go for it, knowing that, as soon as I do, there's no turning back. I'm committed, and I take comfort in knowing that the thunderous tone of the drum will fill any space I've made for my doubts and drown them out. Until about four months ago, I never thought to take up West African djambe drumming as an outlet and for the sake of my mental health and well-being. I'm a novice, but inexplicably, I feel this is what I'd been looking for, and I'm in it for the long haul.

I've found that entering a new phase in my life is exciting but often coupled with sacrifice. The meaningful changes in my life — starting a new job, moving far from home, starting a family, bringing up a child — have come with hard compromises, doubts and societal pressures. Now I factor in the trauma of living in a pandemic world (a divided and, arguably, broken world), and it can feel nearly impossible at times. On any given day, I put on different hats, ensuring needs are met, voices are heard and details are analyzed, and my thoughts run relay-style at warp speed to ensure everything is taken care of in a thoughtful and intentional way. It gets noisy, cluttered and utterly exhausting at times. I've found myself reflecting back on times I was more resilient; the hardships were there, but they were easier to bounce back from.

The closest I've ever come to feeling balanced or in some sort of Zen state was as an undergrad when I was an avid yogi; I built confidence through movement and breath, and I advised my peers to try yoga as a means of stress management. Between undergrad and grad school, I worked as a barista and read Haruki Murakami's books on the train rides to a coffee shop in front of the European Union headquarters on a bustling street in Brussels. I was grounded. I had a strong sense of belonging.

For a period of my life after grad school, my work and creativity were intertwined. I traveled a lot, I inspired kids around the globe, and when people asked me what I did to tap into my creative side, I was able to say, "It's in the job." But this was not a balanced life, and I eventually felt run down. What happened to my easy confidence and assurance? I wished I could sit down, close my eyes and meditate to quiet the mind and sort through all the clutter in my head, but the sheer amount of noise was too intimidating.

COURTESY OF JELENA LUCIN

The author practices on her West African djembe.

It took me a while to figure out that I couldn't go back to the outlets that had worked in the past. Actually, it took someone else giving me permission to try something different. They said, "Forget what's not working … what else do you wish you could do?"

Without thinking, I said, "I want to learn to drum."

This past fall, I went to see a dance studio where my daughter would be taking lessons. I peered through a glass window and saw more than 20 drummers seated, well spaced, in a perfect circle. I was in awe — I hadn't seen a large room full of strangers in a very long time. The sounds thudded dully through the walls, but with every rhythmic beat, I saw the drummers' unity and sense of purpose. They were focused, and each seemed to be a small part of something much bigger. I'm sure that some of the pull I experienced in that moment was my desire to heal from pandemic isolation. By playing the djambe in a group, I thought, I could connect with the people around me without uttering a word.

A drummer connects with the instrument and with the rhythm, getting out of their own head. I'm told the feeling can be transcendent. I'm not quite there yet. However, I have felt the intensity of the djambe drum match exactly what is going on inside me — the stress and anxiety. Any anger and frustration I'm holding on to from the day begins to dissipate. I'm forced to be accountable for the state of my physical body — becoming more aware of the tension I hold. The more relaxed I am, the easier it is to drum well.

The moment I capture a continuous rhythm and I'm in sync with 20 others in a circle, it's empowering, and I can't help but be present and smile. In yoga, there's more space in my mind to drift from one thought to the next, and I struggle to come back to the breath and focus on the sensations — a common challenge for anyone. In drumming, every beat I make replaces a thought, and there's less room for my mind to stray, because I must be entirely focused on the next beat. I drift for a split second, and I lose the rhythm. I get distracted a lot as a beginner, but I keep going. I try again.

Drumming is helping me relearn how to let go, quiet the mind and reconnect with my authentic self. It's not a remedy, but it is a step toward actively seeking better mental health and well-being, and it is exactly what I need in this phase of my life.

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Permission to break down

By Renae Crossing

The effects of fasts on cells are a good analogy for what happens when we step away from work. Let's make intermittent resting a thing.

You're looking at those unpacked boxes cemented as housing blocks on the skyline, determined to be permanent. Clothes lounge like teenagers, and the gray layer of dust is a stratus cloud.

Or maybe your data is half gathered or part processed. Your code is not quite there. Your figures are relatives who have overstayed, and you retreat to the kitchen to escape their gaze: awkward and expectant.

You're tired, and some things have accumulated.

Your cells likewise face that famous economics principle — scarcity — and in these moments they deliver doses of both realism and aspiration. Your body, with all its biochemistry, is still human. Well-oiled machines that they are, even cells conserve energy sometimes by not immediately sorting through proteins that loiter after a job is complete. Not everything is in its place. While it's accurate to picture cells as teeming with organized life, there is actually a degree of clutter. Take comfort.

The memory

I realized the importance of intermittent rest in my first year of graduate school. After working in the lab for a year on my undergraduate thesis, I was teaching secondary school and wanted to talk about science all the time, no longer bookending those conversations into seminars.

Around 1:50 a.m., my housemates would tell me I needed to sleep. I'd finish the lesson on atomic theory for Year 11 Chemistry and close the laptop. Taking a shower became a window in which I could not work.

Late in the year, I went out for dinner for a friend's birthday on a school night. That this was noteworthy is a telling landmark of that time.

