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ASBMB TODAY

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

THE BEST OF BMB 2021

(A SUBJECTIVE LIST)

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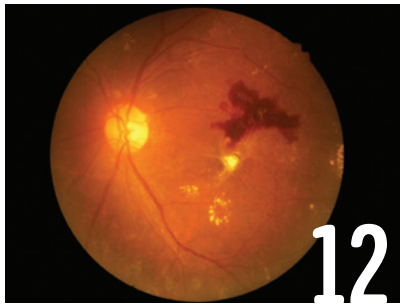

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Our gift to you

By Comfort Dorn

When my older sister and I were about seven and six years old, respectively, what we really wanted for Christmas were Tammy dolls. Tammy was about the same size as Barbie (and had almost as many clothes), but she was considered a more wholesome toy for little girls. She had poofy hair and wore a little turquoise romper. We were obsessed.

My sister was the enterprising one, and she did a fair bit of snooping. A few weeks before the big day, she found the coveted dolls in their hiding place. I wanted to be surprised, but she insisted on showing me and then swore me to secrecy. By Christmas morning, I was an emotional wreck.

But when we tore into our gifts, there were no Tammy dolls to be found. My mother figured out we'd unearthed them, so she took them back to the store and replaced them with far more expensive and tasteful Madame Alexander dolls. You can see where I got my obsession with the element of surprise — not to mention my general anxiety around the giving and receiving of gifts.

December is, of course, the big month for gifts, so I'm tamping down my emotions and trying to get into the spirit. This month's issue is the ASBMB Today team's gift to you, our members and readers. We are so grateful for your unflagging interest and enthusiasm, especially over the past two years. You've kept us motivated through these months of uncertainty.

So tucked into this issue is our roundup of some of the year's most interesting science and our annual gift guide (does giving gift suggestions count as a gift?). We've got profiles of the ASBMB's 15 big award winners to get you excited about the 2022 annual meeting in April in Philadelphia. We also offer two very different essays, by Adele Wolfson and Brooke Morriswood, about the rewards of having undergraduates in the lab. And we wrap it all up with a truly lovely essay by Richard Levy on the pain and rewards of a life in research.

Thanks so much for reading. I hope your holidays overflow with joy and surprises.

CORRECTIONS:

In November's articles about symposia sessions at the 2022 ASBMB Annual Meeting, the names of several speakers were misspelled. A corrected list of speakers starts on page 52 of this issue.

A sidebar in November's feature on the ASBMB Undergraduate Poster Competition incorrectly identified Pamela Mertz of St. Mary's College of Maryland. She is chair of the ASBMB Student Chapters Steering Committee.

ASCB honors Montgomery, Alahari

The American Society for Cell Biology has announced its 2021 slate of award recipients and fellows. Two ASBMB members are on the list.

Beronda Montgomery, the MSU Foundation Professor at Michigan State University, will give the Mentoring Keynote Lecture at the ACSB's 2022 meeting. The lecture highlights "an individual who exemplifies mentoring by their impact on the training of scientists and scholars who belong to underrepresented groups."


MONTGOMERY

Montgomery's lab studies photomorphogenesis, or the growth and development responses of photosynthetic organisms such as plants, algae and cyanobacteria to light cues. Simultaneously, Montgomery applies this line of thinking, investigating how individuals perceive and respond to their environments, to best practices in research mentoring and leadership. She is the author of a recent book, "Lessons from Plants."

Suresh Alahari, a professor at Louisiana State University, is a member of the 2021 cohort of ASCB fellows. His lab studies cancer, with particular focus on a protein called nischarin, which they identified. They study tumor cell migration and adhesion, along with how microRNAs are misregulated in breast cancer.


ALAHARI

Alahari earned a master's degree in human genetics from Andhra University in India and his Ph.D. in molecular biology at Drexel University. After postdoctoral research at the University of North Carolina, Chapel Hill, he joined the faculty there. He has worked at the Louisiana State University Health Sciences Center since 2004.

He is a fellow of the American Academy for the Advancement of Sciences.

Carr moves to UW

Rotonya Carr, a physician–scientist who was until recently an assistant professor of medicine and director of the liver metabolism and fatty liver program at the University of Pennsylvania, has moved to the University of Washington in Seattle. Since Oct. 1, she has headed the university's division of gastroenterology.


CARR

Carr cares for hepatology patients and leads a lab that studies the pathophysiology of fatty liver diseases. Her team is particularly interested in the effects of alcohol on ceramide metabolism and in how proteins associated with lipid droplets affect the development of disease.

After earning her M.D. at Cornell University and completing a residency at Massachusetts General Hospital, Carr spent four years as a practicing physician before returning for fellowship training in gastroenterology at Penn. She joined the faculty at the conclusion of that three-year training period and has worked at Penn for the next 10 years.

She was a member of the first class of junior associate editors of the Journal of Lipid Research and of the first cohort of Lina Obeid memorial awards for young investigators from the International Ceramide Committee.

Kadakia named interim vice provost

Madhavi Kadakia, who served as chair of the biochemistry and molecular biology department at Wright State University in Dayton, Ohio, from 2015 until June of this year, has been named the university's interim vice provost for research.

The Kadakia lab works on signaling pathways in cancer research, focusing on the tumor protein p63. Like the better-known p53, p63 is a transcription factor. Kadakia's research has focused on an N-terminally truncated protein isoform that is most highly expressed in epithelial tissue. The protein is thought to act as a tumor suppressor, keeping cells adhered and preventing migration. Kadakia's group has described microRNAs and coding transcripts that p63 affects.

Kadakia has been associate dean of research affairs at Wright State's medical school since 2019. According to a press release, as head of the pandemic research task force, she was instrumental in getting researchers back onto campus after operations shut down in 2020.


KADAKIA

After receiving bachelor's and master's degrees in microbiology at the University of Mumbai in India, Kadakia earned a Ph.D. in infectious disease and microbiology from the University of Pittsburgh. She shifted into cancer research as a postdoc at the Pittsburgh Cancer Institute and conducted further research at the

Cancer Institute of New Jersey. She has been on the faculty at Wright State since 2002 and was promoted to full professor in 2013. She has served as a board member for the Association of Medical and Graduate Departments of Biochemistry since 2018.

UMich honors Benore, Verma's group

Marilee Benore was one of three University of Michigan faculty members honored this year with the university's Carol Hollenshead Inspire Award for Excellence in promoting equity and social change.

BENORE

Benore is a professor of biochemistry and molecular biology at UM-Dearborn, where she studies vitamin transport using a flock of chickens with a mutation in riboflavin binding protein. The mutation, which is lethal to embryos unless supplementary riboflavin is injected into eggs, has the interesting secondary effect of turning egg whites completely transparent.

Benore also conducts social research in women's persistence in science, technology, engineering and mathematics and has published pedagogical studies as well. She is the former chair of the American Society for Biochemistry and Molecular Biology's Student Chapters subcommittee and is a member of the society's Women in Biochemistry and Molecular Biology Committee.

In addition to honors for UM professors, an educational outreach organization led by grad students and postdocs called Developing Future Biologists received recognition. The group focuses on making developmental biology accessible to undergraduates, and its members include ASBMB member and ASBMB Today contributor **Isha Verma**, a postdoc, along with 10 other graduate students and postdocs.

VERMA

Gunning receives President's Medal

Peter Gunning, a professor at the University of New South Wales Medicine and Health in Sydney, Australia, has received the highest honor of the Australia and New Zealand Society for Cell and Developmental Biology, its President's Medal. The award recognizes Gunning's career-long research on the regulation and function of the actin cytoskeleton.

Gunning's lab studies the actin cytoskeleton and filament proteins called tropomyosins, which in muscle cells help to build the actin–myosin sarcomere. Tropomyosins in nonmuscle cells can affect how strongly actin-binding proteins bind to actin filaments and the activity of myosin motors. Because the cytoskeleton changes dramatically as a normal cell transforms into a cancerous cell, tropomyosins are also possible targets for chemotherapy, and this has led Gunning to form a company developing drugs that target tropomyosins.

GUNNING

In an interview with his university's press office, Gunning said, "I cannot believe we have gone so far in my lifetime from understanding cytoskeletal organization and function through to drug development." In the 1980s, as a postdoctoral fellow at Stanford University, he cloned human actin isoforms and investigated the differences between skeletal and cytoplasmic versions of the proteins. (Prior to that, he studied gene expression in the nervous system as a graduate student at Monash University in Melbourne and then neuronal differentiation at Stanford.)

Gunning is a member of numerous scientific societies, including the American Society for Biochemistry and Molecular Biology and its Australian counterpart, also known as ASBMB, as well as the ANZSCDB and the American Society for Cell Biology. He has served as president of the ASBMB (Australia) and as founding editor of the journal Bioarchitecture. He is the former deputy dean of research and head of the school of medical sciences at UNSW and was the inaugural chair of the research division at the Children's Hospital at Westmead in Sydney.

The award consists of a medal and a talk presented at the recent virtual ANZSCDB meeting in Melbourne.

Johnson delivers Greenberg lecture

Elizabeth Johnson, an assistant professor in the division of nutritional sciences at Cornell University, delivered the 2021 Judith Greenberg Early Career Investigator Lecture at the National Institutes of General Medical Sciences in late September.

JOHNSON

The lecture series highlights the work of early-career grantees at the NIGMS and was named for Judith Greenberg, a former deputy director of the institute who retired in 2020 after working at the National Insti-

HHMI names new investigators

The Howard Hughes Medical Institute announced in September a class of 33 new investigators. Three members of the American Society for Biochemistry and Molecular Biology were on the list.

Shingo Kajimura is a professor at Beth Israel Deaconess Medical Center/Harvard Medical School and the Broad Institute who studies the roles mitochondria-rich brown and beige adipose cells play in organismal metabolism. These tissues are well known to metabolize fat to generate heat; Kajimura's lab of clinicians and basic scientists has shown that they can do more. Beige cells can modulate blood sugar and circulation of other metabolites in a way that suggests implications for diabetes. Kajimura is also interested in adipose tissue development and whether it might be possible to reprogram white adipose cells, which store energy, into brown or beige cells, which are more metabolically active. The lab identified a master regulator for brown and beige fat development and also studies intracellular nutrient trafficking.

KAJIMURA

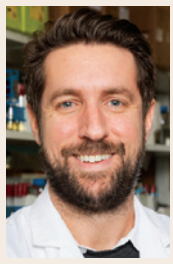
Kajimura earned his Ph.D. at the University of Tokyo. He was a postdoc at Harvard Medical School before joining the faculty at the University of California, San Francisco. He returned to Boston with his lab in the spring of 2020.

Cigall Kadoch is an associate professor at the Dana–Farber Cancer Institute and at Harvard Medical School and a member of the Broad Institute. Her lab studies ATP-dependent chromatin remodeling complexes, macromolecular machines with a dozen or more protein components each. The remodeling complexes — also called switch/sucrose nonfermentable, or SWI/SNF, complexes — can alter DNA accessibility and gene expression by moving nucleosomes along a DNA strand, changing the compaction and organization of chromatin. Mutations in the 29 proteins that can be incorporated into one or more of the complexes within the SWI/SNF family are found in over 20% of human cancers, and some of them serve as the key molecular drivers of select pediatric and adult cancers.

KADOCH

As a graduate student at Stanford University, Kadoch found that these proteins are altered in cancers, affecting oncogenic gene expression. She later joined the faculty at Dana–Farber, where her lab now works on disruption of SWI/SNF complexes and recently solved the structure of one multisubunit SWI/SNF complex and its nucleosome substrate.

Vincent Tagliabracci is an associate professor at the University of Texas Southwestern Medical Center who is interested in discovering novel kinases. His lab studies unusual protein modifications, such as glutamylation and AMPylation, by proteins that resemble kinases. They also have a related line of research into how Legionella lipid kinases alter the host cell membrane as well as other interactions between bacterial effectors and host cells.



TAGLIABRACCI

Tagliabracci earned his Ph.D. in biochemistry and molecular biology at Indiana University, where he studied the role of glycogen phosphate in Lafora disease, a form of epilepsy. He conducted postdoctoral research in Jack Dixon's lab at the University of California, San Diego, studying the mysterious kinase that phosphorylates the protein casein in the Golgi apparatus. (It turned out to be a protein called Fam20c, which governs many other secreted phosphoproteins as well.) He joined the faculty at UT Southwestern in Dallas in 2015. Learn more about his work in a talk he will present at the 2022 ASBMB annual meeting session on signaling.

tutes of Health for 45 years.

Johnson studies how compounds from the gut microbiome become part of host physiology. Specifically, she works on sphingolipids, investigating how lipids from human milk influence microbial metabolism and the effects that interplay goes on to have on infant health.

Johnson studied biology at Spelman College and earned her Ph.D. at Princeton University, working on cell-cycle transcriptomics. She was a postdoc with Ruth Ley and worked on lipid-dependent host–microbe interac-

tions before starting her lab at Cornell in 2018. Her NIH biography noted that she "finds much inspiration from her two small gut microbiome sample generators."

Beitz named a fellow of Sigma Xi

Donald Beitz, a distinguished professor in the animal science and biochemistry departments at Iowa State University, has been named a fellow of the scientific research honor society Sigma Xi.

BEITZ

Preventing metabolic disorders in dairy cows is a focus of Beitz's research. Calving and early milking are apt to cause an energy imbalance as a cow mobilizes nutrients to feed her calf faster than it can eat new food; this can lead to the breakdown of fats and serum ketosis, which can cause fatty liver disease and other health problems.

Beitz has studied dietary changes and other interventions, such as the hormone glucagon, aimed to prevent these disorders from developing. He also studies the effects of dietary interventions on milk composition and collaborates on a project looking for ways to reduce emission of greenhouse gases such as methane and hydrogen sulfide from bovine digestive tracts. His research has been supported over the years by the United States Department of Agriculture, the Wisconsin Milk Marketing Board and other agricultural trade associations.

Soon after earning his doctorate in dairy nutrition and biochemistry at Michigan State University, studying a cell-free protein synthesis system isolated from udders, Beitz took a faculty position at Iowa State in 1967 and has remained a professor there for more than 50 years. He is a member of numerous scientific societies, including the American Society for Biochemistry and Molecular Biology, the American Association for the Advancement of Science, and the American Society for Nutrition, of which he is also a fellow. He has served as president of both the American Dairy Science Association and the Council for Agricultural Science and Technology.

Sigma Xi is a society for science and engineering, founded in the 19th century, which today has about 60,000 members in chapters around the world.

Gertrude Forte

By Courtney Chandler

Gertrude "Trudy" Forte, former editor-in-chief of the Journal of Lipid Research and leading lipoprotein researcher, died June 9. She was 84.

Forte was born Feb. 25, 1937, in Wayne, Pennsylvania. According to her obituary from the Berkeley Lab, she grew up in the countryside, which fostered her love of plants and animals. She attended Immaculata College in Chester County, Pennsylvania, and graduated magna cum laude with a Bachelor of Arts in biology. She received a National Science Foundation predoctoral fellowship award to pursue a Ph.D. in zoology at the University of Pennsylvania.

During graduate school, Forte met and married her husband, John, now deceased, and had two of their three children. In the 1960s, Forte and her family moved to California, and she began her postdoctoral training at the University of California, Berkeley. She had her third child shortly after.

Forte remained at Berkeley for nearly 30 years and was a senior scientist from 1978 to 2004. She then moved to the Children's Hospital Oakland Research Institute, where she worked from 2004 to 2017.

During her tenure at Berkeley, Forte researched the roles lipids and proteins play in cardiovascular disease. She helped develop electron microscopy techniques used to determine the structural features of lipoprotein particles and applied these techniques to study serum lipoproteins from human samples. She also used model systems to demonstrate how high-density lipoprotein, which shuttles cholesterol from the bloodstream to the liver, changes shape as it matures.

Gertrude Forte

After joining CHORI, Forte moved her research in a new direction to take a more applied approach. She developed and tested lipid nanoparticles to be used for drug delivery. One of her projects focused on synthesizing nanoscale particles of low-density lipoprotein to deliver anticancer drugs safely and effectively to tumors in a certain type of brain cancer.

Throughout her career, Forte was awarded more than 30 National Institutes of Health research grants and co-published over 230 research works.

Forte received numerous awards and honors in recognition of her research and professional accomplishments, including the Lawrence Berkeley Laboratory Outstanding Performance Award in 1992, the Associated Western Universities honor of distinguished lecturer in 1994 and the American Heart Association Special Recognition Award in 1999. She was also the first recipient of the annual American Heart Association Mentor of Women Award in 2001.

Forte was editor-in-chief of the Journal of Lipid Research from 1999 to 2003 and was the first woman to serve in this role. She also served as director of research for Lypro Biosciences, a therapeutic development company focusing on developing nanotechnology for better drug delivery, from 2008 to 2017.

Laura Knoff, a former senior research associate who worked with Forte from 1992 to 2000 at Berkeley, remembered her intelligence and mentorship.

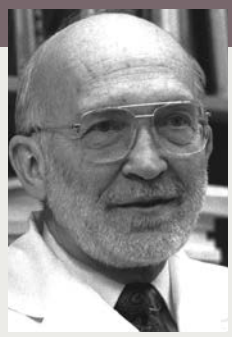
"(I was) in awe of her intellectual abilities and personal stamina," Knoff said. "I learned so much from her. She was truly a role model for women in science and will be sorely missed."

According to a family obituary, Forte was a music enthusiast. She played the piano and sang in the choir of the Saint Mary Magdalen Parish in Berkeley. She also enjoyed supporting local performing arts and attending live performances.

Forte is survived by her three children, their spouses and seven grandchildren.

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.

Jean Wilson



Jean Wilson, a renowned endocrinologist, died June 13.

Wilson was born on Aug. 26, 1932, in Wellington, Texas. After graduating from the University of Texas at Austin with a bachelor's degree in chemistry in 1951, he completed medical school and a residency in internal medicine at the University of Texas Southwestern Medical Center, conducted postdoctoral research for two years at the National Heart Institute under biochemist Sidney Udenfriend, then returned to UT Southwestern as a faculty member. There he continued his research for more than 60 years until retiring in 2011.

Wilson's research centered around male sex hormones called androgens. He discovered the enzyme 5-alpha-reductase, which converts testosterone into the hormone he identified as dihydrotestosterone. He demonstrated that dihydrotestosterone is critical for male sexual maturation and function in many animals.

Wilson also discovered that unchecked dihydrotestosterone production can cause a condition of prostate enlargement. His research contributed to development of the first treatments for prostate disease, a class of pharmaceuticals known as 5-alpha-reductase inhibitors. He also developed methods to quantify cholesterol in the body, contributing to our understanding of how cholesterol is made and degraded.

Wilson was elected to the National Academy of Sciences of the U.S. in 1983 and to the National Academy of Medicine in 1994. He received the Oppenheimer and Koch awards of the Endocrine Society, the Amory Prize of the American Academy of Arts and Sciences, and the Kober Medal of the Association of American Physicians.

Wilson's legacy has been memorialized at UT Southwestern. The Jean D. Wilson Center for Biomedical Research and the J.D. and Maggie E. Wilson distinguished chair in biomedical research were established to promote endocrinology, developmental biology and genetics research with support from Wilson and his sister, the late Margaret Sitton. The Jean D. Wilson, M.D. Award also was created to recognize excellence in research mentorship.

In addition to more than 340 scientific publications, Wilson authored an autobiography titled "The Memoir of a Fortunate Man"; he described growing up in the Texas panhandle, his scientific research and his many hobbies, including ice cream making, bird watching and a passion for opera.

— Courtney Chandler

William Whelan

William "Bill" Joseph Whelan, a renowned biochemist who embodied his own discovery (he was, by nature, a primer), died at his Miami home on June 5.

Whelan was born in Lancashire, England, on Nov. 14, 1924. His mother was a homemaker and his father, from Ireland, made skins for sausages.

Whelan was the first in his family to go to university; he earned three degrees at the University of Birmingham and was appointed as faculty while a graduate student. He then joined the University of North Wales, the University of London Lister Institute, and later the Royal Free Hospital.

Whelan moved to the then 15-year-old Miller School of Medicine at the University of Miami in 1967, remaining its chair of biochemistry until 1991 and retiring as one of its longest-serving faculty in 2019.