The aspiration

The aspiration our cells offer is a paradox. Experts in signaling and production, enjoying a go-go-go lifestyle with side hustle aplenty, even cells benefit from taking a break. In stepping away during a fast from the typical pace of building — of anabolism in its varied forms — our cells may see a host of benefits.

Our cells' response to fasting, laid out clearly in a couple of reviews in the New England Journal of Medicine and the journal Nature, provides a useful analogy: We, too, may take breaks from production. We're not talking months off; I suggest regular, sustainable rest. Consider the Sabbath or a daily practice, a sun salutation or a scheduled walk, after which you can resume with some helpful rewiring.

What might cells' responses to calling a timeout teach us?

Switch your fuel

One weekend in that first grad school year, a teacher friend and I wrote a list of the things we wanted to do in our new city. We decided to visit one place each weekend. In hindsight, the lessons I learned then were just the ones I needed years later when I was studying life science. One day each week was not for planning another experiment or entering more data. It was to switch fuel.

A cell that switches from glucose-derived fuel to ketone bodies in

fasting is later better able to resist metabolic, oxidative, ischemic and proteotoxic stress. It is less prone to getting worked up: inflammation. It is able to grow.

We aren't just what we eat; ponder the sources of all you consume and whether that consumption is passive. The benefits our cells realise after fasting can be mirrored in our own lives by refocusing our fuel from what is constantly coming in — the carbohydrates of media, management or misguided advice — to what we've stored away earlier or never noticed.

In the time stolen from consumption, we can remember what fuels us and ask what gives us energy even as we give. Step away from the things you usually read or hear. Listen to your breath. Consider the lilies. Be beautifully, refreshingly bored. Or put down your book and surrender to the chaos of nieces and nephews. Church pews themselves don't promise renewal, but you can stretch out, with silence, together, and watch the light filtering through stained glass.

Stop accumulating

Another evening, a friend invited a guest speaker to his home. We crammed onto couches in the loft with soft orange light on wooden walls. I listened to her epiphany on rest. She had been completing her Ph.D. in English literature at Cambridge. What she could read was endless; there was no end to further thoughts. Yet by her third year, she chose to rest — read only for pleasure— one day a week. I thought, "If she can choose this, I can too."

When our cells fast, protein production slows. Our cells need not constantly make to stay alive. If we can realize a healthy, evolutionarily conserved equilibrium in our cells, can we realize it for our very selves?

In the frizzled factory of a fasted state, your cells take stock. They throw together a meal from loose ends, clearing clutter. Old proteins forming part of the furniture? Marie Kondo that shit. To one protein, "Thank you for your service." Recycle. To another, "You know what? You still spark joy." Reuse.

I don't think we appreciate the effect this has on the state of our cells. It's not a sentimental second wind for proteins forgotten; the science in the reviews mentioned above suggests it's more like a lifeline, extending quality of life if not lifetimes, through the life-changing magic of lysosomes.

Let's thank the parts of cells that help us do this. Autophagosomes, thank you for gathering with gentleness the old things for sorting. Lysosomes, thank you for having the courage to release aged materials from their former form for reuse. Lipid droplets, thank you for shrinking and expanding in time with our rhythms; you separate and collate lipids that, otherwise accumulating, can be toxic, and in doing so, you relieve us.

Repair and reenter

This time, a drop of memory from when I was in school. My art homework was due the next day, and I was nowhere near done. Dad, relaxed and gentle, suggested I just go to bed. I thought there was no way I could possibly do so, but I did, and I woke up in the morning and finished my homework. My parents knew the power of rest. Mum used to say when I was stressed, "You'll just have to do the best that you can in the time that you have." This is realism with aspiration. Rest, and give your best.

What happens when a cell returns from rest?

A fasting cell repairs DNA. When our cells return to their usual comings and goings after a fast, healthy remodeling occurs. Processes are more efficient. What is essential remains. And we feel better than we did before. It's called refeeding and post-refeeding, and I smile just reading those words.

Disclaimers for days

Let's clear up some mitochondria. Sorry, misconceptions.

Fasting from work may at first not be pleasant. As with a physical fast, you may feel irritable. You may wonder whether intermittent resting is not for you. Scientists want you to know that fasting improves after you've done it a few times. In the case of fasting from work, a shock to your identity may come but not without some productive remodeling. It's worth it.

Has fasting always been about food? Not exactly. Fasting in terms of resting from one's usual rhythms is in many ways a return to the focus of traditional fasts. Since long before the popularization of intermittent fasting, people have fasted less for physical reasons and more to make time for reflection; the biochemical effects of fasting are an apt metaphor for the not-just-physical benefits of taking a break. They are ours to reclaim. Fasting is ours to reclaim, to reframe. We can choose a different focus to yield different fruit.

An individual taste

Sometimes, without carving out time, I've had fasts of various sorts fall into place, and they paid off.

One time, I bought and consumed a host of delicious Middle Eastern sweets in East London. The next day, drinking tea on the sunny couch in the morning, I realised that I didn't need to eat until the afternoon; I had preloaded, accidentally. In that time, I read some, studied the tree outside some, journaled some, prayed some, and pondered some. It was toward the end of one job and the start of another, and I am grateful for the unplanned, golden window of time that dawned from those sweets.

Another time, I didn't drink coffee in the morning, even though I was a teacher, and in the afternoon I played table tennis with some other staff. I never have been known for hand–eye coordination and hated sports for the first half of my childhood, but I won! I felt oddly focused, as though peripheral things were irrelevant and unseeable and sharp-shooter things were streamlined. It's a memory that's stuck with me.

These experiences were unexpected, uneventful, solidifying times of rest.

One day, all that is in our cells will break down, resting in the good earth. Until that final catabolism, let us carve out space to consider what a refreshment from old things, in lieu of constant consumption, can bring to not just our bodies but our spirits.

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Paddleboard lessons

By Allison Frick

I tend to be a melancholy person. Or maybe more angsty and intermittently filled with existential dread.

(If this was a text message, I'd write "LOL" after that statement. You know — like when you say something a little too heavy and want to communicate with a nervous laugh that you didn't really mean it but you don't want to unsay it because it's true? That kind of LOL.)

As far as I can remember, I've always been like this. A teacher in high school once told me I looked like I had the weight of the world on my shoulders. (It was just a really heavy backpack; I had a hard time remembering my locker combination, so it was better to take all my books and binders everywhere. LOL.)

I tried to hide the heavy feelings I had — mimicking people who looked happy, hoping I could be too. As I got older, my anxiety grew and became turmoil and loneliness. In my late 20s into my 30s, I've had the gift of being able to focus on my mental health.

I'm learning how to cope. And I've had a lot of help along the way. I'm incredibly grateful for therapy, an amazing support network, and people in my life who show me more grace and love than I ever thought possible.

And paddleboarding.

I can't remember exactly why I started paddleboarding. I like to try different activities, and at one point, paddleboarding was one of them. I drifted away from it for a time. (See what I did there? LOL, but actually.) During the pandemic, I got to get back into it.

My mom and stepdad kept a sailboat at a marina in Deale, Maryland. When I was a kid, my family had a boat at that marina, and it brought back happy memories to be there. A paddleboard and kayak rental stand had opened, so I figured I'd rent a board. I felt nervous being back on the water, but I kept going back and went as much as I could during the summer of 2020.

Last winter, I used my stimulus check to buy my own board. My excitement about the coming season helped carry me through the winter. I rented a shed to store it just steps away from the dock at my mom and stepdad's new marina, not too far from Deale, in Shady Side. I worried for months about how I was going to get that board in and out of the water, but I clumsily figured it out, and each time I went out on the water, I got a little less nervous.

I ended up spending most of my free time last summer on Parrish Creek. I'd finish work and drive the

Allison still rents boards regularly at Chesapeake Paddle Sports, one of her favorite places. Here she is in May 2021 about to head out for a paddle on Rockhold Creek in Deale, Maryland.

COURTESY OF ALLISON FRICK

ALLISON FRICK

Here's Allison's board during one of her last sunset paddles of 2021 to the beach at Shady Cove Natural Area (Hopkins Cove and Parish Creek) in Shady Side, Maryland.

hour out to the bay, blasting music in my car with the windows down. Usually, I'd make it just in time for a sunset paddle.

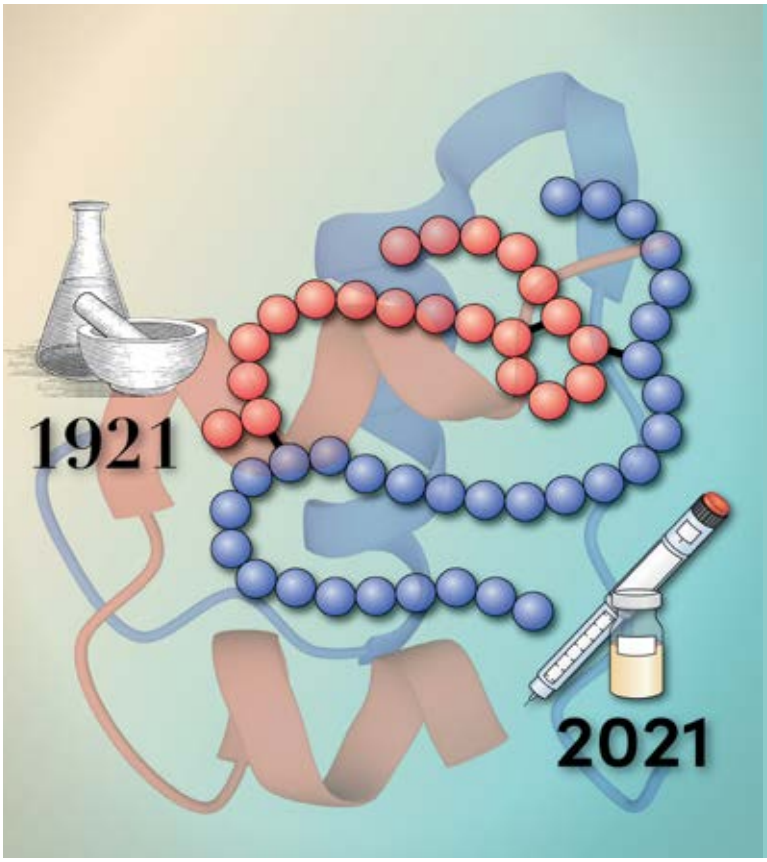
On the weekends, I'd explore the coves around the marina and paddle out to a little beach. I saw cownose rays swim, watched ospreys fly, hung out with horseshoe crabs and kept an eye out for the jellyfish. My favorite thing to do on my mom and dad's sailboat when I was a kid was to count the jellyfish drifting by. I got up to 100 one time. To this day, I am really proud of that unscientific marine-life study. I'm not sure I have the attention span for that as an adult, but I saw a lot of them this past summer.