Whelan worked on important storage molecules in animals and plants, glycogen and starch, respectively. When your stomach is empty, you check the body's metaphorical cupboards, where you can thank glycogenin for putting aside a condensed form of glucose for just such a time.

But catalyzing requires raw materials. In the late 1980s, when funding was dry, his wife, Margaret, suggested he use a newly released pension from his U.K. faculty positions. Whelan expanded his lab and was elected a fellow of the Royal Society in 1992 in part due to a discovery of how to make use of glycogen stores — by glucosyltransferase reactions, in case you were wondering.

Glycogenin is known for drawing things together. Knowing the draw of Florida in winter, Whelan launched a winter conference attracting Nobel laureates, now enjoying its 53rd year. Glycogenin fast-tracks; it is a catalyst. Whelan started an acclaimed program in response to medical shortages, giving Ph.D. students — like glycogen itself — condensed coursework to complete an M.D. faster. And glycogenin is a self-starter; it self-phosphorylates. So, too, was Whelan. He started the journals Trends in Biomedical Science and Federation of European Biochemical Society Letters, and he remained an editor-in-chief of the journal IUBMB Life (and president of the International Union of Biochemistry and Molecular Biology) until 2020, stating he wanted biochemistry to be presented in "crystalline prose."

— Renae Crossing

Get involved with the ASBMB

We encourage all ASBMB members to engage in society activities — big or small. Use our advocacy toolkit to communicate with lawmakers. Start a student chapter at your school. Watch an on-demand webinar. Contribute to our diversity scholarship fund. Learn all the ways you can benefit and help at asbmb.org/membership/get-involved.

Nominations for the ASBMB Honor Society due Jan. 31

Student chapter members are eligible for election into the ASBMB Honor Society, ΧΩΛ. 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 ΧΩΛ

Brady, Coulson and Strahl join JBC in 2022

Donita Brady, Elizabeth Coulson and Brian Strahl will become associate editors for the Journal of Biological Chemistry in January. All three are current editorial board members.

BRADY

Brady is a faculty member at the Perelman School of Medicine at the University of Pennsylvania. She also serves as assistant dean for inclusion, diversity and equity in research. Her areas of specialty are cell signaling and protein kinases in cancer. In 2016, she was named a JBC Herbert Tabor Early Career Investigator Award winner. Also, in April, she will give a talk at the 2022 ASBMB Annual Meeting session on signaling titled "Tracing copper utilization by kinase signal transduction pathways: Implications for cancer cell processes."

COULSON

Coulson is a group leader at the Clem Jones Centre for Ageing Dementia Research and a professor at the Queensland Brain Institute. She also serves as deputy head of the school of biomedical sciences. Her lab studies the degeneration that occurs in cholinergic neurons in the brain and spinal cord. She has been a member of the ASBMB since 2013.

STRAHL

Strahl is a professor at the University of North Carolina School of Medicine, where he also serves as vice chair of the biochemistry and biophysics department. His areas of specialty are chromatin biology and histone modifications. He has been a member of the society since 2005. He won the ASBMB Young Investigator Award in 2006.

Advocating for open science and security in the American research enterprise

In early October, the U.S. House Committee on Science, Space and Technology held an important hearing on balancing open science and research security within the U.S. The ASBMB public affairs staff submitted testimony on this issue urging members of Congress to pass legislation harmonizing disclosure requirements, defining procedures for handling allegations of research misconduct violation and providing the scientific community with evidence-based reports on research integrity violations. Read the testimony at asbmb.org/advocacy/position-statements.

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.

ASBMB welcomes new undergraduate education coordinator

In October, the ASBMB welcomed Tejiri Olafimihan as its new undergraduate education coordinator. In this role, she will support the society's student chapters, undergraduate poster competition at the annual meeting, degree-accreditation program and certification exam.

"I have been an educator for the past five years, and stepping into this role from the classroom as a STEM educator, I'm excited to continue to champion diversity in the scientific community as well as provide students with different resources and opportunities that will empower them to contribute to the next generation of great scientists," Olafimihan said. "I look forward to helping bring about incredible change in the field of life sciences."

ASBMB public affairs 2021: The year in review

By Sarina Neote

From advocating for sustainable science funding to supporting junior scientists, the American Society for Biochemistry and Molecular Biology public affairs team put together this roundup of our policy accomplishments in 2021. Here are the highlights.

Supporting early-career scientists and the research enterprise

The ASBMB took the lead on a bipartisan "dear colleague" letter (a document used by members of Congress to encourage their colleagues to support specific issues) in the House of Representatives advocating for targeted relief for junior scientists affected by the pandemic. Reps. Jamie Raskin, D-Md.; Bill Foster, D-Ill.; and David McKinley, R-W.Va., sent the letter to the House leadership in late May.

In addition to this effort, the ASBMB public affairs staff worked with the society's Public Affairs Advisory Committee to advocate for the passage of the Research Investment to Spark the Economy Act, which, if passed, would provide support for research disrupted by the COVID-19 pandemic.

Supporting international collaboration

The ASBMB public affairs staff wrote and submitted comments to U.S. Customs and Immigration Services outlining significant barriers, such as visa processing delays, that international students and scholars face when trying to study or work in the U.S.

The society also submitted formal testimony for a congressional roundtable, "Researching While Chinese American: Ethnic Profiling, Chinese American Scientists and a New American Brain Drain." In its testimony, the ASBMB emphasized that recent efforts by the Department of Justice targeting Chinese and Chinese American scientists and those who collaborate with Chinese institutions have had a chilling effect on international scientific collaboration, undercutting the U.S.'s role as the global leader in science and technology.

Improving scientific integrity policies

President Joe Biden's administration has focused on restoring trust in science in the federal government and strengthening integrity policies at the science agencies as outlined in his January presidential memo. Per his request, in June, the White House Office of Science and Technology Policy published a notice of request of information to improve the effectiveness of federal scientific integrity policies to enhance public trust in science. The ASBMB submitted formal comments recommending the OSTP strengthen whistleblower protections, refine conflict-of-interest policies, encourage preprints and media engagement, and study and remedy

The end of an era at the NIH

The longtime director of the National Institutes of Health, Francis Collins, announced in the fall that he plans to step down as director and return to running his lab, which focuses on cystic fibrosis. Collins, a physician–scientist, has run the agency for 12 years, serving under three presidents. Before that, he was the director of the National Human Genome Research Institute for 15 years, presiding over the completion of the Human Genome Project.

NATIONAL INSTITUTES OF HEALTH

Francis S. Collins has served as the director of the National Institutes of Health since August 2009.

Collins' signature projects as NIH director have included efforts to address structural racism and sexual harassment, rolling out data-sharing policies, and leadership through the first two years of the COVID-19 pandemic. In a statement, the ASBMB wrote, "Francis Collins has served admirably through some of the most challenging times in the NIH's history. ... a steadfast leader showing grace, tenacity and — on a lighter note — a skill with a guitar unmatched by any other agency leader."

funding inequities.

Shortly after it published this RFI, the OSTP also began creating implementation guidance for federal agencies on clear rules for research security and researcher responsibility. The ASBMB strongly encouraged the OSTP to recommend that federal agencies harmonize conflict-of-interest and conflict-of-commitment disclosure requirements, be transparent about investigative processes on violations of research integrity, and ensure that the Department of Justice's China Initiative does not fuel racial profiling of Chinese, Chinese American, Asian and Asian American scientists.

Commenting on the proposal for ARPA-H

President Biden called for the creation of the Advanced Research Projects Agency for Health, or ARPA-H, dedicated to researching human diseases and focusing on innovative research to address the nation's greatest health challenges. Reps. Diana DeGette, D-Colo., and Fred Upton, R-Mich., released the discussion draft of the bill establishing this new agency and requested feedback from the scientific community. The ASBMB advocated for keeping ARPA-H autonomous and separate from other federal funding agencies and advocated for ARPA-H to create an inclusive research ecosystem that attracts a diverse talent pool.

Sarina Neote (sneote@asbmb.org) is the science policy manager for the ASBMB advocating for diversity in STEM, sustainable funding for scientific research and the STEM workforce.

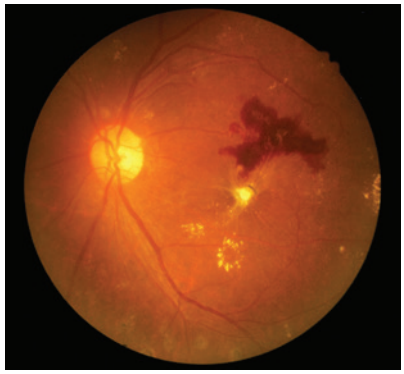
‘Fatty retina’: A root cause of vision loss in diabetes?

By Clay F. Semenkovich & Rithwick Rajagopal

Vision loss in diabetes, one of the most feared complications of this disease, is caused by a progressive pathogenic process known as diabetic retinopathy, or DR. Elevated blood glucose is the predominant risk factor for DR, so many people believe that glucose toxicity is the major contributor to the development of this disease. Yet, to date, no pharmaceuticals specifically targeting glucose-dependent pathways exist for DR.

Diabetes is a disease of broadly disordered metabolism that affects how cells handle lipids, amino acids and signaling networks that regulate growth and proliferation — in addition to its impact on glucose. Accordingly, abnormalities of lipid metabolism are common in diabetes. For example, patients with diabetes often suffer from nonalcoholic fatty liver disease, which is characterized by chronic positive energy balance causing increased lipid synthesis and elevated levels of hepatic triglycerides. Thus, we reasoned that the retina might switch its lipid metabolic programming in response to an abundance of fuel in diabetes.

To test this possibility, our group studied the pathways that govern retinal lipid biogenesis (the process of synthesizing fatty acids from small precursors) during experimental diabetes in mice. In multiple models of diabetes, we observed a roughly 70% increase over controls in the synthesis of retinal palmitate — a ubiquitous saturated fatty acid that forms a basic building block for many lipids. This shift in lipid production was likely due to elevated glucose alone, as isolated retinal tissue exposed to high glucose showed the same increase in palmitate production.



Diabetic retinopathy, shown here, causes vision loss in patients with diabetes.

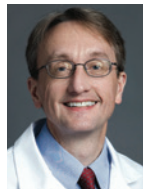
Mechanistically, high glucose levels increased enzymatic activity of two regulatory enzymes: acetyl Co-A carboxylase and fatty acid synthase, or FAS. Mice with partial FAS loss-of-function in rod photoreceptors — the predominant cell type of the retina — were spared from vision loss due to diabetes even though they developed severe systemic metabolic disease on par with control mice. Conversely, mice with FAS gain-of-function developed vision loss in half the time as wild-type mice after induction of diabetes. Taken together, our results implicate increased retinal FAS activity and elevated palmitate as root causes of vision loss in diabetes.

The mechanisms for palmitate toxicity in the retina remain elusive. Unlike in the liver, the diabetic retina does not develop intracellular lipid droplets and does not possess any significant triglyceride stores. Moreover, in comprehensive surveys of membrane lipids in the retina, we found only modest disease-associated changes. Instead, palmitate could elicit pathological signaling either through lipid second messengers or via lipidation of protein messengers. Our group is investigating these possibilities actively.

Our results shed some light on a puzzling feature of human DR: Though glucose is the major risk factor for vision loss in diabetes, it explains only a fraction of the variability in disease progression. Differences among individuals in terms of their retinal lipid biosynthetic flux could account for some of the variance in glucose response.

Future pharmacotherapy to finely tune retinal lipid biogenesis in DR could offer a novel approach to the treatment of an increasingly common cause of visual disability.

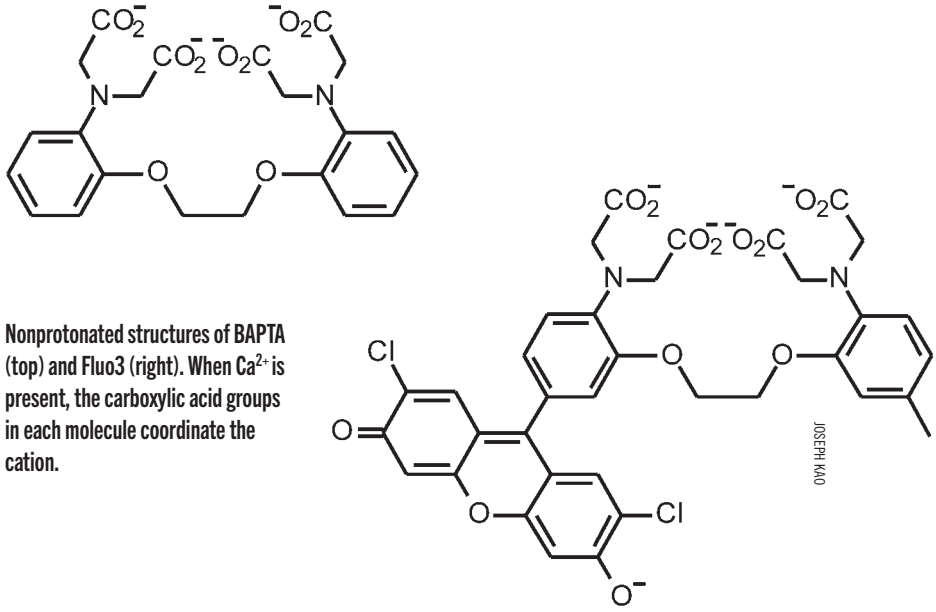
Clay F. Semenkovich (csemenko@wustl.edu) is a professor and division chief of endocrinology at Washington University in St. Louis. He studies lipid metabolism in diabetes, obesity and related disorders.



Rithwick Rajagopal (rajagopalr@wustl.edu) is an assistant professor of ophthalmology at Washington University in St. Louis. His research focuses on abnormalities of neural metabolism as contributors to vision loss in diabetes.

Democratizing calcium visualization

by Laurel Oldach



Nonprotonated structures of BAPTA (top) and Fluo3 (right). When Ca^{2+} is present, the carboxylic acid groups in each molecule coordinate the cation.

At a time when cloning a gene was a feat worthy of a high-impact publication, someone asked Roger Tsien why he studied calcium.

"His somewhat flippant answer was, 'Because it cannot be cloned,'" recalled Joseph Kao, who was a postdoc in Tsien's lab and is now a professor at the University of Maryland. "Early on, he was actually somewhat dismissive of molecular biology."

Tsien, who died in 2016, is best remembered for his contributions to developing a molecular biology icon: green fluorescent protein. His group's work helped transform the protein from a coelenterine curiosity to a laboratory staple and earned Tsien a third of the 2008 Nobel Prize in chemistry. Prior to launching that project in the 1990s, Tsien already had revolutionized the field of calcium sensing.

In the 1970s, Kao said, measuring calcium was "a very rarefied, arcane art" that depended on a deep knowledge of electrophysiology. Today, researchers can use a variety of fluorescent indicators to visualize the activity of calcium and other second messengers in living cells. Many modern indicators derive from a series of probes that Tsien's lab developed.

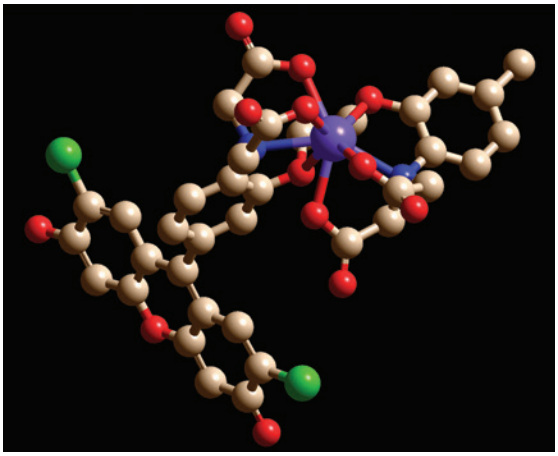
In one **Journal of Biological Chemistry** Classic article on such probes, "Ca^{2+} indicators based on fluoresceins and rhodamines," Akwasi Minta, Kao and Tsien introduced several fluorescent indicators of Ca^{2+} concentration that could be used in cells.

Tsien began to pursue an interest in calcium signaling early in his scientific career. The ion already was known as an important signal carrier central to muscle contraction, synaptic transmission and many other physiological functions.

"Calcium was central to everything — but it was very difficult to measure," Kao said. Tsien considered electrophysiology as an undergraduate, but by the time he started his graduate research at Cambridge, he was focused on chemical approaches.

The first Ca^{2+} chelator Tsien developed, 2-bis(o-aminophenoxy) ethane-N,N,N′,N′-tetraacetic acid, or BAPTA, remains widely used because of its rapid binding kinetics, high selectivity for calcium and insensitivity to pH changes in the physiological range. BAPTA binds calcium through four carboxylate groups.

At the University of California, Berkeley, Tsien led a lab that developed the calcium probes fura-2 and indo-1, which are elaborations of the BAPTA architecture. Both of these molecules are intrinsically fluorescent, but upon binding Ca^{2+}, the shapes of their fluorescence spectra change. The ratio of the fluorescence intensities at two different wavelengths can be calibrated into actual Ca^{2+} concentration. Because such ratiometric measurements are insensitive to the concentration of indicator in the sample, some common experimental artifacts are minimized. Still, Tsien was disappointed that they required long-wavelength ultraviolet excitation, which potentially can harm cells and excite autofluorescence. Tsien was initially reluctant to publish on the new indicators, Kao said, but ultimately yielded to persuasion by postdoc



JOSEPH KAO

Three-dimensional model of Fluo3 binding a Ca^{2+} ion (purple). The structure shows the participation of the two nitrogens (blue) and six oxygens (red) that bind to Ca^{2+}, causing the ion to be enveloped by the chelator.

Martin Poenie.

Tsien was intent on developing a fluorescent Ca^{2+} indicator with excitation in the visible range. Perhaps it could be done by combining BAPTA with the visible fluorescence of already available fluorophores? He recruited postdocs Minta, a chemist, and Kao, a biophysicist, to work on the project.

First, the molecules had to be synthesized. An early synthetic strategy involved a long pressurized incubation in an aluminum instrument that resembled an old-fashioned coffee urn. Kao recalled a time when the chemists left a reaction to run over the weekend, hoping to improve its yield.

"When we came back … there was an imprint where the lid handle had smashed into the ceiling. Somewhere else, we found the lid completely flattened." The reaction also had shattered an internal glass ampule, leaving glass dust all over the lab.

"Subsequently, they found better ways to do that reaction," Kao said.

Even after the molecules were synthesized, the work was not complete. "Roger was a perfectionist," Minta said. "If I did a dye and it had certain imperfections, he made me start all over again."

Some molecules he generated failed to fluoresce or were protonated at near-physiological pH. Minta tweaked and adapted, adding and modifying functional groups until he had two chimeric molecules, derived from the fluorophores rhodamine and fluorescein, that were weakly fluorescent on their own but lit up dramatically when Ca^{2+} bound. The lab dubbed the probes fluo-3 and rhod-2.

Ordinarily, when a molecule absorbs light, the energy is dispersed quickly as molecular motion, or heat. Fluorescence — the release of captured light energy as a photon — requires special circumstances.

"When a molecule absorbs light, an electron is promoted from a lower-energy level into a higher-energy level, leaving a vacancy in the lower level," Kao said. Emission of a photon depends on the excited electron returning to its normal lower-energy state. If an electron elsewhere in the molecule is free to slip into that lower orbital, he said, the excited electron's energy ultimately is lost as heat instead of being emitted as light, a phenomenon known as fluorescence quenching.

In the chimeric molecules, the fluorophore can be quenched by electrons in lone pairs on the BAPTA moiety. But when a positively charged Ca^{2+} ion is present, it forms bonds with those electrons, lowering their energy and making it energetically unfavorable for them to fill the vacancy left by the excited electron. Without competition for the vacated orbital, the excited electron can relax back into it, emitting a photon.

"Calcium allows it to fluoresce beautifully," Minta said. In a test tube, fluo-3's brightness increased by 40- to 100-fold when calcium was added.

In a second paper in the same issue of JBC, Kao and several colleagues tested the probes for live-cell imaging. They found that cells took up the indicators through incubation with the corresponding acetoxymethyl esters and confirmed a dazzling increase in fluorescence when they applied Ca^{2+}-mobilizing agonists.

Fluo-3 quickly was adopted for many uses. By 1995, researchers had reported watching waves of Ca^{2+} activity pass through connected networks of neurons in mouse brain slices, observing cell-cycle initiation in fertilized egg cells, and detecting "Ca^{2+} sparks" — microscopic, elementary Ca^{2+} signals generated by the coordinated opening of small clusters of Ca^{2+}-release channels — on the sarcoplasmic reticulum in heart cells. Kao said the new technologies "made calcium measurement accessible to essentially anyone with a microscope."