Being back at the bay felt like coming home. Being on the water and being in a familiar place brought peace to my soul. When I'm out on the water on my board, I agree with the people who say life is a gift. I smell muddy Chesapeake Bay water, I hear the splash of little fish when they jump, I feel the board and waves under my wobbly feet (which sometimes fall asleep; that's normal, right? LOL), and I see the sunsets.

Paddleboarding gives me a sense of peace and safety within myself that translates to hope and gratitude. The angst, dread and loneliness, they're still there, but with professional help, a support system and a sense that I am loved, I have these precious moments of feeling like everything is going to be OK. It's a little hard to describe, but I know that when I get to my highway exit and see those familiar roads out to the countryside, I'll start to feel it. It's a lightness. My shoulders relax, I smile and I can breathe a little easier. It's a kind of happy I didn't think was possible — contentment, maybe? Joy? I think that's it. It must be.

I'm looking forward to getting back on the water next spring. I sure do love that board, and I'm so glad it's helped teach me what joy feels like.

Allison Frick (africk@asbmb.org) is the ASBMB's multimedia and social media content manager. Follow her on Twitter: @allisonfrick.



100 years since the discovery of insulin

In this special joint issue, we have selected 27 articles published in JBC and JLR over the past century to celebrate the 100th anniversary of the discovery of insulin and the research triumphs that followed.

jbc.org/jbc-and-jlr-100-years

JBC JLR

The Year in JBC: 2021

The COVID-19 pandemic made for yet another tough year, but the authors of the Journal of Biological Chemistry have persisted, producing groundbreaking discoveries and innovative approaches that will have long-lasting impact. Here, the editors of the journal have assembled a collection of articles to showcase just some of the important work published this year.

jbc.org/best-of-2021

Birds of a feather in Philly

Find your flock early — at an interest group session

By Angela Hopp

If you're heading to Philadelphia in April for the 2022 American Society for Biochemistry and Molecular Biology Annual Meeting, you'll need to be ready to hit the ground running. The first day will include a slew of events designed to help attendees with similar research and pedagogical interests make connections — connections the meeting organizers hope will persist long after.

The interest group sessions will start Saturday, April 2. There will be 11 of them (see box), and some will run concurrently.

Daniel Raben of the Johns Hopkins University School of Medicine serves as chair of the ASBMB Meetings Committee and conceived of the interest groups to "incorporate a broader swath of our community." They first launched at the 2021 meeting, which was held virtually.

"There was a concern among some of the ASBMB constituents that they really didn't get a lot of discussions or presentations that focused on what they were really interested in," Raben said. "They almost felt excluded in a way … because of the limited amount of space we have. The interest group events give folks in various specific disciplines and subdisciplines an opportunity to hold a mini symposium before the meeting actually begins."

Marina K. Holz of New York Medical College is one of the 2022 interest group organizers. In 2021, she ran a group focused on signaling with Mythreye Karthikeyan of the University of Alabama at Birmingham.

"I was very excited to organize the interest group in 2021 for several reasons," Holz said. "The first reason was the ability to craft a session with a unique angle. My own research focuses on breast cancer, and I partnered with (Karthikeyan), who studies ovarian cancer and shares my interests in cancer signaling.

"We invited speakers that work at the intersection of the two cancers and could speak about the common mechanisms underlying the pathobiology of these cancers to spark discussion about novel approaches for

ASBMB 2022 interest groups

Chemical biology
Organizers: Minkui Luo, Memorial Sloan Kettering Cancer Center, and Jianmin Gao, Boston College

Enzymology
Organizers: Juan Mendoza, University of Chicago, and Kayunta Johnson, University of Texas at Arlington

Glycobiology
Organizers: Nadine Samara, National Institute of Dental and Craniofacial Research, and Stacy Malaker, Yale University

Lipids
Organizers: Michael Airola, Stony Brook University, and John Burke, University of Victoria

Mitochondria
Organizers: Laura Lackner, Northwestern University, and Oleh Khalimonchuk, University of Nebraska-Lincoln

Neuroscience
Organizers: Jason Yi, Washington University in St. Louis, and Harrison Gabel, Washington University in St. Louis

Protein
Organizers: Lauren Ball, Medical University of South Carolina, and Fangliang Zhang, University of Miami

Research education
Organizers: Ellis Bell, University of San Diego, and Regina Stevens–Truss, Kalamazoo College

Signaling — cancer
Organizers: Marina Holz, New York Medical College, and Mythreye Karthikeyan, University of Alabama, Birmingham

Signaling — physiology and disease
Organizers: Michelle Mendoza, University of Utah Huntsman Cancer Institute, and Robert Zoncu, University of California, Berkeley

Membrane proteins
Organizers: Matthias Buck, Case Western University, and Fran Barrera, University of Tennessee

treatment."

Holz said that the speakers were amazing and that there was a productive discussion with attendees, though the virtual format dampened the interactions, so the two are looking forward to holding an in-person event this year.

"We just finalized our new topic, focusing on novel mechanisms of hormonal signaling in cancer and development, and invited our speakers, who are too thrilled to come to the meeting," Holz said. "Virtual meetings allow for accessibility, and there is a strong argument to continue some of them going forward. However, nothing can replace the personal connections and unfettered exchange of ideas that happen during on-site meetings because science is a collaborative enterprise conducted by scientists who are colleagues and friends."

Danielle L. Schmitt is a postdoc at the University of California, San Diego, who presented her work in 2021 at another signaling interest group that focused on cellular communication in health and disease.

"I really enjoyed the opportunity to share my work with the diverse audience that attends the annual meeting," Schmitt said. "As the interest groups are all under a theme, it was good and really helpful to attend talks that are all related to my work or using similar techniques, and it's always interesting to hear about new work from labs I am more familiar with."

She also attended a separate interest group and noted: "I really enjoyed that the interest groups had a mix of presenters, from established professors to graduate students and postdocs, so you got a range of talks in the session."

For the second year in a row, J. Ellis Bell of the University of San Diego and Regina Stevens–Truss of Kalamazoo College are organizing an interest group on research education. The session is titled "Collaborative Teaching through CURES." (CURES stands for course-based undergraduate research experiences.)

Bell said that the conversations among speakers and attendees that began in 2021 have continued since.

"These interactions have advanced incorporation of CUREs on a number of campuses," he said.

In fact, those connections got the wheels turning for a proposal for the National Science Foundation's Improving Undergraduate STEM Education program "to further study a series of pedagogical questions about using CUREs to give undergraduates authentic research experiences," he said.

Bell added: "We are excited about the 2022 networking event. ... Our goal is to not only continue the discussion and interactions that were started at the 2021 meeting but also identify new pedagogical questions that the community can coalesce around and continue the discussions to broaden the growing network of educators and discipline-based researchers focused on biochemistry education."

Raben noted that, whereas speakers for spotlight talks at the annual meeting are selected based on their abstract submissions, the interest group organizers are given complete freedom to select their topics and speakers because "it's their community."

Submissions of interest group proposals for the 2023 annual meeting will be accepted in the fall.

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

Reminder: Advance registration deadline

Starting in 2023, the five societies will be parting ways. So don't miss this last chance to converse and forge collaborations with scientists from multiple disciplines with shared research interests.

Register by March 18 for a discount on the ASBMB annual meeting at the Experimental Biology conference.

Visit asbmb.org/meetings-events/2022-annual-meeting.

The advocacy town hall is more than a free lunch

By Benjamin Corb

A continuing annual event at this year's American Society for Biochemistry and Molecular Biology Annual Meeting will be our Advocacy Town Hall, hosted by the society's Public Affairs Advisory Committee. Tucked into a scientific meeting, the town hall is an informative and interactive event where ASBMB members have a chance to share their needs and concerns with the ASBMB policy team. It is truly your opportunity to shape our agenda.

The past several years have been a challenge for researchers, students and trainees. From intensified politicization of science to hypercompetitive funding environments to research interruptions caused by the COVID-19 pandemic, today's scientists face a variety of unique obstacles beyond the expected challenges that define basic biomedical research. The ASBMB public affairs department works with science funding agencies, the Biden administration and Congress to develop policy solutions that will improve the research environment for our members.

We are excited to come to Philadelphia — the cradle of American democracy — to share our objectives with the ASBMB membership. Throughout 2022, we plan to work to implement policies that will improve international collaboration in science, identify ways to reimagine science funding for 21st century researchers and their labs, and build a workforce that is diverse and inclusive.

Moreover, we are excited to hear from you about what you need from your public affairs team. What issues do we not know exist that need to be addressed? How can we better serve your needs and improve your research experience? How can we all work together to ensure that policymakers both appreciate how your work improves the lives of Americans and understand the unique challenges you face?

In previous Advocacy Town Hall sessions, ASBMB members have started thoughtful conversations among attendees and staff on topics ranging from how scientists can get more involved in advocating for their future and careers to how organizations like the ASBMB can do more to support scientists with issues such as the unique needs of women and minority researchers. We've also shared advice on sources of funding and career development.

Benjamin Corb, the ASBMB's director of public affairs, leads the Advocacy Town Hall at the 2019 ASBMB Annual Meeting.

This event is more than an opportunity to grab a lunch on us between science talks. Come for the sandwich, but stay for the dialogue.

Benjamin Corb (bcorb@asbmb.org) is the ASBMB's director of public affairs. Follow him on Twitter: @bwcorb.

Finding science in Philadelphia

By Racheal D'Souza

You might have already heard that the American Society for Biochemistry and Molecular Biology will hold its 2022 meeting in Philadelphia April 2–5. If you think your curious mind will be looking for some fun science, technology, engineering and math–related activities outside the convention hall, look no farther than the top science museums in Philly — a city where many great ideas were born.

Steeped in the history of science, Philadelphia is the home of many firsts in the United States — first hospital (1751), medical school (1765), women's medical school (1850), college of pharmacy (1821), medical library (1751) and even the nation's first zoo (1874). Philly also is ranked by SmartAsset as the best city in America for diversity in STEM fields.