Tsien was disappointed, however, that the new probes changed only in intensity, not in excitation or emission wavelength, upon Ca^{2+} binding; he had hoped to be able to do ratiometric imaging.

"Roger was almost always dissatisfied with any product that you made," Kao said. "He had a perfect conception of how they should behave, and then they would fall short on one or another aspect, and he'd be a little rueful: 'If only we had discovered how to do this.'"

Tsien finally got his visible ratiometric Ca^{2+} sensor about 10 years later. It was based on GFP and the calcium-binding protein calmodulin; though calcium could not be cloned, cloning turned out to be useful in its study after all.

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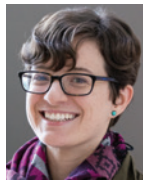

Salivary proteins may hold key to targeting tick-borne diseases

By Nivedita Uday Hegdekar

When Ingrid Dijkgraaf's research group was searching for molecules that could inhibit chemokines, a group of small signaling proteins involved in the development of atherosclerosis, they stumbled upon an unusual source: tick saliva.

As blood-sucking parasites, ticks transmit more than a dozen serious diseases, including Lyme disease, typhus and tick-borne meningoencephalitis, to both animals and humans. They also produce proteins in their saliva that help them avoid being spotted by the host's immune system.

Several years ago, Dijkgraaf's group, including then–graduate student Stephen Denisov, found that evasins, a family of those proteins that help ticks skirt detection, also could neutralize chemokines involved in atherosclerosis.

"Tick saliva contains chemokine-binding compounds," said Dijkgraaf, an associate professor at the University of Maastricht. "Millions of years of evolution have already developed, probably, the most ideal compound to target atherosclerosis. This shows how nature could help researchers unravel molecular mechanisms. They can be the starting point for development of therapeutics and chemical agents."

Dijkgraaf began investigating other proteins in the saliva of ticks. Several years ago, one of her collaborators, Ben Mans, a professor at the University of Pretoria, South Africa, isolated BaSO4-adsorbing protein 1, or BSAP1, from tick saliva and described its anticoagulant activities. However, its structure was yet undetermined, and Dijkgraaf saw this as an excellent research opportunity.

Denisov, by then a postdoctoral fellow in Dijkgraaf's lab, had extensive experience in structural biology and undertook the project.

"After Dr. Mans gave us the sequence, we were able to synthesize this protein chemically," Denisov said. "Once we elucidated the structure, we carried out additional studies to characterize its activity."

Denisov discovered that parts of the BSAP1 protein were similar to others, such as tick salivary lectin complement pathway inhibitor, or TSLPI, Salp14. He carried out assays to distinguish TSLPI Salp14 and BSAP1on a functional level and found that the BSAP1 and TSLP1 proteins both inhibit the lectin complement pathway and thus prevent the host's immune system from recognizing an invasive tick bite. However, the Salp14 protein has a double function — it is an inhibitor of both the lectin complement pathway and the host coagulation cascade, which means it also prevents clotting of the host's blood at the site of the bite.

Denisov's data collectively support a mechanism by which tick saliva proteins can evade the host immune system. The findings recently were published as a research paper in the **Journal of Biological Chemistry**.

For next steps, Dijkgraaf wants to study the precise molecular mechanism by which the salivary proteins inhibit the host immune system and potentially use these proteins for development of anti-tick vaccines.

SCOTT BAUER, U.S. DEPARTMENT OF AGRICULTURE

Ixodes scapularis, commonly known as the deer tick or black-legged tick, is a vector for Lyme and other diseases.

Her collaborator Joppe W. Hovius, an infectious disease specialist at the University of Amsterdam, is an expert on the TSLPI protein.

"His work has shown that the TSLPI protein helps Borrelia bacterium to move from the ticks to the host and cause Lyme disease," Dijkgraaf said. "Hence, if we could inhibit this protein by antibodies or some medication, then maybe we can also inhibit the transmission of the Borrelia bacterium from tick and host."

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A new way of looking at HDL in pregnancy

By Jessica Desamero

For a fetus to develop, many changes must occur in the pregnant person's body. Lipoproteins have been well studied in pregnancy, but the changes in molecules that make up high-density lipoprotein, or HDL, tend to be overlooked. In a recent study published in the **Journal of Lipid Research**, however, researchers at the University of Cincinnati College of Medicine show how HDL metabolism changes to support fetal development.

Laura Woollett, John Melchior and their team started with a shift from looking at the fetus to studying lipoproteins in the mother. They thought HDL also might play a role in pregnancy. Many things that can go wrong, such as early birth and preeclampsia, a serious blood pressure condition, have an element of increased inflammation. Among its diverse functions, HDL is antioxidative and anti-inflammatory, so the team aims to identify women who have these adverse effects due to abnormal HDL.

"There are no biomarkers … and there are no treatments," Woollett said, "so this is a very novel way that we could help identify who might be at risk early on and why."

HDL particles are composed of lipids and proteins that act differently but look similar. Melchior compares viewing them to looking at a highway from an airplane. "You can see all these different cars and trucks on the road, and we know they have different functions," he said. "But from that altitude they all look the same, so we use some fancy techniques to zoom in on these particles and get a better idea of which ones are traveling through the system."

The team compared changes in lipoprotein subspecies in plasma collected from nonpregnant women and women in their second trimester. Using nuclear magnetic resonance spectroscopy, or NMR, they found that HDL particles were notably larger in pregnant women. Given that HDL is the most compositionally diverse of the lipoproteins, they went on to isolate the different HDLs using high-resolution gel filtration chromatography. Analyzing the phospholipid distribution in fractions of separated plasma, they found a considerable increase in large-sized HDL in pregnant women similar to that found using NMR. The researchers then used liquid chromatography–mass spectrometry to identify and analyze 87 HDL-associated proteins in the gel filtration fractions. Visualization of these data via a heat map showed remarkable changes in the abundance of several protein clusters in pregnant women compared with nonpregnant women.

These results show the impact of pregnancy on the size and protein composition of HDL particles and their distinct subspecies. Compositional alteration likely affects HDL function in multiple metabolic pathways. Woollett said, "The HDL, we think, is having an impact on various immune cells that are mediating inflammation as well as cells of the placenta or the maternal fetal interface, meaning that HDL could be affecting a lot of different cell types involved in the maintenance of pregnancy."

The researchers think the proteins that tell HDL particles to perform their functions could serve as biomarkers. "For instance," Melchior said, "if you see a really concerning rise or fall in a specific subspecies of HDL that we've defined, … that's a great molecular marker for being able to trigger a more comprehensive examination of what's going on. We can develop an assay to rapidly measure that and quickly determine if the mother is at risk for early labor and/or preeclampsia."

DOI: 10.1016/j.jlr.2021.100107

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What's growing in your mouth might change with your health

A tech-enabled deep dive into dental plaques

By Ken Hallenbeck

The small molecules, sugars and proteins produced by the microorganisms living in your mouth provide information about your health — and not just your oral health.

An interdisciplinary team of researchers at the University of Wisconsin–Madison, the Morgridge Institute for Research, and the Marshfield Clinic Research Institute report that the dental plaques of diabetic patients are measurably different from those of healthy volunteers.

Using state-of-the-art sample processing techniques, Katherine Overmyer and colleagues performed in-depth multiomics analysis on samples from Marshfield Clinic dental patients. The results confirm several trends previously reported in the oral microbiome field but also break new ground.

The goal was to understand "how you can use the mouth and things in the mouth to look at systemic disease," Overmyer said. To that end, they collaborated with Marshfield Clinic researchers to collect samples from patients with periodontal disease, patients with diabetes and patients that had both conditions.

"Part of the work was to look for significantly changing microbes, or microbial proteins associated with periodontal disease and diabetes," she said. "And we found some that were consistent with what is in the literature."

The multiomics analyses — 16S rDNA sequencing, metabolomics, lipidomics and proteomics — provided the researchers with unparalleled insight into tiny clinical samples.

Overmyer said that expert sample analysis is key to success: "You get a tiny little spec of a (sample) — how can you get the most out of that?"

The study, published in the journal **Molecular & Cellular Proteomics**, represents the first application of multipronged analytical methods to the oral microbiome.

Joshua Coon, one of the study's corresponding authors, noted that the applications for multiomics analysis are already exciting, but work toward wider adoption is important.

"Moving forward, we are working on technology that would allow us to have one mass spectrometer, one chromatography setup, and out would come all three compound classes in one data set," Coon said. "That is going to be key in making a multiomic setup more accessible. You won't have to have three mass spectrometers to be able to look at these things."

And once every lab can collect multiomics data? The next horizon is clinical or at-home devices.

"We don't live in a world right now where these technologies are available" outside the lab, Coon said, "but the take-home is that we can tell a lot about someone by looking at something like a (dental) plaque." Collecting molecular data during daily rituals such as tooth-brushing could provide early warning of oral and even systemic disease.

While the at-home use of mass spectrometry and other such analytical techniques is likely decades away, enabling other research labs to perform such detailed analysis is the first step toward that future. Overmyer is on the task. "We are working to make (multiomics) data more accessible," she said, "so if you have a mass spectrometer you can collect those data."

DOI: 10.1016/j.mcpro.2021.100126

Ken Hallenbeck (khallenbeck@reimaginescience.org) earned a Ph.D. in pharmaceutical sciences from the University of California, San Francisco, and now is an early drug discovery researcher. Follow him on Twitter: @kenkhallenbeck.

From the journals

By Isabel Casas, Anna Hu & Shravanti Suresh

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

Making pain meds with microbes

The pain medicines codeine and morphine are closely related benzylisoquinoline alkaloids, or BIAs, derived from opium poppy. Microbial biosynthesis systems to produce these medicines are an area of active research, given that agricultural methods are affected by climate, supply chain and geopolitical instability. But this emerging synthetic biology strategy requires having a detailed understanding of the biosynthetic pathway in the plant.

Codeinone reductase, or COR, catalyzes the last step of the biosynthetic pathway, but the determinants that mediate substrate recognition and catalysis are not well defined.

Samuel C. Carr and colleagues at the University of Calgary in Canada recently reported the crystal structure of apo-COR in the **Journal of Biological Chemistry**.

They performed structural comparisons to closely related plant aldo-keto reductases, or AKRs, and distantly related homologs, revealing a novel conformation in one of the loops adjacent to the BIA binding pocket. The authors used site-directed mutagenesis and identified specific substitutions in COR that led to changes on AKR activity for both substrates, codeinone and neopinone.

The authors wrote: "The deeper understanding of structure–function relationships in COR should lead to further improvements in the performance of microbial BIA biosynthesis systems. … Although still not commercially viable, microbial biosynthesis systems are quickly gaining ground on the traditional agricultural methods of obtaining these medicines and will one day lead to a pharmaceutical production process (that) is more environmentally friendly, globally equitable and easier to secure from illicit diversion." *DOI: 10.1016/j.jbc.2021.101211*

Leptin landmarks and obesity genetics

Since the discovery of leptin, a hormone that regulates appetite, fat storage and glucose levels, researchers have studied its associated Lepr gene to learn about the varied mechanisms behind obesity. Lepr encodes for a leptin receptor protein and mutations such as the $Lepr^{db/db}$, a diabetes mutation that models obesity. Claudia Berger and an international team recently published a paper in the **Journal of Lipid Research** describing a novel Lepr mutation that led to even more extreme body weight and impaired glucose metabolism outcomes than the established db/db model.

Through genetic crossing of specific mouse breeds and quantitative trait locus analyses, the researchers identified a spontaneous base pair deletion that results in premature protein truncation. They called this mutation $Lepr^{L536Hfs*6}$ and found that the affected mice were more obese than db/db mice, had worse glucose metabolism and experienced higher cholesterol levels. The model also can be used to study fatty liver disease and other metabolic conditions.

To study effects of a heterozygous Lepr mutation, the collaborators crossed their mouse strains ($Lepr^{L536Hfs*6/wt}$ and $Lepr^{db/wt}$) for $Lepr^{L536Hfs*6/db}$ mice. Heterozygosity led to a higher level of obesity and impaired glucose metabolism than expected given the parental models, although the researchers need to do more studies to explain the mechanisms behind this result. Altogether, this research could be used to analyze obesity risk factors in humans. *DOI: 10.1016/j.jlr.2021.100105*

IMProv brings structural databases together

A popular technique used to validate direct interactions in protein complexes is cross-linking mass spectrometry, or XL-MS, which typically will detect linked residues while integrating these networks with structural techniques to generate accurate models of high-level molecular processes. XL-MS can overcome ambiguity in modest-resolution cryo-EM density maps and add more information to extrapolate X-ray maps into more accurate models.

In a recent paper in the journal **Molecular & Cellular Proteomics**, Daniel S. Ziemianowicz and colleagues at the University of Califor-

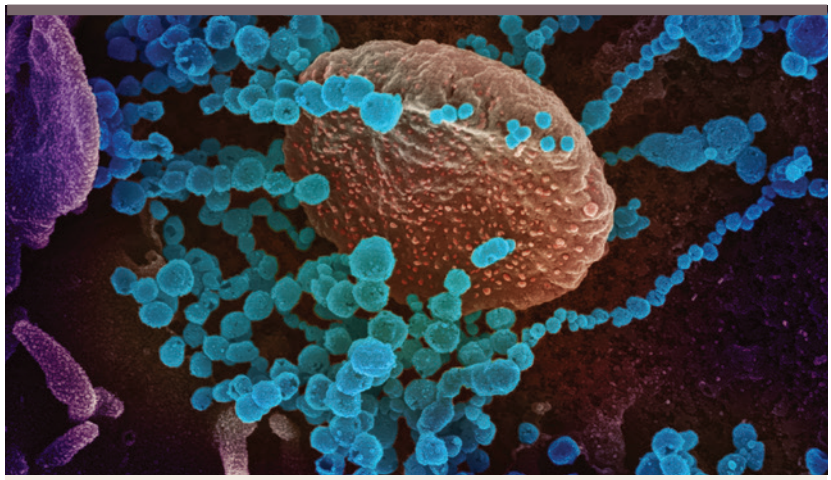
nia, San Francisco, and the University of Calgary, Canada, describe a new tool known as IMProv that can integrate cryo-EM densities, existing structures and cross-linking data. This addresses the effect of underlying protein dynamics on cross-linking. To use this resource, a user provides the sequence information for each protein building block and available partial or homologous structures. IMProv generates models using four steps: building a Python modeling interface, creating corresponding directories, using a SLURM bash script to model on a high-performance cluster and combining all of the above to generate the final model.

The authors show how IMProv could fill some gaps in the current model of the polycomb repressive complex 2. Overall, this resource will serve as an effective tool to develop existing data repositories and enable the use of cross-linking data to interpret and model structural data with greater precision.
DOI: 10.1016/j.mcpro.2021.100139

Sex-specific differences in glucose homeostasis

Metabolic syndrome is a cluster of conditions that increase the risk of heart disease, stroke and diabetes. It is well established that sex as a physiologic factor is associated strongly with metabolic syndrome.

Hv1 is a voltage-gated proton channel involved in insulin secretion. Huimin Pang and colleagues at Nankai University in China previously showed that male mice with Hv1 knocked out end up with hyperglycemia and insulin intolerance. But they wanted to know if this was also true for female knockout mice and, if so or if not, what role sex



NIAID-RML

This scanning electron microscope image shows SARS-CoV-2 (round blue objects) emerging from the surface of cells cultured in the lab. SARS-CoV-2 is the virus that causes COVID-19.

A global proteomics approach to COVID-19 and host signaling pathways

COVID-19 has taken over the world as the largest global pandemic of our time. While the inflammatory implications of SARS-CoV-2 have been well studied, researchers do not yet understand the effect of the virus on signaling pathways. This is crucial, since COVID-19 manifests in severities ranging from asymptomatic infection to multiorgan failure. Immune response to a viral antigen is wide-ranging, from an interferon-mediated antiviral response to downstream events that activate transcription factors. This eventually leads to an inhibition of replication, transcription and translation of the viral genome, followed by its degradation and recruitment of immune cells.

In a recent study in the journal **Molecular & Cellular Proteomics**, Patrick M.Vanderboom and colleagues at the Mayo Clinic compared SARS-CoV-2 negative and positive patient samples to analyze molecular features of the host response. A global proteomics approach was used to characterize the influence of this infection, and samples were obtained from the nasopharynx due to the proximity to the lungs, where this COVID-19 most often progresses to severity.

When they subjected these samples to mass spectrometry, the researchers found 7,582 proteins, of which 143 were upregulated and 80 were downregulated in patients who had COVID-19. The upregulated proteins were involved mostly in interferon signaling. In particular, the authors monitored two specific molecules, RIG-1 and STAT1, involved in interferon signaling and found that the levels of these proteins correlate with viral loads.

The authors said that while these studies provide definitive information about the signaling pathways that are affected by SARS-CoV-2 infections, they will need to do more research to understand completely the pathogenesis of the virus and its potential outcomes in individual patients.
DOI: 10.1016/j.mcpro.2021.100134

— Shravanti Suresh

New lipid markers of liver disease

Nonalcoholic fatty liver disease, or NAFLD, also known as hepatic steatosis, affects up to 30% of adults worldwide and, left untreated, can lead to cirrhosis or liver cancer. Despite its prevalence, researchers do not yet understand the mechanisms behind its progression. As the name suggests, in this form of liver disease, fat accumulates in the liver without any associated alcohol intake. NAFLD itself can be separated into two subcategories: nonalcoholic fatty liver, or NAFL, characterized by fat accumulation without inflammation, and the more severe nonalcoholic steatohepatitis, or NASH. NAFL can develop into NASH, resulting in inflammation and fibrosis of the liver.

Olga Vvedenskaya, Tim Daniel Rose and a team of researchers from Austria and Germany investigated several hundred lipids to find markers of the NAFL-to-NASH progression and published their results in the **Journal of Lipid Research**.

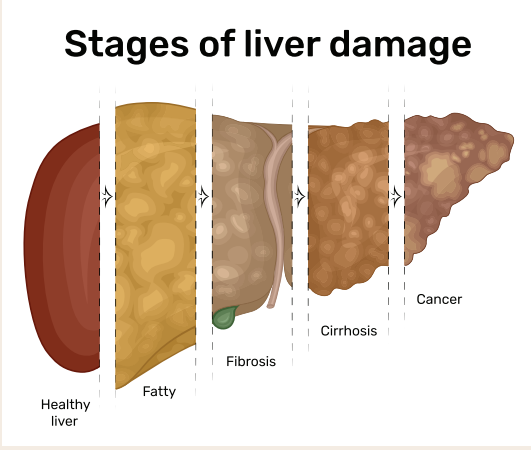
The scientists analyzed histology data from 365 Caucasian patients, drawing out 316 lipids from 22 major classes of membrane and energy storage lipids. Based on liver fat content and inflammation, the patient profiles were divided into four main groups: normal control, healthy obese, NAFL and NASH.

The researchers performed bicluster analysis on these 316 lipid species using molar quantities of lipid types in each of the four patient groups measured with high-resolution mass spectrometry. This showed that the quantity of neutral lipids steadily increased from normal to NAFL and NASH patients, while most membrane lipids remained almost unchanged. Additionally, they found two sphingomyelins that were tied closely to disease progression and might distinguish patient groups with only slightly less specificity than when considering all the lipids together.

Finally, the team created an open library of liver lipids and identified several that indicate early and late-stage NAFL, potentially aiding in the early identification, understanding of pathogenesis mechanisms, and prevention of this disease.

DOI: 10.1016/j.jlr.2021.100104

— Anna Hu



The stages of liver damage from a healthy liver to cancerous. Left untreated, nonalcoholic fatty liver disease can progress from a fatty liver to one of these health outcomes.

steroids play in the results.

The team recently reported in the **Journal of Biological Chemistry** that, in fact, fasting blood glucose levels in females were lower than those for males despite decreased insulin secretion in both sexes. In addition, they found that knockout mice of both sexes had increased expression of gluconeogenesis-related genes in liver compared with wild-type mice.

This sex-related difference in glucose homeostasis is associated with the glucose metabolism in liver tissue, the authors say, likely due to the physiological levels of testosterone in knockout male mice.

DOI: 10.1016/j.jbc.2021.101212

Fatty acid versatility extends to Type 2 diabetes

Fatty acids, a lipid type found throughout our cells, may be more versatile than previously thought. Pratik Aryal of Beth Israel Deaconess Medical Center and Harvard Medical School and a team of researchers investigated a score of lipids that fall

under the umbrella of fatty acid esters of hydroxy fatty acids, or FAHFAs. Publishing their findings in the **Journal of Lipid Research**, the team showed that FAHFAs' biological properties are important for Type 2 diabetes.

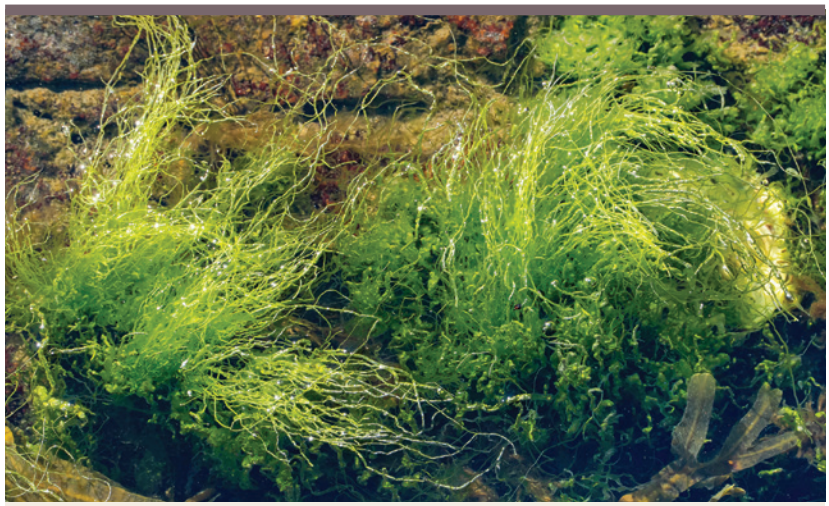
Some FAHFAs are known to have anti-diabetic and anti-inflammatory effects, making them a clinically relevant subject of study. But with several hundred variations (isomers) of these lipids across multiple FAHFA families, plenty have not been tested yet.

The researchers found that, in addition to several known anti-diabetic isomers, some others increased insulin secretion in a pancreatic cell line. Robust insulin secretion is critical for normal blood sugar control. Several FAHFAs also increased insulin-stimulated glucose uptake in adipocytes (fat-storage cells) – that is, these FAHFAs improved insulin sensitivity. Reduced sensitivity, or insulin resistance, increases Type 2 diabetes risk and risk for cardiovascular disease, Alzheimer's disease and cancer. This work could lead to use of FAHFAs as treatment for metabolic diseases such as Type 2 diabetes.

DOI: 10.1016/j.jlr.2021.100108

Automating and optimizing protein–protein studies

When protein interactions occur in intrinsically disordered regions, it's often through short linear motifs, known as SLiMs, which are both tedious and challenging to study. Researchers must incubate individual peptide spots with the protein extract on a cellulose membrane and then retrieve them for further analysis. This time-consuming procedure limits the number of samples that can be analyzed at a time.



W. CARTER/WIKIMEDIA COMMONS

Gutweed is just one of many types of green algae. Sea animals, including manatees, and humans have incorporated so-called sea lettuce into their diets.

Breaking down seaweed: An alternative enzyme cascade

Marine algae are responsible for half of the global photosynthetic carbohydrate production. The Ulva species — commonly known as sea lettuce — grow quickly and produce large amounts of carbohydrate-rich biomass, making them an emerging renewable energy and carbon resource.

To exploit this potential energy source, researchers must better understand the metabolic processes leading to the seaweed's degradation by microbes in nature. That's what motivated Marcus Bäumgen, Theresa Dutschei and colleagues at Germany's University Greifswald to undertake a recent study published in the **Journal of Biological Chemistry**.

A few years ago, the same team reported a complex enzymatic cascade that enables a marine flavobacterium to degrade the algal polysaccharide ulvan. In the new JBC paper, the Greifswald team reported their discovery of a separate degradation pathway for ulvan oligosaccharides in that same marine bacterium, Formosa agariphila. The authors found a new dehydratase — P29_PDnc — acting on the nonreducing end of ulvan oligosaccharides.

"This elucidation of an alternative degradation pathway illustrates the complexity of the biological systems for marine ulvan degradation," the authors wrote. "It indicates the necessity of backup mechanisms for metabolic processes in order to get access and compete for the diversity of complex marine carbon sources in nature."

The team's research shows that this dehydratase is involved in degrading carboxylated polysaccharides into monosaccharides, providing further insights into the molecular mechanisms of the ocean's carbon cycle.

"The characterizations of ulvan-active enzymes and the clarification of their substrate scopes allow using these enzymes for the production of ulvan-derived chemical products from currently rarely used green algal biomass," the authors wrote.

DOI: 10.1016/j.jbc.2021.101210

— Isabel Casas

To overcome these shortcomings, Evelyn Ramberger, Lorena Suarez–Artiles, Daniel Perez–Hernandez and colleagues at Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Germany, have developed an optimized method for using protein interaction screen on a peptide matrix, or PRISMA, in combination with quantitative mass spectrometry.

PRISMA is a new way to study point mutations and post-translational modifications within protein interaction motifs and to map these motifs.

In a recent paper in the journal **Molecular & Cellular Proteomics**, the authors write that PRISMA can be automated and allow the detection of phosphorylation-dependent interactors of certain proteins or mutation-dependent interactions of certain peptides. The authors propose that the transfer of this method from manual low-throughput procedures to an automated, microwell format with a high-throughput output retrieval will enable researchers to use PRISMA to explore disordered protein functions more efficiently. This method could contribute to deciphering the protein networks dependent on these short motifs that are involved in signaling processes and diseases.

DOI: 10.1016/j.mcpro.2021.100135

A piece of the centromere recruitment puzzle

The transcription of noncoding RNA at the centromere, a chromosomal locus essential for accurate segregation of chromosomes during cell division, is an important step for appropriate centromere function. Alterations in this function lead to genomic instability and aneuploidy, frequently observed in human cancers.

Shuhei Ishikura and colleagues at Fukuoka University in Japan in 2020 determined that zinc-finger transcriptional regulator ZFAT binds to the centromere to regulate ncRNA transcription. However, it has not been clear how ZFAT is recruited to the centromere.

Recently, the team reported in the **Journal of Biological Chemistry** that the centromeric protein CENP-B is an essential player in this process.

The authors performed ectopic expression and co-immunoprecipitation analysis, suggesting that ZFAT requires and interacts with CENP-B for ncRNA transcription. CENP-B knockdown showed decreased ncRNA expression levels at the centromere.

"Furthermore, the evident interaction between ZFAT and CENP-B was observed in both human and mouse cells," they wrote.

The researchers conclude that CENP-B helps establish ZFAT centromeric localization to regulate ncRNA transcription.

DOI: 10.1016/j.jbc.2021.101213

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Upcoming ASBMB events and deadlines

DECEMBER

6	**DEUEL** early registration deadline
6	ASBMB annual meeting travel award deadline
7	**Art of Science Communication** course applications accepted
15	ASBMB annual meeting last-chance abstract submissions open

JANUARY

10	**DEUEL** abstract deadline
27	ASBMB annual meeting last-chance abstract deadline
24	Marion Sewer scholarship applications now accepted
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
27	*National Protein Day*
28	*Rare Disease Day*

ASBMB

FEATURE

THE BEST OF BMB 2021

(A SUBJECTIVE LIST)

By Laurel Oldach

After the past year, some of us at ASBMB Today are feeling a little behind in our scientific reading. Perhaps you, too, have been preoccupied with pandemic concerns, or with how to teach remotely, organize childcare for a quarantined kid or keep experiments moving forward when the only pipette tips you can buy don't fit.

Whatever the reason, it can be helpful to pause and reflect. That's why we decided to look back at the year that was and ask the experts what exciting science we might have missed.

We asked members of the American Society for Biochemistry and Molecular Biology Council and editors of ASBMB journals to reflect on 2021 and tell us what stood out to them in the biochemistry and molecular biology literature. Year-end lists are always subjective, and it can take many years for the true impact of a finding to become clear. Still, this list reflects a field alive with discoveries driven by new computational tools and molecular techniques, a number of recent advances in structural biology, and, of course, widespread interest in treating and preventing diseases, most of all COVID-19.

You can find links to each study in the web version of this article at asbmb.org/asbmb-today.

Protein folding in silico

After winning the CASP14 protein structure prediction competition in November 2020 by accurately predicting numerous protein structures that had been solved experimentally and kept secret, the program AlphaFold was published in the journal Nature in July. The program's developers at the Google affiliate Deep Mind also launched a protein structure database in partnership with the European Bioinformatics Institute. In August, an academic group based at the University of Washington published a related approach called RoseTTAfold in the journal Science.

Both programs depend on machine learning to extract rules from an enormous number of previously solved structures and predict new ones.

Biologists expect to use this computational advance to save time in solving future structures, predict protein–protein interactions, and perhaps design drugs. Michael Airola, a structural biologist at Stony Brook University who works on challenging proteins that bind to lipids, said the program offers testable hypotheses his lab has found useful.

Vanderbilt University biochemist Fred Guengerich said, "It is modeling and the proof is in the predictability." Still, he wrote, his lab used an AlphaFold model in a recent paper "in the absence of a real structure available."

Structure prediction isn't just for proteins, either. Karin Musier–Forsyth, a biochemist at Ohio State University, pointed out another deep learning effort "somewhat analogous to the AlphaFold breakthrough, but for RNA," which also was published in Science in August.

Glycosyltransferases find a new target

Another molecule unexpectedly has joined the crowded milieu on the cell surface — although evidence suggests it may have been there all along.

While testing to see whether RNA in the cytoplasm might be modified with a small, reversible sugar group, researchers in chemist Carolyn Bertozzi's lab at Stanford University found large, RNase-sensitive glycosylated molecules on the surface of several immortalized cell lines. The find suggested that the surface glycome includes RNA molecules with complex carbohydrate modifications only seen on proteins until now. The modified RNAs are from a noncoding family that genetic studies have linked to autoimmune disorders; the team found that they bind to a receptor class called sialic acid binding immunoglobulin type lectins, or siglecs. The research, preprinted in 2019, was published in the journal Cell in June.

Bertozzi told ASBMB Today contributor Ankita Arora, "Once again, we are humbled by how little we know about biology."

The finding satisfied an initially skeptical Bertozzi and eventually peer reviewers, but some scientists remain cautious. University of Georgia glycobiologist Gerald Hart wrote, "I hope Carolyn's findings are correct, but until they are repeated by others, a healthy dose of skepticism is warranted. … The field missing a large N-linked type glycan seems hard to fathom, but we all need to keep an open mind."

Mass in vivo transfection

Development of a new type of vaccine, an advance that was realized in 2020, began to have an impact on daily life in 2021. Two mRNA-based vaccines that confer robust immunity to SARS-CoV-2, along with a more conventional peptide antigen vaccine, became available to healthcare workers in late December 2020 and were, within the U.S., widely available for adults by May.

Many researchers joked about receiving their transfections, a term for an often-used lab technique that delivers nucleic acids in liposomes that can reach the cytoplasm through endocytosis.

While public health practitioners still are grappling with vaccine hesitancy and misinformation, researchers in the pharmaceutical industry regard the shots' efficacy as a key proof of concept. Companies such as Moderna have begun to work on other therapies, including more vaccines, that can be delivered in mRNA form.

'Nothing is undruggable'

Some goals take a long time to reach. Scientists have known since the early 1980s that the Ras family of GTPases, which activate growth signals, can be powerful oncogenes. Ras mutations are involved in about one-third of cancers.

Yet for decades, the search for a way to block cancer-related signaling by one member of the Ras family, a mutant KRas called G12C, without harming healthy tissues failed miserably. Because KRas has a smooth surface and few ligand-binding pockets, medicinal chemists began to think it might be impossible to design an inhibitor to block its activity. But this year, two small-molecule inhibitors targeting KRas G12C were approved to treat certain cancers. University of California, San Francisco, chemist Charles Craik, who nominated the advance, wrote, "These breakthrough drugs

have changed the course of management of KRas driven cancers and open the way for additional approaches of combination therapies to benefit patient care."

In other feats of small-molecule design, targeted protein degradation has expanded beyond proteome-targeting chimeras, or PROTACs, to include small molecules that tee their targets up for lysosomal or macroautophagy-based degradation, according to a March review article in RSC Chemical Biology. Meanwhile, researchers also have reported a small-molecule drug candidate that can block the interaction between protease PCSK9, which regulates low-density lipoprotein receptor levels, and its target, the LDL receptor. "Nothing is undruggable," remarked Jay Bradner, the president of Novartis' research arm, while announcing the publication in the journal Cell Chemical Biology in September.

A daisy chain of knots, loops and petaloids

Single-stranded RNA is never as straight as cartoons make it look. Instead, the molecule tends to base pair over short stretches, forming loops, hairpins and other secondary structures that can impart function. Several groups have reported the secondary structure of the SARS-CoV-2 single-stranded RNA genome both within virions and in host cells. Together, the studies show that the genome's secondary structure involves numerous stem-and-loop elements concatenated into what one research team called "petaloid structures" in their June study in the journal Nature Communications. The genome further folds into an approximately spherical tertiary structure to fit into virus capsids.

A study published late in December 2020 in Nucleic Acids Research reported on a number of structural elements that might present druggable pockets, crevices on the face of the viral genome that small molecules could slip into to act, perhaps, as therapeutics. Musier–Forsyth, who nominated these studies, called them "quite impressive."

Three cheers for cryo-EM

While the technique has been around for a few years, cryo-electron microscopy continues to dazzle researchers with its speed and clarity in determining structures. Craik wrote, "Major technological efforts … facilitated achieving the goal of determining protein structures at atomic resolution and started a 'resolution revolution,' which forever changed the landscape of structural biology."

Several scientists pointed to its impact, especially advances in understanding protein complexes. As an example, Craik cited the "breakneck speed" with which structures of the SARS-CoV-2 spike protein bound to human ACE2 receptor were published in 2020, just months after the virus initially was isolated.

The technique also is offering new insights into long-standing questions. Binks Wattenberg, a biochemist at Virginia Commonwealth University, nominated a pair of papers that appeared in March in Nature Structural and Molecular Biology on the structure of a serine palmitoyltransferase complex. "This structure reveals so much about how this critical enzyme is regulated by accessory subunits," Wattenberg wrote, adding that it also "illustrates the accumulating power of cryo-electron microscopy for determining the structures of multisubunit membrane proteins."

This year, researchers at the Rockefeller University reported in September in the journal Science on a cryo-EM structure of three stages of the giant ribonucleoprotein complex called the small subunit processome, a precursor to the mature ribosome. Ribosome assembly is a complex and intricate process, with pieces coming together a few at a time into a massive molecular machine, each of whose two subunits includes 30 or more proteins built on an RNA core. Many chaperones that help to build the ribosome fall away before the mature ribosome is complete.

The series of structures the researchers found helps to unravel the steps in ribosome assembly and the structure of intermediates. Yale biophysicist Susan Baserga, who nominated this finding, wrote, "Twenty years after my laboratory purified and named (the SSU processome) in yeast, we have the human structure. Very exciting!"

Getting therapeutic proteins into the brain

The blood–brain barrier is a major hurdle for treating certain diseases. Tight junctions between blood vessel endothelial cells play a protective role, shielding the brain from pathogens and from circulating molecules that are useful for whole-body physiology but toxic to neurons. Still, the barrier can make it extremely difficult for researchers to deliver drugs into the brain.

Matthew Gentry, a biochemist at the University of Kentucky, nominated an approach to evade the blood–brain barrier that was published in the journal Cell by researchers at Denali Therapeutics and several universities in September. The approach takes advantage of the brain's mechanism for importing necessary iron. The vascular endothelia have a receptor for the iron carrier protein transferrin. Denali used a protein chimera made of the transferrin receptor binding domain and a therapeutic cargo protein to deliver a replacement for the lysosomal protein progranulin in mice. The chimeric protein restored ordinary lipid levels and showed some tissue-level restoration of health in the animals' brains. Progranulin deficiency can cause frontotemporal dementia in humans, so the results are of clinical interest. The company has announced that it is testing candidate drugs to treat other lysosomal storage disorders as well.

Genomic data from innumerable patients

Broad Institute proteomics director Steven Carr wrote, "I think the advances made by the NCI-CPTAC consortium deserve special mention."

The Clinical Proteomic Tumor Analysis Consortium, or CPTAC, sponsored by the National Cancer Institute, is a massive collaboration aimed at proteogenomic analysis of a variety of common cancer types. The combination of DNA sequences, proteomes, post-translational modifications and RNA-seq data for individual patients, often matched to adjacent healthy tissue, gives deep insight into how cancer develops. The project was launched in 2014, and its data had been used in at least 740 publications in 2021 when this issue of ASBMB Today went to press.

This year, proteogenomics studies using the data have given detailed portraits of what goes wrong in pancreatic ductal adenocarcino-

ma, lung squamous cell carcinoma and glioblastoma. Each study includes data on 100 tumors or more and identifies patterns of potential molecular vulnerability that promise to help future patients. Other studies aim to guide treatment or cancer staging, and still others offer mechanistic insights into disease phenotypes such as treatment resistance. Carr wrote, "The information that's been provided … has been pretty amazing, and has highlighted (how) proteomics adds to and goes beyond genomic methods."

Lipids and virology

A virus would not make it far without its host cell. Add to that the fact that humans tend to change more slowly than viruses, and it becomes clear why understanding how host cell factors contribute to viral pathogenesis can help to develop broad-spectrum antivirals.

Looking back on this year, University of Wisconsin metabolic biochemist James Ntambi wrote, "The close link of lipid metabolism to virology noted this year is beginning to excite me."

In addition to the lipid nanoparticles that encapsulate mRNA vaccines, Ntambi highlighted a September article in the journal Nature Metabolism that reported that fatty acid synthase, which produces palmitate through a series of steps, is a crucial enzyme for SARS-CoV-2 replication. The virus spread less completely through a cell culture with fatty acid synthase inhibited, and the same inhibitor — approved as a treatment for obesity — also reduced viral titers in mice. The study's authors pointed out that palmitoylation is an important modification for the function of the viral spike protein.

Ntambi wrote, "What this says is that the lipid biosynthetic pathway could be seen as a potential antiviral strategy for COVID-19 treatment."

Proximity proteomics

Protein–protein interactions drive a lot of biology but can be difficult to capture. They are often fleeting, may involve only glancing contact and sometimes affect only a modified subset of the two binding partners. Al Burlingame, a professor at the University of California, San Francisco, nominated proximity labeling coupled to proteomics for highlighting at year's end. These methods use radicals, affinity tags or other often complementary processes to modify molecules close to an introduced bait protein.

Using proximity proteomics, researchers can conduct subcellular proteomics and other narrowly focused investigations. Some of the studies published and preprinted this year include studies of lipid raft signaling, mitochondrial RNA anchoring, interactions between surface proteins at the synapse, and assembly of the kinetochore.

In a March article in Chemical Society Reviews, scholars led by David MacMillan and Tom Muir wrote that the development of proximity proteomics illustrates how "the union of chemistry and biology can present powerful tools that can impact human health."

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

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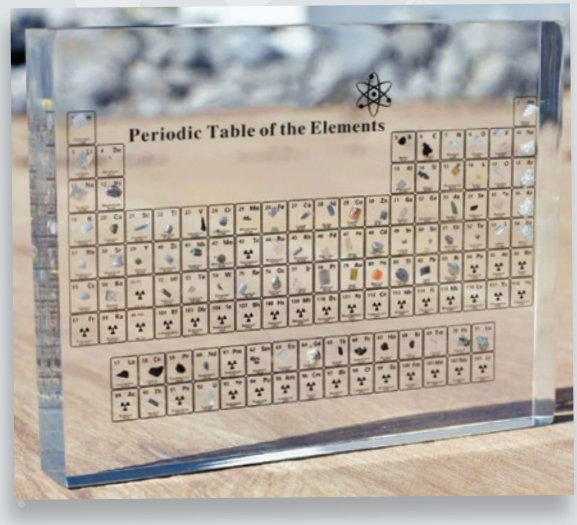

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Season's greetings!
We hope this gift guide helps you knock your holiday giving out of the park.