Here are a few sites you might want to check out in April.

Academy of Natural Sciences of Drexel University

1900 Benjamin Franklin Pkwy. / ansp.org

A world leader in environmental science and biodiversity, the Academy of Natural Sciences of Drexel University is the nation's oldest natural history museum. The academy's collection includes more than 18 billion specimens and about 100 living animals.

ACADEMY OF NATURAL SCIENCES OF DREXEL UNIVERSITY

This fully constructed Tyrannosaurus rex stands in Dinosaur Hall at the Academy of Natural Sciences of Drexel University.

Science History Institute

315 Chestnut Street / sciencehistory.org

Preserving and expanding the knowledge and understanding of chemistry, history and life sciences, the Science History Institute (formally known as the Chemical Heritage Foundation Museum) includes a museum, library, archive and research center. The institute has a collection of some of the oldest landmark instruments, such as a Beckman model G pH meter, Mettler B5 single-pan balance and Perkin-Elmer model 125 infrared grating spectrophotometer. The institute also has varied holdings relevant to the history of chemistry including alchemical books and fine-art depictions of Early Modern alchemists.

SCIENCE HISTORY INSTITUTE

Arnold Beckman invented this model G pH meter in the 1930s at the request of a chemist from the California citrus industry who needed an accurate way to measure the acidity of his product.

Mütter Museum

19 S. 22nd Street / muttermuseum.org

Located in the Center City of Philly, the Mütter Museum focuses on medical history, with a vast collection of anatomical and pathological specimens, wax models and antique medical instruments in a 19th century setting that helps visitors understand and appreciate how the human body works. The museum, which started with 1,700 objects and a donation of $30,000, now has grown to house a collection of 25,000 specimens.

MÜTTER MUSEUM

The skeleton of a Philadelphia woman with a rare bone disorder (left) was donated to the museum.

Penn Museum

3260 South St. / penn.museum

The Penn Museum has a plethora of archaeological and anthropological collections. Its archives include 2,500 feet of written records documenting more than 300 expeditions to destinations all over the globe. More than 15 galleries exhibit diverse artifacts and objects from around the world and through the ages, celebrating cultural richness and artistic diversity. Penn Museum has an extensive collection of coprolites (fossilized feces of animals that lived millions of years ago). Archaeologists study them to understand the existence of different plant species from long ago.

MARY HARRSCH, FLICKR

This Etruscan gold necklace dating from fifth to fourth century B.C. is on display at the Penn Museum.

The Franklin Institute

222 N 20th St / fi.edu

The Franklin Institute was founded in 1824 to honor Benjamin Franklin. Boasting an extensive collection of artifacts from the Wright brothers' workshop, the Franklin Institute Science Museum is one of the nation's oldest premier centers for science and research. The institute hosts the 10-in-10 Live Science Show with 10 different science demonstrations in 10 minutes. Interactive exhibits focus on everything from astronomy to the science behind sports, all with the goal of encouraging learning in a fun way.

FRANKLIN INSTITUTE

The Giant Heart, a walk-through exhibit, has been on display at the Franklin Institute since 1953.

Hill–Physick House

321 S. 4th Street / philalandmarks.org/physick-house

This historic house museum belonged to the "father of American surgery," Dr. Philip Syng Physick. The free-standing four-story Federal-style brick house was built in 1786 and was declared a National Historic Landmark in 1976. The house features some of the most interesting artifacts from the life of Dr. Physick and the fascinating melodrama of his personal life, which makes the museum a must visit.

PHILADELPHIA SOCIETY FOR PRESERVATION OF LANDMARKS

The Hill–Physick House is in Philadelphia's Society Hill neighborhood.

Racheal D'Souza (rdsouza2@buffalo.edu) is an associate scientist working on CRISPR, with a strong interest in writing.

ASBMB EXEMPLARY CONTRIBUTIONS TO EDUCATION AWARD

Provost makes chemistry accessible

By Martina G. Efeyini

So he could attend college and begin his career in science, Joseph Provost enlisted in the U.S. Army, serving in the military police. He finished his duty as a chemical warfare officer and commander of a mechanized infantry company in the Minnesota National Guard.

"Going from high school into the Army helped me learn discipline and focus," Provost said. "Also, being an officer helped me with leadership and management skills."

Provost, recipient of the 2022 ASBMB Award for Exemplary Contributions to Education, is a professor at the University of San Diego. For 27 years, he has worked in undergraduate education, teaching numerous biology, chemistry and biochemistry courses while maintaining a federally funded research lab focusing on lung cancer and fibrosis.

Provost earned his Ph.D. from the University of North Dakota School of Medicine and Health Sciences and then did a postdoc in John Exton's lab at the Vanderbilt University Medical School. In 1997, he became a professor at Minnesota State University Moorhead before moving to the USD, where he chairs the chemistry and biochemistry department.

"When I got to Moorhead, the university was starting to build a culture of undergraduate mentored faculty research," Provost said. "I helped create and build the biochemistry/biotechnology program and a serious redesign that was very successful."

The USD faculty has also created a fantastic place to learn and do research, he said.

Because neither of his parents finished high school, Provost recognizes the challenges some students face. He enjoys helping underrepresented, first-generation and transfer undergraduates gain confidence in science, using uses various approaches to make learning engaging and accessible to all.

"He uses innovative pedagogy to get his students' attention," Ellis Bell wrote of Provost in his nomination letter. "He trains students without 'cherry-picking' the best."

Provost serves on the ASBMB Education and Professional Development Committee, co-established Student Chapters, co-developed the fellowship and accreditation programs, co-led and judged the undergraduate poster competition, and is on the Membership Committee.

"My goal has always been to do what it takes to help students and work with faculty and help them," Provost said, "or create opportunities for people to do cool things."

'It's all about the students'

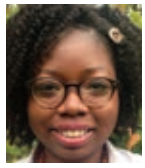
Whether it's arranging a trip for a student's medical school interview, inviting a student to join his lab or offering a listening ear to a faculty member, Joe Provost is always available to help.

Provost has trained more 180 undergraduates and high school and middle school teachers. He also has mentored faculty and served as a program and departmental external reviewer for 13 universities and colleges.

At the 2022 ASBMB annual meeting, Provost's talk will focus on his work in undergraduate education. He will highlight his innovative pedagogy, training and mentoring so other educators can have resources to support their students.

"I love the community that ASBMB brings together — it's helping students. So, the focus of my talk is, 'It's all about the students,'" he said. "Everything I've done, everything we've done … It's all been driven to support students."

JOSEPH PROVOST



Martina G. Efeyini (mefeyini@gmail.com) is a toxicologist, science communicator and advocate for the next generation of scientists. She works at the University of Maryland, Baltimore, CURE Scholars Program and is a careers columnist for ASBMB Today. Follow her on Twitter: @mefeyini.

2022 science policy priorities

By Rick Page

The Public Affairs Advisory Committee of the American Society for Biochemistry and Molecular Biology advocates for government policies that support and provide flexibility to scientists and ensure the sustainability of American research. Many legislators and policymakers lack scientific training, so science policy advocates must seize opportunities to guide and inform evidence-based policy.

Here are some policy priorities that the ASBMB PAAC and public affairs staff will focus on in 2022.

Sustainable funding

The PAAC will focus its advocacy efforts on three major issues in federal agency funding: the rising cost of research, the increased administrative burden of the grant process and lack of flexibility within grant mechanisms.

The modular National Institutes of Health grant has not kept pace with inflation, so the PAAC is developing recommendations to ensure grants can support research, such as requiring that the NIH revisit the modular grant budget every 10 years.

Investigators need the flexibility to change research directions so we can continue to capitalize on the federal government's investments in their training. The PAAC will urge the NIH to develop transitional funding opportunities, similar to a new National Science Foundation mechanism, that allow investigators to train in a new area with strong promise for impact.

Training the next generation

A shrinking postdoc job market, pandemic challenges, and the mental health burden and high-stress environments faced by early-career scientists are sapping the vitality of American research. The PAAC will focus on policy solutions to address these challenges, particularly lack of benefits and inconsistent salaries for postdoctoral fellows. Although postdoc salaries have become more standardized in recent years, benefits still vary widely. The PAAC will advocate for other federal funding agencies to adopt the NIH's salary recommendations and for funding to study postdoc management, salaries.

A related effort involves working to address challenges graduate students face, including mental health and food insecurity. A startling number of grad students experience food or housing insecurity, and the pandemic has taken a toll on the well-being of trainees. Efforts in this space will leverage the ASBMB's relationships with the NIH to advocate for better support for our most at-risk trainees.

International collaboration

Free collaboration across borders is essential for science to advance, but investigators and institutions must navigate a burdensome patchwork of polices to remain compliant with restrictions. The PAAC will advocate for harmonizing these policies and continued support of international students, scholars and collaboration.

The ASBMB will work to ensure that Deferred Action for Childhood Arrivals, or DACA, students can contribute to the American research enterprise and that immigration policy welcomes anyone who wants to study science in the U.S. The public affairs department has worked closely with federal agencies to improve research security policies without hindering international collaboration and will continue to do so.

Diversity and inclusion

As we work to increase diversity of science faculty at U.S. institutions, we must ensure equity in competition for grants. The PAAC will partner with the NIH Center for Scientific Review to collect data on the diversity of NIH grant reviewers and evaluate whether that diversity reflects goals that move the grant system toward greater equity.

The PAAC also will advocate that the NIH and NSF increase funding for and develop grant mechanisms that provide funding to historically Black colleges and universities, minority-serving institutions, primarily undergraduate institutions and emerging research institutions. Diversifying the pool of researchers and institutions receiving federal funding for research will ensure that we are training a diverse pool of undergraduates who will continue in science, technology, engineering and mathematics careers and become future leaders of science.

Rick Page (pagerc@miamioh.edu) is a professor in the chemistry and biochemistry department at Miami University and chair of the ASBMB's Public Affairs Advisory Committee. Follow him on Twitter: @ThePageLab.

'I could not ask for more'

By Laurel Oldach

Moderna may have been a little-known biotech company before the COVID-19 pandemic, but its name is a household word now. ASBMB Today asked Hardik Jani, who has worked at the company since 2017, about his experience helping to develop the company's revolutionary vaccines.