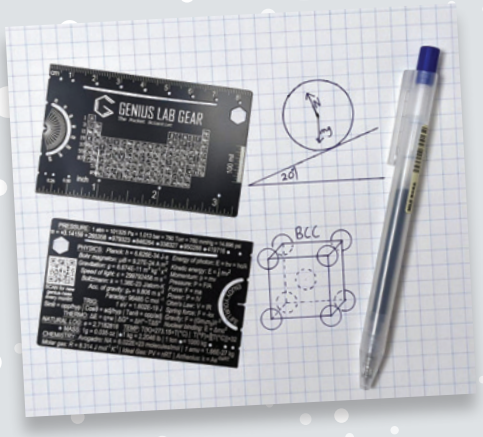
All these gifts can be delivered right to the recipient's door. Whether it's for your favorite scientist or a treat for yourself, get gifting!

1. Multicolor scientist socks, $60.50 | ties.com **2.** Periodic table with real elements, $84.95 | niagarablue.com **3.** Genome Dorothy dress, $64.99 | svahausa.com **4.** Human brain with labels paperweight, $57.99 | amazon.com **5.** DNA bracelet, $15.40 | etsy.com/shop/LeBuaJewelrytoo **6.** The pocket scientist: Ruler scale & unit conversion, $11.99 | amazon.com **7.** Genetics & DNA softcover notebook, $24.95 | etsy.com/shop/CognitiveSurplus **8.** Conical flask earrings, $14.13 | etsy.com/shop/ChemisTreeCrafts **9.** 2022 This day in science calendar, $12.60 | amazon.com **10.** Scientist rainbow shirt, $23 | etsy.com/shop/SciencePlusCoffee

For even more great giving ideas (including lots of gifts for kids), check out our expanded guide at asbmb.org/asbmbtoday.

2021 HOLIDAY GIFT GUIDE

By Racheal D'Souza



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(Stephanie Paxson and Allison Frick contributed to this guide.)

33
ASBMB Leadership Award (early-career)
Lea Vacca Michel
Rochester Institute of Technology School of Chemistry and Materials Science

34
ASBMB Leadership Award (mid-career)
Marlene Belfort
University of Albany's RNA Institute

35
Walter A. Shaw Young Investigator Award in Lipid Research
Michael Airola
Stony Brook University

36
Avanti Award in Lipids
Alex Toker
Beth Israel Deaconess Medical Center and Harvard Medical School

37
DeLano Award for Computational Biosciences
Tatyana Sharpee
Salk Institute for Biological Studies

38
Ruth Kirschstein Diversity in Science Award
Tracy Johnson
UCLA and Howard Hughes Medical Institute

39
William C. Rose Award
J. Martin Bollinger Jr.
Pennsylvania State University

40
ASBMB Exemplary Contributions to Education Award
Joseph Provost
University of San Diego

41
ASBMB–Merck Award
Robert V. Farese Jr. and Tobias C. Walther
Harvard Medical School and the Harvard T.H. Chan School of Public Health; associate members of the Broad Institute of MIT and Harvard

42
ASBMB Young Investigator Award
Greg G. Wang
University of North Carolina School of Medicine

43
Mildred Cohn Award in Biological Chemistry
Janet Smith
University of Michigan Medical School

44
Earl and Thressa Stadtman Distinguished Scientist Award
Kathleen Collins
University of California, Berkeley

45
Bert and Natalie Vallee Award in Biomedical Science
Elaine Fuchs
Rockefeller University and Howard Hughes Medical Institute

46
Herbert Tabor Research Award
Susan S. Taylor
University of California, San Diego

47
Alice and C. C. Wang Award in Molecular Parasitology
John Boothroyd
Stanford University

48
Career-development programming at the annual meeting

51
Pubs workshop to cover images, words and reach

52
Symposia session speakers

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Interest groups at #ASBMB2022

ASBMB EARLY-CAREER LEADERSHIP AWARD

Michel strives to be a better mentor

By Connor O'Hara

Lea Michel's family is a priority. Born in Korea and raised in Rochester, New York, Michel has extended the traditional definition of family to include all her students at Rochester Institute of Technology. She grew up close to the campus and attended yearly ice-skating camps run by RIT. Her passion for science and learning, however, was developed off the ice.

Michel attended an all-girls high school where she thrived in math and science. Her physics teacher, Mr. Hendrick, constantly reminded his students of the many women doing incredible things in the field and in other branches of science.

"So many girls grow up doubting if they belong in science, especially physical science," Michel said. "I had no doubts."

That fearless approach propelled Michel into her own lab at RIT, and for her commitment to helping other women advance in biochemistry and molecular biology, she has won the 2022 ASBMB Early-Career Leadership Award.

Michel performed undergraduate research in the lab of the only female physics professor then at Colgate University, Beth Parks, whom she considers a role model. After studying abroad, Michel realized that she was missing something by doing physics alone. She wanted to pursue science that was applicable to life and human health, so she transitioned in graduate school to Kara Bren's lab at the University of Rochester, where she found the perfect combination in biophysics.

In Bren's lab, Michel learned the value of the teamwork and cooperation that she strives for in her own lab. Now an associate professor in the school of chemistry and materials science, she said landing a faculty position at RIT was like winning the lottery; more than a decade later, she works to retain historically disadvantaged students in science and has a lab of diverse students.

Michel tries not to get too comfortable with her methods, she said. Her advice to others: "Get outside of your comfort zone" and "be brave." Much work remains to bring and retain women, first-generation, and deaf and hard-of-hearing students (RIT's National Technical Institute for the Deaf is the first and largest technological college in the world for deaf students) in science and math, she said, and she strives to support her lab family at RIT in the same way that impactful mentors helped her.

LEA MICHEL

Bacterial proteins in sepsis

Lea Michel's research lab has several ongoing projects, and one of the team's principal studies is attempting to identify biomarkers for diagnosing sepsis at earlier stages in development.

Bacterial sepsis is a leading cause of death in hospitals around the world. Gram-negative sepsis, or GNS, induces a hyperimmune response due in part to its lipopolysaccharide endotoxin and accounts for just under half of the total cases of bacterial sepsis. Michel's lab is using biophysical and biochemical methods to better understand the pathology of GNS and the release of peptidoglycan-associated lipoprotein, or Pal, from E. coli that contributes to the dramatic and deadly inflammatory response.

Other particles released from Gram-negative bacteria include outer membrane vesicles, which Michel and her lab also consider an attractive and distinguishing biomarker for use one day in the clinic.

Connor O'Hara (oharacp@mymail.vcu.edu) is a graduate student in the department of medicinal chemistry at the school of pharmacy at Virginia Commonwealth University. Follow him on Twitter: @oharacp_vcu.

ASBMB MID-CAREER LEADERSHIP AWARD

Belfort strikes the right balance

By Connor O'Hara

Growing up the daughter of German immigrants in apartheid South Africa, Marlene Belfort cut open her toy dolls to get a better look at what was on the inside. She also saw her mother face the challenges of "putting in a good day's work," as she put it, while supporting a family. These experiences inspired Belfort to aim for success both professionally and in her home life.

Her early curiosity propelled Belfort to the University of Cape Town, where she pursued an honors course that yielded her bachelor's and master's degrees. Some at UCT dismissed her pursuit of science degrees, as it was a common principle then that "women were for maternity, not for chemistry," as one teaching assistant informed her. Yet her drive to learn and better herself has led her to rewarding experiences — up to and including receiving the 2022 ASBMB Mid-Career Leadership Award.

To expand her professional opportunities beyond Cape Town, Belfort decided to join her longtime boyfriend Georges in California for her doctorate. Confronted with deciding whether to stay at Northwestern University in Chicago, where she did her postdoc, the couple — now parents of three sons — took work at different organizations in the more affordable city of Albany, New York, which seemed to be "a reasonable place to raise kids and get them started" before they moved to the next stop on their journey.

MARLENE BELFORT

Excising the facts about introns and inteins

Marlene Belfort said she has had a rewarding career identifying and characterizing the functional roles of both introns (noncoding intragenic sequences) and inteins (internal protein segments), molecular entities that are analogous in their ability to excise and self-splice from nucleic acids and proteins, respectively.

In her lab, Belfort studies the properties, structure, function and regulation of these entities as they relate to the behavior and evolution of organisms that contain them. With her husband, Georges Belfort, she has demonstrated applications of both entities related to biotechnology and disease, including the highly cited exploration of intein fusion for simplified protein purification methods.

"Then here we are, 43 years later," Belfort said.

"We both needed to work extremely hard to maintain our careers," she said, but they were also rewarded. At the translational interface between chemical engineering and biology, the Belforts have supported each other in grants, manuscripts and advising students.

"When my children were little, I kept thinking I was messing up all the time," Belfort said, but she now believes, "having a scientific career made me a better mom, and having kids to balance out my life made me a better scientist."

Now a distinguished professor and director of the Life Sciences Research Program at the State University of New York at Albany, Belfort said she enjoys taking care of people and organizations. She steadfastly has promoted the careers of women and underrepresented people in science and is thrilled to receive an award she describes as "particularly meaningful."

"If I can help people strike that right balance and integrate meaningful lives with their scientific careers, that's something that gives me great joy."

Connor O'Hara (oharacp@mymail.vcu.edu) is a graduate student in the department of medicinal chemistry at the school of pharmacy at Virginia Commonwealth University. Follow him on Twitter: @oharacp_vcu.

WALTER A. SHAW YOUNG INVESTIGATOR AWARD IN LIPID RESEARCH

Airola learns from failure

By Laurel Oldach

You can't say Michael Airola wasn't warned.

While trying to develop a research program that would differentiate his own lab from his postdoctoral mentor's, he set out to determine the structure of phospholipase D.

"I cautioned Mike that there was an elephant graveyard of grad students and postdocs who had attempted to solve these structures," Michael Frohman, who had discovered the protein 20 years prior, wrote in a recommendation letter.

But Airola, who received the ASBMB's 2022 Walter A. Shaw Young Investigator Award in Lipid Research, said, "I was optimistic … I thought, 'we have a chance; we had an interesting idea, and I don't think anyone has tried that, so we should try it.'"

That idea was to remove a section from the middle of the protein that appeared to have high intrinsic disorder. The more orderly portions left behind crystallized beautifully.

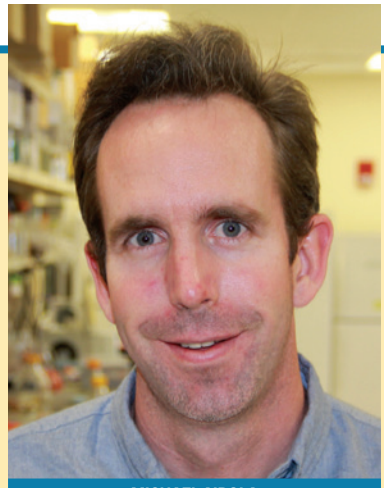
When it became clear that the approach would work, Airola said, he told graduate student Forrest Bowling, "It looks like you may have a successful Ph.D. project." Bowling, he recalled, answered, "What do you mean, this 'could be' a Ph.D. project? Why do you think I joined your lab?"

Airola knew that not every graduate student answers their first research question — especially if it depends on crystallizing a protein. He had started his own dissertation interested in the structural biology of circadian signaling in human cells. "Through failure, I learned quite a bit," he said.

He transitioned to a question about bacterial chemotaxis; studying a transmembrane signaling system got him interested in membrane biology, which brought him to Yusuf Hannun's lab at Stony Brook University. As a postdoc, Airola determined the structure of two sphingolipid-metabolizing enzymes. Later, he landed a job as a professor at Stony Brook. Both Hannun and his wife and collaborator, the late Lina Obeid, were supportive and influential mentors, Airola said.

Airola's own collaborations to boost graduate students and postdocs have included co-organizing a weekly virtual seminar series in lipid research that as many as 500 researchers attended at the height of pandemic lockdowns.

On the hunt for structures



MICHAEL AIROLA

As a professor, Michael Airola has pursued new structures, focusing on lipid-modifying proteins — both phospholipase D and a phosphatase called lipin — that are important for signaling yet challenging to study. He is interested in lipid droplet proteins and in how new sequence-based structure prediction tools will help generate hypotheses about which parts of a protein might be critical to its structure. Could such tools, plus creative approaches, put hitherto impossible structures within reach?

"I'm very aware that some projects aren't going to work," Airola said. "But I also don't want to work on things that are just easy."

As a mentor, it's a balancing act to help trainees select projects. "I try to help guide them through all the things I learned through failing to help them succeed — but then, we're not afraid to say, 'this isn't working, let's shelve it for a little bit and let's try something else.'"

The strategy seems to work. In a letter nominating Airola for the Shaw award, Yusuf Hannun wrote, "All of his graduate students are excelling and driven, and everything they touch seems to turn to gold."

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AVANTI AWARD IN LIPIDS

Toker recognized for 'seminal contributions' to lipid biology

By Courtney Chandler

Alex Toker always has been interested in science, and he recalls many days spent at the Natural History Museum in London, where he grew up. Yet it wasn't until his postdoctoral years spent under the mentorship of Lewis Cantley that he decided to make research his career.

"I just had kind of an epiphany and decided this is what I want to do for the rest of my life," Toker said. "I loved basic science and discovering things."

In 1988, Cantley won the American Society for Biochemistry and Molecular Biology's Avanti Award in Lipids. Toker, now a professor at Harvard Medical School and editor-in-chief of the Journal of Biological Chemistry, will receive the same award in 2022. Toker is being recognized for his work on lipid signaling and particularly his studies on phosphatidylinositol 3-OH kinase, or PI3K, and serine/threonine kinase AKT signaling in cancer.

Vytas Bankaitis, a distinguished professor and chair in chemistry at Texas A&M University and winner of the 2019 Avanti Award, wrote in his nomination letter that Toker deserved the award for his "seminal contributions to the lipid field" and "steadfast professionalism." Toker received word about the award while on vacation in New Hampshire.

"I was just so proud and ecstatic and filled with a sense of achievement and recognition by my peers," Toker said. "It really is a culmination of 20-plus years of running a laboratory, and, considering the past recipients, it is truly humbling."

The discovery aspect of research still drives him, and he enjoys the independence and creativity scientific research can bring. He is also passionate about mentoring.

"The greatest source of joy and pride and the most satisfying aspect of my career is really the training of the scientists and students that I've had in my laboratory," he said.

Toker credits his family, trainees, mentors and colleagues with helping him get to where he is today.

He also serves as associate director of the Cancer Research Institute at the Beth Israel Deaconess Medical Center and program advisor for the Biological and Biomedical Sciences Graduate Program at Harvard Medical School.

Pathways past and future

Alex Toker's research focuses on understanding how intracellular signaling pathways affect cancer cell behavior. During his postdoc work, he identified that a protein kinase called Akt, also known as protein kinase B, or PKB, was activated by lipid products of the PI3K pathway, thus linking the two signaling pathways.

The two pathways, together with the mammalian target of rapamycin, or mTOR, pathway, collectively control cellular metabolism, proliferation and growth, and survival. All are dysregulated in certain types of cancer.

In his award talk, Toker plans to start at his seminal discovery linking lipid mediators with specific signaling and move through his subsequent work characterizing Akt and other pathways in the cell and in cancer. He also will focus on where he thinks the field is going and ongoing studies in his lab aimed at designing therapeutic interventions targeting the pathway.

ALEX TOKER

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DELANO AWARD FOR COMPUTATIONAL BIOSCIENCES

Sharpee sees many ways of looking at a tree

By Laurel Oldach

You might not think a book called "Einstein Gravity in a Nutshell" would offer much insight into how the brain works. Tatyana Sharpee would disagree.

"For many years, this was my Saturday reading," Sharpee said, smiling, after she pulled the book from her home office bookshelf during an interview. Nothing but the title suggests a nutshell-sized quantity of information; the tome is several inches thick and almost 900 pages long.

In a letter nominating Sharpee for the American Society for Biochemistry and Molecular Biology's 2022 Delano Award for Computational Biosciences, fellow Salk professor Tony Hunter describes her studies as developing "a cohesive description of how biological systems strive for efficiency in information transmission at both local and network-wide scales." A second letter from Duke neuroscientist Nicolas Brunel called her "one of the leading computational neuroscientists of her generation."

Computational neuroscience is a fair distance from where Sharpee started. "I grew up wanting to be a physicist — that was the only option," she said.

Her parents in Ukraine both were physicists, and her grandparents were mathematicians. She earned a Ph.D. in theoretical physics at Michigan State University before beginning a postdoc in computational neuroscience.

"The transition from physics to biology was not an easy one," she said — not because the subject was more challenging but because stepping away from her lifelong intention to be a physicist provoked self-doubt and what she called "some kind of existential crisis."

These days, however, she sees the switch as an opportunity to bring lessons learned in physics into a new field. "I think that's the wonderful part about science, that you can start in one area, and then diffuse to other disciplines."

Sharpee also derives insight from working with colleagues, whose diverse perspectives she values. "Because each one of us has a different trajectory in science, our approaches to the same problem will be different," Sharpee said. "I hear, for example, that if you ask two photographers to photograph the same tree, the two photographs will come out very different. The same thing happens with scientists."

TATYANA SHARPEE

Applying geometry to biology

Tatyana Sharpee, a professor at the Salk Institute who trained as a physicist before transitioning into computational neurosciences, uses many concepts drawn from physics to explain biological phenomena.

One area she has found fruitful is applying hyperbolic geometry to biological questions. Hyperbolic geometry rests on parameters far removed from the Euclidean geometry most of us learn in high school. For starters, whereas in Euclidean geometry just one straight line can pass through any given point without crossing a second straight line, in hyperbolic space, infinitely many can do so.

Sharpee applies this conceptual framework to biological problems that involve compressing multidimensional signals into fewer dimensions — such as neural encoding of sensory input or visualizing gene expression in disease.

"I am deeply honored to receive the DeLano award," Sharpee said, because Warren L. DeLano widened the adoption of advanced quantitative analyses of biological data in an open and reproducible manner.

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RUTH KIRSCHSTEIN DIVERSITY IN SCIENCE AWARD

Johnson wants every student to feel they belong

By Adriana Bankston

Throughout her career, Tracy Johnson has observed the lack of diversity and of role models from diverse backgrounds in science. Motivated by her own mentors, she is committed to giving back. "They never questioned that I belonged in science," she said.

In recognition of her commitment to the belief that science "should be equally accessible to people from underrepresented backgrounds," Johnson has won the American Society for Biochemistry and Molecular Biology's 2022 Ruth Kirschstein Diversity in Science Award. Sonia Flores, chair of the ASBMB's Minority Affairs Committee, nominated Johnson for the award, noting that she is "the epitome of a scientist who has had an illustrious research career and who has dedicated her life to inspire and be a role model for those individuals who would never have thought they could choose research as a career."

Students from marginalized groups often lack exposure to research and a sense of belonging to the scientific community, Johnson said, and this affects their persistence. To address these issues, she started the four-year undergraduate Pathways to Success Program at UCLA, which includes early exposure to research and mentoring. As a result, Johnson said, students feel empowered to pursue scientific careers and to fulfill their professional passions and interests.

Integrating two loves: RNA and teaching

Tracy Johnson's lab has long been interested in basic mechanisms of gene expression and how the spliceosome functions to create mature messenger RNA. Work in the lab is focused on understanding the dynamic rearrangements of the spliceosome, the relationships between chromatin modification and spliceosome assembly and catalysis, and elucidating how these splicing mechanisms converge to allow the cell to respond to its environment.

Johnson has been able to integrate her love of RNA with her passion for teaching by developing courses in which first-year students engage in authentic research experiences exploring basic mechanisms of RNA splicing. This approach to engaging students in research is a key feature of the UCLA-HHMI Pathways to Success Program. Her talk at the ASBMB annual meeting will be titled "Beyond Diversity: Building a Culture of Inclusion in Science."

TRACY JOHNSON

Born in the Midwest, Johnson grew up in California. As an undergraduate student at the University of California, San Diego, she gained research experience that cemented her goal of pursuing a scientific career. She earned her Ph.D. at UC Berkeley and performed postdoctoral training at the California Institute of Technology followed by faculty appointments first at UC San Diego and then at UCLA, where last year she was appointed the dean of life sciences. She is also a Howard Hughes Medical Institute professor and chair of the executive board of the HHMI Society of Professors, which offers her additional opportunities to think about systemic change in science education.