1 What has changed the most at Moderna during the pandemic?

Moderna's values of being collaborative, bold, relentless and curious have always been a constant. I believe these values have been a guiding force for our success even after so many years and exponential growth of the company. I would say nothing has changed for me or Moderna.

2 Tell me about your role?

I'm a principal research associate in the platform automation center of excellence, finding automated solutions for manual assays. I lead collaborations with the infectious disease team to transfer enzyme-linked immunosorbent assays to an automated platform to increase sample capacity to help us evaluate our preclinical vaccines and understand the underlying science.

I was proud to be a part of the COVID-19 vaccine team. It's a great feeling. But we still have a long way to go. We have a crazy pipeline and many programs, with many people working tirelessly to make a difference.

Hardik Jani

CURRENT POSITION
Principal research associate, Moderna

CAREER PATH
M.S., biotechnology, University of Houston–Clear Lake

First job: Senior research assistant, Base Pair Biotechnologies

FAVORITE MOLECULE OR PROTEIN
Nucleic acids, especially RNA. "The world just witnessed what mRNA technology can achieve. And it's going to transform how medicine works."

3 What's been most challenging?

Due to the pandemic, we had to improvise. It was tough for me to manage work–life balance; I have a 2-year-old baby, and I sometimes feel I missed out on the best phase of her life.

People would come in early, work in shifts, sometimes come on weekends. It was challenging, but the goal pushed us hard. I would say it was not a challenge but an honor that after so much hard work we were able to develop a vaccine that actually works to treat patients.

4 What was it like when the clinical trial results were announced?

To be honest, I was really emotional. I still get goosebumps. It was the proudest moment of my life.

It was also a bittersweet project. So many lives were lost. I believe in destiny; I was certain that we were chosen to fight this pandemic. I am extremely proud, humbled and honored to be a part of this incredible team.

5 Thinking back, what made you pursue a science career?

I finished high school in India in early 2000. The biotech field was new, but there was always that spark. Knowing what I know now, if I had to go back in time, I would either be a scientist or a singer; those are my passions.

I'm trained in Hindustani classical music. I make a point to spend one hour every Sunday with my daughter going over ragas. I'm practicing, and she's learning something. It's the best feeling to have both your passions in your life. I could not ask for more.

(This interview has been edited and condensed. Read a longer version at asbmb.org/asbmbtoday.)

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

CLASSIFIEDS

Staff Scientist Babu Group
St. Jude Children's Research Hospital

M. Madan Babu's Group and the Center for Data Driven Discovery in the Department of Structural Biology are actively recruiting highly driven and talented individuals who are motivated to explore the intersection between data science and biology in a multidisciplinary and diverse working environment. Multiple experimental and computational positions are available at the Masters and Ph.D. levels in data science, cancer genetics, human genetics, omics, network biology, synthetic biology, molecular biology and cell biology.

https://careers.asbmb.org/job/staff-scientist-babu-group/60115265/

Assistant Professor of Biochemistry
California State University, Fullerton

The Department of Chemistry and Biochemistry at California State University Fullerton invites applications for a full-time tenure-track Assistant Professor position in biochemistry to begin in Fall 2022. Applicants shall have a Ph.D. in either biochemistry, chemical biology, biological chemistry or a closely related field, and relevant postdoctoral or equivalent experience at the time of appointment. The successful candidate will maintain an active research program involving undergraduate and M.S. students while committed to excellence in teaching biochemistry at the undergraduate and graduate level.

https://careers.asbmb.org/job/assistant-professor-of-biochemistry/60144384/

Postdoctoral Research Fellow
New York Blood Center

The Lindsley F. Kimball Research Institute (LFKRI) Principal Investigators are seeking highly motivated and exceptionally creative candidates to lead cutting-edge research projects in the field of blood cellular therapy, inflammation and immunology, and hematopoietic stem cell (HSC) biology.

https://careers.asbmb.org/job/postdoctoral-research-fellow/59622232/

Research Scientist (Cardiovascular & Cancer)
University of Washington

The focus of the Research Scientist Associate position within the Fujise Lab is to work as a team to bring fortilin from bench to bedside. The Research Scientist will report to and work closely with the Principal Investigator, who will mentor him/her for his/her professional goals and development. Excellent people and communication skills are critical for success.

https://careers.asbmb.org/job/research-scientist-cardiovascular-cancer/60064815/

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

2022 ASBMB Annual Meeting

APRIL 2–5 | PHILADELPHIA

Programming for 2022

Join thousands of scientists from multiple disciplines with shared research interests. Present your latest findings, hear inspiring lectures, participate in workshops, and form new bonds that will help you achieve the most important work of your career.

Four days of discoveries and dialogues. All ASBMB meeting programming is designed *for scientists by scientists.*

Award lectures. Celebrate scientific leaders and mentors. These high-profile speakers will cover impactful research and education and diversity initiatives.

Scientific tracks. Deepen your knowledge of significant research trends during daily sessions curated by pioneers and innovators.

Workshops. Leading experts will offer practical advice for adopting the latest tools, software, methodologies and best practices to propel your work from bench to publication.

Important deadlines:

Last-chance abstract submission deadline: Jan. 27
Early registration deadline: Feb. 7

asbmb.org/annual-meeting

ASBMB

EB Experimental Biology

The ASBMB annual meeting is held in conjunction with Experimental Biology.