"My dream is that every student who starts in the sciences leaves feeling like they belong and that they've been supported," Johnson said. "As an educator and leader, I aspire to provide every student with an educational experience that sets them up for whatever career they choose."

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WILLIAM C. ROSE AWARD

Bollinger built a bioinorganic powerhouse

By Laurel Oldach

Factories apply high heat and tremendous pressure to turn atmospheric nitrogen into ammonia — something bacteria do every day at ambient temperatures in the dirt, powering the global nitrogen cycle.

Martin Bollinger doesn't work on the nitrogen cycle. But he does use it to explain to undergraduates the tremendous power of redox metalloenzymes, such as the ones nitrogen-fixing microbes use. He, too, seems to favor an environment that gets things done with less heat and pressure than commonly are considered necessary.

His joint group with Carsten Krebs reported recently in Science the mechanism a microbial enzyme uses to make ethylene, a two-carbon molecule used as a building block in numerous industrial syntheses, which currently is produced from petroleum.

"It's the coolest mechanism I've ever been involved in working out," Bollinger said, adding that he had no hand in the experiments — it was all the work of student Rachelle Copeland, with an assist from postdoc Shengbin Zhou. "That was a great mentoring story," Bollinger said, "because all we did was get out of her way."

Talk to him long enough and you'll notice this is a habit: Bollinger always mentions not just the work done in his laboratory but the name of the trainee or colleague who did it.

Bollinger is the recipient of the American Society for Biochemistry and Molecular Biology's 2022 William C. Rose Award, which recognizes outstanding research contributions and a demonstrated commitment to mentoring. Colleague Squire Booker nominated Bollinger for the Rose Award. "Marty has been an incredible mentor to students and postdocs, and particularly women and women of color," Booker noted.

Bollinger founded a bioinorganic chemistry research group at Pennsylvania State University. Booker, the second member of the group, said Bollinger has been key in lobbying university administration on its behalf.

Colleague Joseph Cotruvo Jr. wrote in a recommendation letter, "Marty has been the guiding force in turning Penn State into a powerhouse in bioinorganic chemistry — the best place in the country, and probably the world, to do research in this field."

Contributing to the tight-knit, collaborative group of researchers, Bollinger said, is one of his proudest accomplishments. "I'm sure it's not completely unique, but it's very, very rare. … It comes from a common mindset where it's not all about me; it's about everyone succeeding, and keeping your ego in check, and promoting younger people."

Multiple activities from a pared-down source

Among other metalloproteins, Martin Bollinger's research group studies mononuclear nonheme iron oxygenases, enzymes that depend on one iron ion that is not coordinated by a porphyrin. Enzymes in this class can add hydroxyl groups, convert single bonds to double bonds, create or expand rings, or generate special functional groups such as endoperoxides or isonitriles — and sometimes do more than one of these transformations, depending on the substrate.

"The overarching goal has been to understand how you can, from essentially one structural scaffold and a simple cofactor and co-substrate, elicit these multiple activities," Bollinger said of his work.

MARTIN BOLLINGER

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ASBMB EXEMPLARY CONTRIBUTIONS TO EDUCATION AWARD

Provost makes chemistry accessible

By Martina G. Efeyini

Before becoming a science educator, Joseph Provost enlisted in the Alabama Army National Guard and worked as an active-duty policeman. After earning a bachelor's degree from Bemidji State University in Minnesota, he served in the U.S. Army Reserve for 19 years.

"Going from high school into the Army helped me learn discipline and focus that I didn't have before," Provost said. "Something particularly helpful in the research lab and the classroom."

Provost, recipient of the 2022 ASBMB Award for Exemplary Contributions to Education, is the department chair and a professor of chemistry and biochemistry at the University of San Diego. For 27 years, he has worked in undergraduate education.

Provost earned his Ph.D. from the University of North Dakota School of Medicine and Health Sciences and then did a postdoc at the Vanderbilt University Medical School. In 1997, he became a professor of chemistry and biology at Minnesota State University, Moorhead.

"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."

As a professor, he helps first-generation and transfer undergraduates gain confidence in science. He uses mind maps, flipped classrooms, course-based undergraduate research experiences and just-in-time teaching to make learning accessible.

"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. When the pandemic started, he led a group to curate resources for ASBMB and shared them with the biochemistry and molecular biology community worldwide.

"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'

Joseph Provost is an innovator, leader and educator respected by the ASBMB and the global biochemistry and molecular biology community. 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, he is always available to help.

Provost has trained undergraduates and high school and middle school teachers. He also has mentored faculty and served as a program and departmental external reviewer for 12 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 that 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.

ASBMB–MERCK AWARD

Farese and Walther find depth in a droplet

By Renae Crossing

"Tobi was a very rare type of person. … When you do a sabbatical many people in the lab ignore you, but Tobi ... without hesitation, said, 'I'll help you. Let's go.'"

In this way, Tobias Walther's simple question ("What are you working on?") to Robert Farese Jr. started a long-term collaboration that has become the forefront research group in a new field of biology: how and why our cells make little droplets, called lipid droplets, and why that matters.

In the early 1990s, Farese had been studying enzymes that make oils. In his science, as in his photography, Farese looks deeply at everyday things others pass over. Lipid droplets had been observed under microscopes since the 1800s, but Farese said, "When I went to the textbooks and tried to learn about them as organelles, I couldn't find anything."

Farese and Walther converged from complementary paths: one a U.S. lipid biologist with an M.D., the other a German chemist and biochemist who was a postdoc at the time. Additionally pooling structural biology, biophysics, proteomics, enzymology and physiology, over time they created excellent science.

"We stand on the shoulders of some amazing scientists," Walther said, "but they didn't have the tools that we have."

For what they've done with these tools, Walther and Farese, now running a joint lab at Harvard University and both associate members of the Broad Institute, have won the American Society for Biochemistry and Molecular Biology's 2022 ASBMB–Merck Award.

Droplets by nature are isolated, but good science isn't. For Walther, "It's about the work and not (the two of us) ... many people in our lab have contributed." Farese attributes asking good questions to their "constant creative dialogue … ping ponging" ideas for experiments. Both buck egomania in science, appreciating a congratulatory note from mentors over a press release.

Feedback on the science itself, says Walther, is what shows "we're on the right track." That track increasingly has shown that there's depth in a droplet, and there's yet more to be found.

ROBERT FARESE JR.

TOBIAS WALTHER

Two make one

Two enzymes inside us, DGAT1 and DGAT2, like Tobias Walther and Robert Farese Jr., converge with their distinct pathways to work on a common process: encasing energy-rich molecules safely in lipid droplets. (And one of them is shaped like a butterfly.) Lipids left alone to accumulate can be toxic, so it's safer to bundle them together.

Inside lipid droplets are fats, or triacylglycerides: esters of fatty acids and glycerol. Their presence makes cells an emulsion, Farese explains, and while we know in terms of physics how emulsions form, in biochemistry, questions arise about "how nature evolved proteins and lipids to govern that process in a regulated way."

Knowing how fats are metabolized has consequences: mutated versions of DGAT1 cause congenital diarrhea syndrome, and physicians may soon block DGAT2 to treat nonalcoholic fatty liver disease; the latter is in clinical trials. Overactive versions of DGAT enzymes will have plants and microbes producing oils for food or fuel for us.

And regarding obesity and conditions where people are underweight, Walther wants people to know, "We're making a lot of progress, and there's a lot of hope."

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

ASBMB YOUNG INVESTIGATOR AWARD

Wang's work is fueled by interest in cells

By Shravanti Suresh

Greg Wang is fascinated by the molecular biology of cells and the many levels of modifications they encompass to regulate gene expression.

"Follow your heart and do what interests you the most," he said.

Wang followed his heart from China, where he earned undergraduate and master's degrees, to the University of California, San Diego, where he pursued basic research to understand how the cell works. During his Ph.D. in biomedical sciences, he showed that nuclear receptor binding SET domain 1, a family of histone methylase transferase proteins, is directly linked to transcriptional regulation of the Hox-A locus and histone modification dysregulation leading to cancer formation.

Now an associate professor at the University of North Carolina at Chapel Hill, Wang studies a number of chromatin-modulating enzyme machineries and histone reader proteins that have been shown to be critical for chromatin/gene regulation and often altered in disease states. He also studies phase separation of transcription factors, which is critically involved in pathogenesis. For these works, he has been named the winner of the American Society for Biochemistry and Molecular Biology's 2022 ASBMB Young Investigator Award.

"Whenever you pick a question to work on, the more fundamental and broader the question is, the more you will learn in the process of answering it," Wang advises early-career scientists. The energy and curiosity of his students and postdocs fuel his fascination for chromatin biology, he said, and those lab members are leading his foray into molecular medicine.

The ASBMB award adds to a growing list of accolades including the Yang Family Biomedical Scholar award and the Phillip and Ruth Hettleman Prize, both from UNC in 2019; the Leukemia & Lymphoma Society Scholar award in 2018; and the American Cancer Society Research Scholar award in 2016.

GREG WANG

Three projects with a chromatin focus

At the ASBMB annual meeting, Greg Wang will talk about his quest to answer questions in the field of chromatin biology and chromatin's effect on gene (de)regulation and cancer formation.

Post-translational modification of histones leads to changes in chromatin, which lead to fine-tuning of DNA-templated pathways. The misregulation of histone modifications can lead to oncogenesis due to misperception in cell identity and deregulation of gene-expression profiles. Wang was among the first to show that the deregulation of certain histone reader proteins is causal for initiating cancer.

The Wang lab also uses small-molecule inhibitors to target enzymes that modify histones. Along with collaborators, they have developed a set of epigenetic inhibitors via proteolysis targeting chimera, known as PROTAC, which can inhibit and degrade target oncoproteins in tumor cells.

Wang is also interested in how cancer cells use phase separation by acquiring mutations, allowing the cells to enhance a genomic targeting of oncogenic transcription factors and form a distorted chromatin 3D structure during tumorous transformation.

At the annual meeting, Wang will talk about his research integrating these major projects: cellular crosstalk involving chromatin regulation, phase separation that results in 3D chromatin organization and the development of small molecules to target oncoproteins in tumor cells.

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MILDRED COHN AWARD IN BIOLOGICAL CHEMISTRY

Smith unravels secrets of nature's catalysts

By Arti Dumbrepatil

When Janet Smith was an undergraduate at Indiana University of Pennsylvania, she attended a seminar on cytochrome c structure, sequence and phylogeny. "I thought proteins were just wonderful," she said. "I was fascinated by the structural details and how the conservation of cytochrome c sequences mapped to the 3D structure, but didn't have an opportunity to study protein structure until I was a postdoc. It's the discovery … Sometimes you look at a new protein structure and immediately say, 'Oh, wow. Now I get it.' It's a great thrill."

Some four decades later, Smith was still busy piecing together protein structural puzzles when she learned she had won the American Society for Biochemistry and Molecular Biology's 2022 Mildred Cohn Award in Biological Chemistry.

"It was a complete surprise, a very pleasant surprise," she said, describing the award as "a recognition of my service activities to help advance the structural biology field."

In her lab at the University of Michigan, Smith and her team use X-ray crystallography, notably the multi-wavelength anomalous diffraction method and its single-wavelength counterpart, known as MAD and SAD, to solve structures of proteins such as biosynthetic enzymes for natural products and primary metabolites. As a new assistant professor, her first research projects required specialized synchrotron beamlines, leading to her effort to develop high-performance beamlines for macromolecular crystallography.

"One of the most satisfying aspects of my career has been to watch my field change from 'protein crystallography' to 'structural biology,'" Smith said. "I have been fortunate to see protein structure become prospective in biochemistry and molecular biology, no longer retrospective."

Smith lectures internationally on structural biology and synchrotron radiation and mentors young women in science and young crystallographers, even if they don't work in her lab. Mentoring is her hardest job, she said. "Science changes … and it can be difficult to choose a path in research. I advise new students to choose any experimental area where they enjoy the work, and to consider what fields they think will be strong in 20 years. And then look at the intersection. And be fearless about changing course as science — and they — change."

Deciphering structural puzzles

Janet Smith's lab studies the biological function of proteins at the molecular level. They use X-ray crystallography to solve protein 3D structures and then aim to explain what the proteins do and how they do it.

"We try to explain the function of a protein in terms of the 3D structure, and then test ideas about mechanism with biochemical and other experiments," Smith said. She has used this approach to understand the mechanism and regulation of several enzymes by solving their crystal structures.

JANET SMITH

In her award lecture, "Proteins in the Interplay of Viruses as Pathogens and Us as Hosts: 'Us vs. Them,'" Smith will discuss her recent research, she said. Her lab's study of viral proteins has revealed some unexpected mechanisms underlying host–virus interactions and subsequent immune response mechanisms.

"I will probably talk on one or two systems that we have investigated," she said, "and highlight the structural features of proteins that humans make to fight RNA viruses."

Arti Dumbrepatil (artidumbre@gmail.com) is a science writer covering topics ranging from nanorobots to virology. She has a Ph.D. in biochemistry and writes for Microbiome Digest and Bio Voice News. Follow her on Twitter: @rtisciwrites.

EARL AND THRESSA STADTMAN DISTINGUISHED SCIENTIST AWARD

Telomerase studies led Collins to discoveries in genetic elements

By Nicole Lynn

Almost half the human genome owes its origin to retroelements — components of the eukaryotic genome capable of mobilizing via an RNA intermediate to other portions of genetic DNA, where they can be inserted.

After two and a half decades of research on telomerase, the enzyme responsible for maintaining telomeric DNA integrity during replication, Kathleen Collins at the University of California, Berkeley, expanded her research to focus on genetic retroelements in eukaryotes. Collins' journey into this largely unexplored field began about five years ago, after she and her colleagues reached long-sought insights in their telomerase research.

"Our time studying telomerase provided us expertise, for example, a better understanding of protein–RNA interactions," Collins said, "and we wanted to know if we can answer questions about retroelements using our knowledge of telomerase."

For her contributions to telomerase and the RNA field, Collins will receive the American Society for Biochemistry and Molecular Biology's 2022 Earl and Thressa Stadtman Distinguished Scientist Award, which recognizes outstanding achievements in basic research.

Collins comes from a family of academics; however, her interest in biology emerged from a love of science, technology, engineering and math as well as learning and the pursuit of truth. As a researcher and educator, Collins encourages her students to place themselves continuously in the way of information — for example, at conferences and office hours or with experts and peers — because a person never knows where their best lessons will come from.

"The number of insights I have had in my work that came from lecturing or preparing to teach, are huge," she said. "It's why I believe teaching and research go so well together."

As a mentor, Collins enjoys sharing advice; she motivates her students to put themselves out there with regard to science, reminding them that they needn't be shy or worry about imposing as long as they are respectful. One motto she shares with students: "No question is too stupid, except one that goes unasked."

KATHLEEN COLLINS

Investigating retroelements in the eukaryotic genome

In the context of evolution, retroelements can be described as opportunistic genetic elements that carry themselves as passengers in the genomes of their hosts. As humans evolved, these elements were silenced to maintain the integrity of our genome; however, a large number still exist in our DNA.

After many years investigating the enzyme telomerase, including its specific mechanisms on the chromosome, Kathleen Collins and her lab noticed its connection to retroelements.

"It's crucial to think of telomerase as a ribonucleoprotein because it is a co-folding protein and RNA mixture," Collins said. "Telomerase is the non-selfish version compared to what we see with eukaryotic retroelements."

Collins' lab is paving the way in eukaryotic retroelement research, focusing in particular on non–long terminal repeat retroelement reverse transcriptases and their ribonucleoprotein complexes. Collins hopes to harness the targeting specificity observed in these enzymes for future use in gene therapy.

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BERT AND NATALIE VALLEE AWARD IN BIOMEDICAL SCIENCE

Fuchs goes boldly where no stem cell biologist has gone before

By Alyson Smith

Elaine Fuchs, a professor of mammalian cell biology and development at the Rockefeller University, has won the 2022 Bert and Natalie Vallee Award in Biomedical Science for her foundational research showing how stem cells create, maintain and repair our skin.

"I began my career in biochemistry and slowly migrated into stem cell research and cancer, so for me to receive this award from the ASBMB is really special," Fuchs said. "I look forward to being at the annual meeting and talking about the work that we have been doing over four decades."

In her nominating letter, Helen Blau, a professor at Stanford University School of Medicine, wrote, "Innovation is a hallmark of Fuchs' work. She has repeatedly exploited a diversity of approaches to probe old questions in new ways."

A desire to impact human health motivated Fuchs' career transitions: from physical chemistry as an undergraduate to the biochemistry of bacterial sporulation as a Ph.D. student to skin cell biology as a postdoc and in her own lab. Each transition required a leap into the scientific unknown.

"You can never solve an equation about life," Fuchs said. "It took me much of my career to realize that that's what I enjoy most about biology. There are always new questions that emerge from each experiment."

Although Fuchs no longer works at the bench, she is as passionate about her research as when she started her lab 40 years ago. She continues to inspire junior researchers to become fearless in their approach to science.

ELAINE FUCHS

Exploring the secrets of skin disease

As an assistant professor, Elaine Fuchs used the nascent recombinant DNA technology to hunt for genes behind human skin disorders. Her lab focused on keratins, the major structural proteins in skin cells, identifying mutations that disrupt keratin assembly and the skin's unique protective qualities.

By engineering transgenic mice with keratin mutations and comparing their pathologies with images in dermatology textbooks — an unconventional approach in the early 1990s — Fuchs and her lab discovered the mutations underlying several human skin disorders. These landmark studies unlocked a new paradigm of studying mutated proteins in mice to define the genetic bases of human disease.

Fuchs' lab then explored how stem cells create, remodel and repair the epithelial barrier at the skin surface and how these processes go awry in cancer. Her team aims to find drugs that target cancerous epithelial stem cells with minimal harm to normal stem cells, leading to more effective and safer treatments.

Most recently, Fuchs' lab discovered an epigenetic memory recorded within the chromatin of tissue stem cells after stress. It provides new insights into chronic disorders like psoriasis, atopic dermatitis, asthma and inflammatory bowel disease. In her nominating letter, Mina Bissel of the Lawrence Berkeley National Laboratory wrote, "Fuchs' team continues to develop and adapt new tools and technology to tackle big questions in stem cell biology."

Alyson Smith (alysonscsmith@gmail.com) is a Ph.D. graduate in cell biology from Scripps Research in La Jolla, California. She now works as a scientific writer for Vala Sciences Inc. Follow her on Twitter: @cellbionerd.

HERBERT TABOR RESEARCH AWARD

Taylor's career began as med school detour

By Nivedita Uday Hegdekar

Susan Taylor's career spans over 50 years of groundbreaking research, accolades and accomplishments. But she never intended to follow this path.

As a freshman at the University of Wisconsin, Taylor dreamed of becoming a physician. Charles Sorum, her chemistry professor, solidified her foundation in the field. "He was a big influence in my life and inspired me to major in chemistry, despite it being an unconventional choice for a woman in the 1960s," Taylor said.

During her senior year, Taylor's fiancé accepted a job at the National Institutes of Health in Maryland. Having missed the Johns Hopkins Medical School deadline, she applied to the Hopkins graduate school, where she completed doctoral research on lipids and became a biochemist.

"I still had my heart set on medical school," Taylor said. "However, my husband accepted a position in Cambridge, England, so I decided to hold off … for a few more years."

As a postdoc with Brian Hartley at the Laboratory of Molecular Biology, Taylor discovered protein chemistry and structural biology — and shelved her med school plans for good.

"My two years in Cambridge taught me how to think about science across disciplines," she said.

Taylor returned to the U.S. as a postdoc at the University of California, San Diego, where she remained and is now a distinguished professor in two departments: chemistry and biochemistry and pharmacology.

For her excellence in research and contributions to the scientific community, Taylor will receive the American Society for Biochemistry and Molecular Biology's 2022 Herbert Tabor Research Award.

A passionate advocate for interdisciplinary science, especially for training the next generation of scientists, Taylor is especially conscientious about recruiting and mentoring underrepresented students.

She looks back fondly on her professional journey.

"I have had the good fortune of collaborating with so many creative scientists from various disciplines," she said. "Over the years, we have supported and learned from each other."

SUSAN TAYLOR

Fascination with a signaling molecule

When Susan Taylor was a postdoctoral fellow at the fledgling University of California, San Diego, her advisor, Nathan Kaplan, introduced her to cAMP-dependent protein kinase, or PKA, a signaling molecule that regulates glycogen, lipid metabolism and many other things within cells.

"I became fascinated with this highly allosteric enzyme and decided to characterize it further," Taylor said. She and PKA became lifelong partners.

In her own lab, Taylor led studies that elucidated the structure and function of PKA. Following identification of active site residues in the catalytic and regulatory subunits, she and her collaborators solved the structure of the PKA C-subunit in 1991 — the first protein kinase structure. She subsequently solved structures of higher complexity, culminating in full-length functionally nonredundant holoenzymes.

Unraveling the dynamics and allosteric signaling and demonstrating how these correlate with disease phenotypes has been a continuing theme of the Taylor lab. Most recently, using high-resolution imaging in retina and brain, she has further defined isoform specificity and, in particular, has focused on the previously uncharacterized Cβ isoform, which accounts for about 50% of PKA signaling in brain.

Nivedita Uday Hegdekar (nivedita.hegdekar@umaryland.edu) is a graduate student at the University of Maryland working toward a Ph.D. in biochemistry and molecular biology and an M.S. in patent law. Follow her on Twitter @NiveditaHegdek1.

ALICE AND C.C. WANG AWARD IN MOLECULAR PARASITOLOGY

Boothroyd honored for Toxoplasma gondii research

By Anna Tancredi

In his lab's early years, John Boothroyd worked with both the protozoan that causes African sleeping sickness, Trypanosoma brucei, and the parasite that causes toxoplasmosis, Toxoplasma gondii. His team was one of the first to report mRNA trans-splicing and polycistronic transcription in eukaryotes from their trypanosome research. But about a decade later, Boothroyd started to feel that the trypanosome research field was becoming saturated; he wanted to go back to his early interest in intracellular biochemistry, so he focused his research on the less-explored Toxoplasma. Since then, his lab has made great strides in understanding host–parasite interactions.

Boothroyd has won the American Society for Biochemistry and Molecular Biology's 2022 Alice and C.C. Wang Award for his seminal contributions to molecular parasitology both in the laboratory and in the greater community.

After earning his Ph.D. at the University of Edinburgh in 1979, Boothroyd was a scientist at the Wellcome Research Laboratories in the United Kingdom for three years before moving to Stanford University, where he's worked for almost four decades. He is now a professor of microbiology and immunology and associate vice-provost for graduate education and postdoctoral affairs.

On top of his research contributions, Boothroyd aims to better the lives of students and faculty by altering how we view mentorship in the sciences. "One of my passions is to change the academic culture to recognize that mentoring is a really important and really hard job, and that people can benefit from receiving explicit training," he said.

Elected to the National Academy of Sciences in 2016, Boothroyd continues his work to create a supportive, inclusive scientific community at a national level.

In his own lab, Boothroyd has a team-oriented approach, saying, "I strongly feel that awards like this are to the team, not me."

In this strain, virulence varies greatly

Toxoplasma gondii has a diverse range of hosts; it can infect nearly any warm-blooded animal, including humans. An estimated 40 million people in the United States are infected with the parasite. Though many cases are asymptomatic, severe toxoplasmosis can be fatal for pregnant individuals or those with weakened immune systems, so it is crucial to understand how these parasites work. John Boothroyd and his team at Stanford want to understand what makes some strains of Toxoplasma so virulent and how the host immune system and the parasite interact.

JOHN BOOTHROYD

In their most recent publication, the team used single-cell transcriptomic analysis to examine how host cell gene expression changes upon infection by Toxoplasma gondii. They compared the transcription of Toxoplasma-infected cells with cells that were injected but not invaded by Toxoplasma. While previous studies only had assessed gene expression days after infection, Boothroyd's team measured transcription within one to three hours. They found that transcription of host immune and cellular stress response genes increases upon injection of rhoptry effector proteins. Exactly how these effectors are introduced into the host cell is one of the lab's current focuses.

Anna Tancredi (tancredi.annac@gmail.com) received a bachelor's degree in molecular biology from Kenyon College. Follow her on Twitter: @popscicle_xyz.

Career-development programming at the annual meeting

By Kirsten Block, Jelena Lucin & Ciearra Smith

No scientific conference is complete without a healthy dose of professional development. The annual meeting of the American Society for Biochemistry and Molecular Biology in April in Philadelphia offers a collection of programming to meet a variety of needs for members of all career stages and interests. This year, the lingering effects of COVID-19 as well as diversity, equity and inclusion come into focus throughout our programming.

Take time to connect with other attendees, sharpen your transferable skills, reflect on the year that was, and consider what the future holds for higher education and the biomedical science research workforce.

Diversity, equity and inclusion

The ASBMB is committed to supporting and enhancing diversity, equity and inclusion in the fields of biochemistry and molecular biology. We continue these efforts with a pair of events at the annual meeting that critically examine barriers experienced by women and historically excluded groups in the science, technology, engineering and mathematics workforce.

The evolution of work–life integration in the time of COVID-19

Integrating work and personal life is challenging and has been made even more so for women during the COVID-19 pandemic. The ASBMB Women in Biochemistry and Molecular Biology Committee is hosting its annual networking dinner and a panel discussion titled "The Evolution of Work/Life Integration in the Time of COVID-19."

Lea Vacca Michel of the Rochester Institute of Technology, winner of the society's Early-Career Leadership Award, and Marlene Belfort of the University at Albany, winner of the Mid-Career Leadership Award, will be panelists.

They will be joined by members at various career levels to discuss their experiences with integrating work and their personal lives during the pandemic.

Attendees are encouraged to weigh in during the discussion.

Race and mental health in STEM

STEM graduate students and postdoctoral fellows, particularly those of color, often experience microaggressions, discrimination and harassment in the workplace, which can lead to adverse mental health outcomes. We must support these scientists by encouraging dialogue and taking action. In this session, sponsored by the ASBMB's Maximizing Opportunities for Scientific and Academic Independent Careers, or MOSAIC, program, panelists Cirleen DeBlaere of Georgia State University, Carlota Ocampo of Trinity Washington University and Stephen Quaye of Ohio State University will lead insightful discussions pertaining to the intersectionality of race and mental health of STEM trainees.

Education and professional development

Whether you are looking to enhance your professional skills or think broadly about higher education, workshops hosted by the ASBMB Education and Professional Development Committee have you covered.

Approaches to teaching in the biosciences using different course modalities

Learn to work outside your teaching comfort zone using different modalities. Using sample lessons, attendees will learn how to take a traditional lesson taught using one modality and adapt it to another. This workshop will examine evidence-based practices reported in the literature, and attendees are encouraged to share their own practices and experiences. What works well, and what hasn't? What are the advantages or disadvantages of employing different modalities? In addition to identifying new strategies to use in the classroom, attendees will walk away with new connections in the education community.

Increasing diversity through master's degree programs

The National Science Foundation created the Scholarships in Science, Technology, Engineering and Mathematics program with a goal to broaden participation in the STEM workforce. The NSF program funds institutions of higher education to enable them both to provide scholarships and to implement and adapt evidence-based curricular and co-curricular activities to boost recruitment, retention and success of low-income students. In this workshop, recipients of an S-STEM grant will share their experience developing a research-based master's degree program and its impact on enhancing diversity within their department. They also will discuss future steps in sustaining the program beyond the lifetime of the grant.

Becoming the boss of your career

The past two years may have left many feeling adrift in their career progression. This workshop's goal is to encourage, support and empower attendees to take charge of their careers. Facilitator Erica Gobrogge of Van Andel Institute will focus on practical and actionable strategies for setting and achieving your career goals and effectively advocating for your career to your mentor(s), colleagues and institutional leadership. Attendees will develop their own goals, draft action plans and practice navigating potentially challenging conversations necessary to achieve their goals.

Pedagogical lessons learned during the time of COVID-19

Higher education experienced unprecedented disruption in spring 2020 when schools were forced to close and virtual instruction replaced classroom learning. What can we learn from the experiences and creative teaching strategies employed out of necessity when schools were shuttered? What worked, what didn't, and what misconceptions were proved wrong through more than a year of distance learning? As we consider what the new normal in BMB education will look like in the future, we must reflect on the experiences of faculty members and students living and learning through disruption. In this session, a series of short talks building upon a virtual issue from the journal Biochemistry and Molecular Biology Education will set the stage for an open discussion for all attendees.

Outreach

The ASBMB Science Outreach and Communication Committee is dedicated to empowering members of the society to engage their local community and communicate their science effectively. The committee aims to equip members with the tools and resources needed to be successful, and it will be offering several opportunities during this year's annual meeting.

The power of storytelling

Storytelling is an essential component of communication. It can be used to connect with a diverse audience and make challenging subjects more accessible. Mastering storytelling requires creative flexibility, dexterity with language and willingness to get personal. Learn how to incorporate yourself as a scientist into your science story in a way that strengthens your message without sacrificing scientific integrity. This interactive session will lead participants through hands-on storytelling training that is based on one of the modules from the ASBMB course The Art of Science Communication.

Transforming scientific research into equitable outreach

How do you transform your passion for science into equitable outreach? This interactive session will cover the importance of science outreach and its impacts on enhancing diversity, equity and inclusion within the biomedical science research workforce. Chelsey Spriggs, co-founder of Black in Microbiology (#BlackInMicro) and a member of the first cohort of the ASBMB MOSAIC program, will share her

journey as a role model for underrepresented students interested in biological research. She will describe how she has engaged in outreach and mentorship and how, through her work as a board member of the Black in Microbiologists Association, she aims to enhance the visibility of Black scientists in the field. Be ready to have a thoughtful discussion with your peers and brainstorm ways to use science outreach as a vehicle to equity and inclusion.

Experimental Biology Career Central

One great benefit of meeting with other societies at the Experimental Biology conference is being able to take part in programming at Career Central. The ASBMB will do its part by presenting a quartet of bite-size sessions focused on developing key skills to support your career progression and exploring different career paths available to those with scientific training.

The art of the interview: Ask great questions, give great answers and enjoy the process

No matter where you are in your career, having great interview skills can help you make the next step. When it comes down to brass tacks, an interview is just a conversation. Laurel Oldach, a scientist-turned-science-writer at the ASBMB, will talk about both sides of interviewing: how you can make the most of informational interviews that you conduct and how you can feel more relaxed and prepared when you're the interviewee.

Exploring careers in science publishing

Ever wonder what it is like to work behind the scenes to bring research to publication? Join members of the ASBMB publications staff to explore the variety of positions in publishing that benefit from scientific training. Speakers will share insights into the different roles, the day-to-day and how to make the leap from research to publishing.

Managing your mentoring relationships through mentoring up

Once you have found a mentor, what comes next in making the most of this relationship? Richard McGee of Northwestern University Feinberg School of Medicine will focus on the essential and critical elements of effective mentoring relationships, with an emphasis on mentoring up — how students and postdocs can use these principles to guide and help their mentors provide what they are seeking from them.

Science policy skills — helpful for scipol and beyond

Whether you are interested in science policy as a possible career or enjoy advocacy to support your science, there is a subset of skills necessary to make you an attractive job candidate or skilled advocate. But did you know that those same skills can help you be a better scientist too? Join ASBMB Public Affairs Director Benjamin Corb, Policy Manger Sarina Neote and members of the society's Public Affairs Advisory Committee to learn about how to improve those soft skills — and apply them no matter where your career takes you.

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

Jelena Lucin (jlucin@asbmb.org) is the ASBMB's outreach and education coordinator. Follow her on Twitter: @Jelena23Lucin.

Ciearra Smith (csmith@asbmb.org) is the ASBMB's manager of diversity, equity and inclusion. Follow her on Twitter: @CB_witha_PhD.

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!

Pubs workshop to cover images, words and reach

By Stephanie Paxson

Will my data stand the test of time?

Is my writing clear, compelling and engaging?

Will I be able to reach an audience that will give my research its greatest impact?

These are questions authors ask themselves when preparing manuscripts for publication.

The American Society for Biochemistry and Molecular Biology is home to the Journal of Biological Chemistry, the Journal of Lipid Research, and Molecular & Cellular Proteomics. In a 90-minute workshop at the ASBMB 2022 annual meeting, members of the society's publications staff will offer insights into the publication pipeline and provide you with tips on three essential topics: presenting data, writing well and sharing your work.

Collecting, storing and presenting data: The workshop will begin with the visual essentials for publication — figures and data presentation best practices. We will provide suggestions on how to prepare images and what you need to think about for image acquisition and storage and figure preparation. We will tell you how to find the right exposure, resolution and software for your images.

Editing text for clarity and reach: The title and abstract are the portal to any manuscript. How can you create compelling, broadly accessible text for your target audience? We will go over the key elements that make a good title and abstract. Participants will have an opportunity to review examples and work with the presenters to create engaging text that people will want to read.

Sharing your work: Over the past 20 months, we've learned how to operate virtually and create online communities. Once your paper is published, you can use online platforms to share your research and make it more visible. We will show participants how to use social media and online platforms to communicate their science.

The ASBMB wants to help you achieve your publication goals as part of our mission to bring enduring research to the scientific community. We can't wait to see you in Philadelphia — and be sure to follow us on twitter @ASBMB for all the latest updates on #ASBMB2022.

Stephanie Paxson (spaxson@asbmb.org) is the ASBMB's journal marketing associate. Follow her on Twitter: @stephaniepaxson.

Symposia session speakers

Education and professional development

Developing a collaborative environment to facilitate inclusive departmental communication — ***Todd Weaver***, *University of Wisconsin–La Crosse*

Creative strategies to perform an inclusive faculty search — ***Anita Corbett***, *Emory University*

Creative approaches to perform an inclusive faculty search — ***Wendy Gilbert***, *Yale University*

Peer collaboration and review: A guide to iterative improvement in learning — ***Dan Bernstein***, *University of Kansas*

What makes a competitive applicant? Assessing students for graduate/professional school applications — ***Erin Sayer***, *University of Nebraska–Lincoln*

Developing BMB assessment questions for use in the undergraduate classroom — ***Victoria Moore***, *Elon University*

Enzymology

Riboflavin catabolism: The destruction of an icon — ***Tadhg Begley***, *Texas A&M University*

Repairing enzymes using spare parts — ***Catherine Drennan***, *Massachusetts Institute of Technology*

Machinery in motion: New insights into mitochondrial proteostasis — ***Gabriel Lander***, *Scripps Research Institute*

An aerobic strategy for C-H bond functionalization — ***Jennifer Bridwell–Rabb***, *University of Michigan*

Structural biology of natural product biosynthetic enzymes — ***Janet Smith***, *University of Michigan*

Correlated motions in enzymes — ***Nozomi Ando***, *Cornell University*

Nickel pincer nucleotide: biosynthesis and function — ***Robert Hausinger***, *Michigan State University*

Bacterial biosynthesis of natural products — ***Katherine Ryan***, *University of British Columbia*

Glycobiology

Nanoscale physical biology of the cellular glycocalyx — ***Matthew J. Paszek***, *Cornell University*

MALDI imaging mass spectrometry mapping of the glycocalyx — ***Richard R. Drake***, *Medical University of South Carolina*

Genetic and small molecule strategies to edit the glycocalyx — ***Sriram Neelamegham***, *State University of New York at Buffalo*

Enzymatic removal of cell surface antigens as a route towards universal O type blood and organs — ***Stephen Withers***, *University of British Columbia*

Hypersialylation of tumor cells promotes pancreatic cancer progression — ***Susan Bellis***, *University of Alabama at Birmingham*

Receptor N-glycosylation links metabolism with signaling — ***James Dennis***, *Lunenfeld Tanenbaum Research Institute*

Modeling the mucinous glycocalyx to unravel receptor pattern recognition by influenza A viruses — ***Kamil Godula***, *University of California, San Diego*

Cell surface glycan engineering reveals that matriglycan alone can recapitulate dystroglycan binding and function — ***Geert-Jan Boons***, *University of Georgia*

The glycocalyx in tumor progression and metastasis — ***Valerie Weaver***, *University of California, San Francisco*

The heparaase/syndecan-1 axis in cancer progression — ***Ralph D. Sanderson***, *University of Alabama at Birmingham*

Reprogramming T cells to target glycans and overcome glycan-mediated immunosuppression for cancer therapy — ***Avery Posey***, *University of Pennsylvania*

Orchestrated intragranular restructuring of mucins during secretory granule maturation — ***Kelly Ten Hagen***, *National Institute of Dental and Craniofacial Research*

Membranes/Lipids

Regulation of PIP2 homeostasis at ER-plasma membrane contacts by Nir proteins — ***Jen Liou***, *University of Texas Southwestern Medical Center*

Roles for inter-organelle contacts in organizing metabolism — ***W. Mike Henne***, *University of Texas Southwestern Medical Center*

Systematic analysis of membrane contact sites — ***Maya Schuldiner**, Weizmann Institute of Science*

Novel pathways of intracellular membrane lipid transport and neurodegenerative diseases — ***Pietro De Camilli**, Yale University School of Medicine; Howard Hughes Medical Institute*

Chemical tools for understanding phospholipase D signaling — ***Jeremy Baskin**, Cornell University*

Control of the cellular lipid landscape by inositol lipids — ***Tamas Balla**, National Institutes of Health*

Volume electron microscopy analysis reveals a new type of membrane junction required for mixing of parental genomes after fertilization — ***Orna Cohen–Fix**, National Institute of Diabetes and Digestive and Kidney Diseases*

Automatic whole cell organelle segmentation in volumetric electron microscopy — ***Aubrey Weigel,** Howard Hughes Medical Institute Janelia Research Campus*

Regulation of membrane dynamics via phosphoinositide signaling cascades — ***Lois Weisman**, University of Michigan*

Novel mechanisms in phosphoinositide turnover — ***Raghu Padinjat**, National Centre for Biological Sciences*

Regulation of COPII dynamics in development and disease — ***Anjon Audhya**, University of Wisconsin–Madison*

Intracellular trafficking during neutrophil chemotaxis — ***Carole Parent**, University of Michigan*

Metabolism

Interplay between metabolism and gene expression — ***Marian Walhout**, University of Massachusetts Medical School*

Identifying toxic metabolites and their roles in disease — ***Dohoon Kim**, University of Massachusetts Medical School*

Transcriptional regulation of primary and specialized metabolism — ***Siobhan Brady**, University of California, Davis*

Interorgan crosstalk and metabolism regulation in Drosophila — ***Norbert Perrimon**, Harvard University*

Metabolic adaptation to oxidative stress at the host-microbe interface — ***Stavroula Hatzios**, Yale University*

Deconvoluting host-gut microbiota co-metabolism — ***Pamela Chang**, Cornell University*

The tiny pharmacists within: how the human gut microbiome impacts drug metabolism and disposition — ***Peter Turnbaugh**, University of California, San Francisco*

Metabolic outliers in human disease — ***Ralph DeBerardinis**, University of Texas Southwestern Medical Center*

Lipid metabolism and ferroptosis — ***Scott Dixon**, Stanford University*

Too much and never enough: Synthetic excess and metabolic inefficiency of aneuploidy in tumorigenesis — ***Emma Watson**, Harvard Medical School*

Uncovering conditional vulnerabilities in cancer — ***Jason Cantor**, University of Wisconsin*

The genetics of tumor suppression by p53 — ***Maureen Murphy**, Wistar Institute*

Protein machines and disorder

In situ structural analysis of the nuclear pore complex — ***Martin Beck**, Max Planck Institute of Biophysics*

Molecular-scale structure of a high-curvature membrane — ***Adam Frost**, University of California, San Francisco*

Structure and function of DNA transposition assemblies — ***Orsolya Barabas**, University of Geneva*

Structural adventures in bacterial protein secretion and motility — ***Susan Lea**, National Institutes of Health*

Building the microtubule cytoskeleton via phase transitions — ***Sabine Petry**, Princeton University*

Structured and disordered proteins collaborate to drive membrane remodeling — ***Jeanne Stachowiak**, University of Texas at Austin*

Phase separation shapes form and function of the nucleolus — ***Richard Kriwacki**, St. Jude Children's Research Hospital*

Decoding plasticity of the dark proteome — ***Edward Lemke**, Johannes Gutenberg University*

Phase behavior of intrinsically disordered prion-like domains — ***Tanja Mittag**, St. Jude Children's Research Hospital*

Regulation of translation and deadenylation via biomolecular condensates — ***Julie Forman–Kay**, Hospital for Sick Children*

Polyubiquitin effects on phase transitions of shuttle protein UBQLN2 — ***Carlos Castañeda**, Syracuse University*

The role of phase transitions in transcription — ***Ibrahim Cissé**, California Institute of Technology*

Organelles

The degradation of misfolded proteins in the ER — ***Jeffrey Brodsky**, University of Pittsburgh*

Post-translational control of HMG CoA reductase, the rate-limiting enzyme of cholesterol synthesis — ***Russell DeBose–Boyd**, University of Texas Southwest Medical Center*

Signaling principles, signal decoding and integration revealed by stress — ***Diego Acosta–Alver**, University of California, Santa Barbara*

The role of rhomboid pseudoproteases in ERADicating misfolded membrane substrates — ***Sonya Neal**, University of California, San Diego*

Mechanisms of membrane protein sorting — ***Sichen (Susan) Shao**, Harvard Medical School*

Peroxisomal quality control in Arabidopsis — ***Bonnie Bartel**, Rice University*

Mitochondrial-derived compartments protect cells from nutrient stress — ***Adam Hughes**, University of Utah*

Regulation of mitochondrial genome synthesis in animal cells — ***Samantha Lewis**, University of California, Berkeley*

Mechanisms of stress granule regulation by ribosome-associated quality control factors — ***Stephanie Moon**, University of Michigan*

Control of translation by ubiquitin during oxidative stress — ***Gustavo Silva**, Duke University*

Proteins directing lipid fluxes at the ER-lipid droplet continuum — ***Elina Ikonen**, University of Helsinki*

The interconnected dynamics of ribonucleoprotein condensates and the endoplasmic reticulum — ***Jason Lee**, Baylor College of Medicine*

RNA/DNA

Cracking the nucleus: Finding order in chaos — ***Clodagh O'Shea**, Salk Institute*

EM structures of nucleosomes with chaperones — ***Karolin Luger**, University of Colorado Boulder*

Structural mechanism of human telomerase holoenzyme — ***Kelly Nguyen**, Medical Research Council Laboratory of Molecular Biology*

Studying DNA-related processes on DNA curtains — ***Ilya Finkelstein**, University of Texas at Austin*

m6A in the action of regulating the regulators — ***Kathy (Fange) Liu**, University of Pennsylvania*

Regulation of noncoding RNA in space and time — ***John Rinn**, University of Colorado Boulder*

RNA methylation multitasking on chromatin — ***Blerta Xhemalce**, University of Texas at Austin*

RNA methylation in gene expression regulation — ***Chuan He**, University of Pennsylvania*

Visualizing RNA in life cells — ***Timothy Stasevich**, Colorado State University*

Visualizing the dynamic genome during development — ***Alistair Boettiger**, Stanford University*

3D in situ RNA sequencing — ***Xiao Wang**, Broad Institute; Massachusetts Institute of Technology*

Engineering the repetitive 3D genome in human disease — ***Jennifer Phillips–Cremins**, University of Pennsylvania*

Signaling

Expanding the kinome — ***Vincent Tagliabracci**, University of Texas Southwestern Medical Center*

Structural basis for signaling by the HER3 pseudokinase — ***Natalia Jura**, University of California, San Francisco*

Tracing copper utilization by kinase signal transduction pathways: Implications for cancer cell processes — ***Donita C. Brady**, University of Pennsylvania*

Non-canonical ubiquitination — ***Satpal Virdee**, University of Dundee*

Large scale phosphoproteomics, dynamics and function — ***Judit Villén**, University of Washington*

CRISPR sensors for signaling — ***Stéphane Angers**, University of Toronto*

Proximity-dependent sensors for signaling — ***Anne-Claude Gingras**, Lunenfeld–Tanenbaum Research Institute*

Proteome-scale amino-acid resolution footprinting of protein-binding sites in the intrinsically disordered regions — ***Ylva Ivarsson**, Uppsala University*

Catalytic degradation in pseudoenzymes — ***Patrick Eyers**, University of Liverpool*

Cell signaling by protein tyrosine phosphatases — ***Hayley Sharpe**, Babraham Institute, Cambridge*

Defining pseudoenzymes in glycosylation pathways — ***Natarajan Kannan**, University of Georgia*

Tackling adversity: Tales of the epigenome

A sex-specific role for long noncoding RNA in depression susceptibility and resilience — ***Orna Laster**, Icahn School of Medicine at Mount Sinai*

Rethinking the stress paradigm: Exploring new connections between epigenetic adaption and cellular stress — ***Kaushik Ragunathan**, University of Michigan*

Live fast, die young: The role of epigenetics in stress and aging — ***Anthony Zannas**, University of North Carolina*

Sex-dimorphism in aging: are we missing half of the picture? — ***Bérénice Benayoun**, University of Southern California*

Intergenerational inheritance of altered metabolism phenotypes after early-life stress in Caenorhabditis elegans — ***Sarah Hall**, Syracuse University*

Epigenetic mediators of risk for metabolic disease — ***Mary Elizabeth Patti**, Harvard University*

Consequences of early-life starvation on adult lipid metabolism — ***Ryan Baugh**, Duke University*

Extracellular vesicles as stress signals: Identifying novel systemic mechanisms of trauma programming — ***Tracey Bale**, University of Maryland*

Programmed epigenetic risk: Can stress exposures in utero predispose infants to obesity and metabolic diseases — ***Kristen Boyle**, Colorado University, Anschutz Medical School*

The role of maternal factors in epigenetic programming of neurodevelopment — ***Patrick McGowan**, University of Toronto*

Epigenetic marks identify asthma susceptibility in African Americans — ***Ivanna Yang**, Colorado University, Anschutz Medical School*

Chronic stress, omics, and asthma — ***Juan Celedon**, Children's Hospital of Pittsburgh*

Early-life stress and epigenomic regulation of behavior — ***Julie-Anne Balouek**, Princeton University*

Interest groups at #ASBMB2022

On the first day of the 2022 ASBMB Annual Meeting, which will be held in conjunction with Experimental Biology in April in Philadelphia, the society will offer in-person networking events based upon attendees scientific interests.

The goal of these two- and three-hour events is to bring together people with similar research interests to present, discuss and interact.

The interest groups and their organizers are listed below. Keep an eye on the ASBMB meeting website for speaker lineups, locations and times. All will be held on Saturday, April 2.

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

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

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

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

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

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

Proteins
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
Organizers: **Marina Holz**, New York Medical College, and **Mathreye Karthikeyan**, University of Alabama, Birmingham

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

Structural biology
Organizers: **Fran Barrera**, University of Tennessee, and **Matthias Buck**, Case Western University

The joys of doing research with undergraduates

By Adele J. Wolfson

WELLESLEY COLLEGE

Adele Wolfson, standing second from right, poses with members of her lab in 2012. One of the lab's recently published papers had Yu Liu, front row second from right, as first author.

Although I now have been retired for a few years, I had two publications come out recently with former undergraduates as first authors. This prompts me to reflect on undergraduate research experiences from a faculty member's point of view.

Much has been written about the benefits of undergraduate research for students. It is considered a high-impact practice, and multiple projects exist to expand the opportunity to all students via course-based undergraduate research experiences, known as CUREs, or other models.

We see less discussion of what undergraduate research does for faculty. And such discussions tend to focus on the disadvantages for faculty — students in the lab decrease productivity, it's not fair that faculty in other fields don't have to involve undergraduates in their scholarship, by the time students know enough to be helpful they have graduated, and so on.

These complaints all contain some truth and should be taken into account by administrators when it comes to tenure and promotion decisions. But I have found many reasons to work with undergraduates, and it is not exaggerating to use the term "joys" in the title of this essay.

Among the many reasons to work with undergraduates:

They are impatient. They have four years at most in the lab. Those who already know about research will be knocking on your door the first day they are on campus, and those who learn about research when they take classes will be even more anxious to make up for lost time. This impatience is a great impetus for a new faculty member to get moving on research when they might otherwise be overwhelmed with course preparation and settling in. I never would have gotten into my own lab during my first semester teaching if it hadn't been for students eager to get involved.

They force you to think in short, self-contained projects. Not all research projects are suitable for undergraduates; for example, you likely will not want to build new instruments or develop new animal models (although both are possible if your tenure committee is patient). But small projects that can be completed in a few years can accumulate to major findings and are nice to have in hand for preliminary data. Some of my publications resulted from individual student projects, each following up on a single amino acid substitution in an enzyme or the effects of stresses on a single bacterial strain. Numerous CUREs are based on this principle: many small contributions to a larger project.

They are enthusiastic and will do anything in the lab. You don't want to stick your undergraduates with

all the menial tasks, but there is certainly lots of routine work, such as making solutions and ordering/unpacking supplies, that they are happy to do as long as they are learning and contributing.

They do not require lots of monetary resources. Unlike graduate students, for whom you might have to pay tuition and stipends, undergraduates usually do not need much funding. Resources for summer stipends and work-study can be found, and if the students are earning academic credit for research, the credit is their compensation.

Their careers are not bound up in yours. You probably will write them recommendation letters, but undergraduates are unlikely to rely on your reputation in the same way that grad students and postdocs do. This means they are freer to leave for another lab (or leave research altogether) without hard feelings, which is likely healthy for you and your department.

They offer a different lens through which to see the students in your classes. That is to say, they help you to be a better teacher. Students who traditionally are considered successful in academic work have a certain set of skills and attitudes, which may or may not be the same as the skills and attitudes needed to succeed in research. They might be afraid of failure and often don't like to ask for help. Students who are perhaps not the top of their class in terms of grades but are great in the lab recognize mistakes as opportunities to learn and are likely to embrace collaboration. Working with such students has helped me appreciate the many types of intelligence among the students in my classes and prompted me to include more teamwork and revision in assignments. By talking informally with them in the lab, I gained insight into students' thinking about scientific ideas and misconceptions.

They create a community that allows you to see the potential scientist in every student. Undergraduate research is powerful because just being part of a research group helps to build a student's identity as a scientist. This is particularly important for students from groups that historically have been excluded from scientific fields. But this is a two-way transaction; I also have benefitted from seeing students in my labs who broadened my definition of a scientist — whether students of color, those with disabilities or those returning to school after years at home or in the workforce.

I am sure my colleagues who regularly work with undergraduates in their labs will find my catalog of advantages to be commonsensical and will add more to the list. But for those faculty just starting out in academic careers, especially those who have spent their training exclusively in graduate institutions, I hope that these ideas will spark an interest in working with undergraduates and perhaps building a research program around them.

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Mentoring the next generation

By Brooke Morriswood

My lab might be closing soon because of insufficient research productivity. Is it really because I supervised too many undergraduate students? And if so, should I regret it?

I've been a group leader for seven years. I've been 100% self-funded the whole time, and in that period, nobody has been in my group longer than about nine months. I'm paid by what's known as a "golden handcuffs" grant; it covers my salary, but I'm not allowed to apply for other sources of funding. When I was awarded that grant three years ago, my request for an accompanying Ph.D. stipend was rejected.

So I adapted. I started doing more teaching and realized I loved it. No, not quite that. It was hard, and it was a hell of a steep learning curve (especially the practical classes), but it felt meaningful. I felt that I was giving something back.

As I did more teaching, slowly getting the hang of it in an unfamiliar academic environment, I began to receive a stream of enquiries for undergraduate and master's positions in the group. I had no postdocs or Ph.D.s, so I supervised them all myself.

More than that, I quickly realized that's how I wanted it. All but one year of my postgraduate and postdoctoral time was spent in research institutes, and I was very lucky to have done my Ph.D. at the Medical Research Council Laboratory of Molecular Biology in Cambridge, England, where group leaders were encouraged and to some extent expected to still be active at the bench. Being directly supervised by my Ph.D. mentor — who was actually very close to retirement at the time — had made a big impression on me. I wanted to replicate that training experience.

The only way I could be sure that every student coming through my group acquired the information I thought was important, not only learned how to use techniques but also understood them, and adhered to the professional standards I applied to myself was to look after the students personally. With this approach, I found that I could supervise a maximum of three students at a time.

Over these past seven years I've personally supervised seven master's students, seven undergraduates and 19 five-week rotation projects, over 30 students in all. I supervised more than 20 of those students in the three years since I started teaching more.

And I've gotten really, really good at supervising. Right now, we are putting the finishing touches to a research paper exploring the interplay between the cytoskeleton and endocytic machinery in the eukaryotic parasite Trypanosoma brucei that has literally two soccer teams' worth of authors. That's because it's been painstakingly assembled by all of those undergraduate students working in sequence.

But it hasn't come quickly enough. I found out recently that my grant renewal application has been unsuccessful, so the entire future of the group is uncertain. One reviewer recommended funding with high priority and the addition of a Ph.D. stipend, while the other placed it in the bottom 50% of reviewed applications and considered it not internationally competitive; both agreed that my recent publication record was weak. As ever, there are reasons but no excuses.

Such setbacks invite a degree of reflection. I've asked around, and one common thread has emerged: My mistake, so it goes, is that I have not spent enough time at the bench myself. By choosing to supervise undergraduates instead of cloistering myself, I have lost time and productivity.

There's a grain of truth to this. My productivity is roughly what it would have been if I'd worked alone at the bench full time. But when things are going well and the students are bedded in, I have six hands, and we are more productive than if I were working alone with the two hands at the ends of my arms.

Plus, as a group leader it's not possible to work full time at the bench. There's not just the teaching; there are all the myriad other bits and bobs that go with being a contributing, engaged and helpful member of a department. Would that department view me as an asset if I had refused to do those things? I doubt it. But in seeking to be a good colleague and a good mentor, I may have sabotaged my research career.

Besides these questions of productivity, though, supervising undergraduates in the lab is really, really great fun. It's fun communicating the basics, reassuring to realize that I still understand them (there's a selfish case

for teaching and mentoring, after all), and an entertaining challenge trying to enthuse students about a topic.

And it's important too. The coronavirus pandemic has shown how integral science is to contemporary society and how important an informed and supportive public is. We need people going out into the wider world knowing how science works, believing it's important and trusting its practitioners.

I've often heard group leaders in postdoc-rich environments complaining that we train too many Ph.D.s. They're wrong. If there's a glut of Ph.D.s on the academic job market, then it means we're telling them that academia is the default route and we're not highlighting other career options clearly enough.

I'm also hearing more and more (often from colleagues in research-intensive environments) that the quality of incoming Ph.D.s isn't high enough. Research techniques are getting more sophisticated, so more and more expert training is needed at an earlier stage. We need to involve undergraduates as early as possible. We need to expose them to frontline research early on so that they gain relevant experience and inculcate the right standards.

There is value to making sure that undergraduates get high-quality training not just for research but for society at large. I could have been at a bench on my own these last few years, but I'm happier that I've sent out 30 students who know how science feels and how good science is done.

Yes, I've been dumb. I'm guilty of doing the job the way I think it should be done instead of looking at how I was supposed to be doing it. It took time, apparently too much time, to learn how to do all this efficiently, and I made a lot of the usual new group leader mistakes along the way. I don't think the choice between doing it alone or doing it with undergraduates was the problem. I think the main problem was not having even a single Ph.D. student this whole time.

I don't know if I could have done better with the hand I was given, and I'm happy with the way I played it. I had a hell of a lot more fun interacting with all those young scientists than I would have done working alone every day of the week.

If this is the end, then it doesn't feel like such a bad hill for my academic career to die on. I believe in the potential of young scientists. I believe they deserve the best possible introduction to bench science. I believe they benefit enormously from close interaction with experienced scientists, and I believe this is something I can do to make a difference.

I'm not going to change my approach. Wish me luck.

This essay is adapted from Brooke Morriswood's blog, Total Internal Reflection.

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Science is a human endeavor

Lessons learned from the dogged pursuit of a Nobel laureate's error

By H. Richard Levy

The general public may think of science as a cold, heartless endeavor and of scientists as individuals concerned solely with cold facts, but of course this is not true. Many of us are passionate about our work. We exhibit the same foibles as nonscientists: hubris, jealousy, competition, exhilaration, disappointment. Much of what we do depends on human interactions, and our work is affected by the lives and deaths of our colleagues and peers.

One of the most frustrating periods of my research career occurred in the early 1980s. While reviewing scientific literature in the late 1970s for a review I was writing about the enzyme glucose 6-phosphate dehydrogenase, or G6PD, for the series Advances in Enzymology, I ran across a paper published in 1974 by Leonard Eggleston and Hans Krebs that aroused my interest. It purported to describe a novel mechanism for the regulation of hepatic G6PD by an unidentified factor.

In March 1977, I wrote to Krebs asking whether any further unpublished work had been done that I could cite in my review. He replied that since Eggleston had died the work had been in abeyance but that he recently had taken it up again and was trying to identify the factor. He would keep me apprised of any progress. In September, he wrote again that he had nothing new to report; a few attempts to identify the factor had been unsuccessful.

I decided that we would take up this problem in my lab. We did so and encountered baffling difficulties that took long to resolve in a process that included both gratification and grief.

WIKIMEDIA COMMONS

Hans Krebs, shown here in his 1953 official Nobel Prize portrait, was a pioneer in the study of cellular respiration and discovered the citric acid and urea cycles.

Meeting a giant

Krebs, one of the giants of 20th century biochemistry, was born in Hildesheim, Germany, in 1900. As a Jew, he was forced to resign his position at the University of Freiburg soon after Hitler came to power in 1933. He went to the University of Cambridge in England and then to the University of Sheffield, where he produced his most widely recognized work, the elucidation of the metabolic pathway that became known as the Krebs cycle. In 1953, he was awarded the Nobel Prize in physiology and medicine.

A year later, I was a graduate student at the University of Chicago when Krebs came to spend a month in the biochemistry department. We graduate students had a biochemistry club, and that year I was its president (the title was actually "dictator"). We invited him to give a talk, which he did. This is how I first met him. I met him several times subsequently and was always impressed that he remembered me and details about me.

When I was on sabbatical leave at Oxford University in 1973–1974, Krebs had a position at the Radcliff Infirmary, and I talked with him on several occasions. He had led Oxford's biochemistry department until his mandatory retirement in 1967.

Finding the flaw

I thought — correctly, as it turned out — that the research following up on Krebs' work would be too risky a problem to give to a graduate student, so I asked my technician, Melody Christoff, to undertake the experiments.

The essence of Krebs' finding can be summarized as follows: G6PD plays an important role in carbohydrate and lipid metabolism in several tissues including the liver. It catalyzes the oxidation of glucose 6-phosphate using the coenzyme nicotinamide adenine dinucleotide phosphate, or $NADP^+$, which thereby is reduced to NADPH. NADPH is a potent $NADP^+$-competitive inhibitor of G6PD, and in mammalian tissues, it is present in concentrations 100 times greater than that of $NADP^+$. Under these conditions, G6PD should be totally inhibited, yet it is known to be highly active.

Krebs' experiments sought to resolve this paradox. The Eggleston and Krebs paper reported that rat liver extracts contain an unidentified,

macromolecular, highly unstable cofactor, which together with oxidized glutathione overcomes this NADPH inhibition, thus providing a physiological explanation for this paradox. My goal was to identify this cofactor.

First, though, we had to repeat Krebs' experiments. We devoted enormous time and effort but were unable to confirm certain key findings. I consulted with several colleagues to no avail.

Ultimately, by following minutely every facet of the experimental protocols in the paper, we found two mutually reinforcing errors that had allowed the authors to make their interpretation. The first error was one in basic enzyme kinetics: a large correction they made for the reaction rate in the absence of glucose 6-phosphate that, because of the saturating substrate concentration they used, was unnecessary and thus incorrect. The second error was that their use of $ZnCl_2$ to inhibit endogenous glutathione reductase led to an interfering absorbance at the same wavelength used to measure the enzyme activity. It was critical to inhibit glutathione reductase in their experiments because this enzyme catalyzes the oxidation of NADPH in the presence of oxidized glutathione, thereby removing the inhibitory NADPH; but because of its interfering absorbance, $ZnCl_2$ was an inappropriate choice.

When we took these two artifacts into consideration, we were able to reconcile Krebs and Eggleston's data with ours but proved that their conclusions were incorrect.

A gracious concession

In September 1980, I wrote a detailed letter to Krebs about our findings and conclusions. I mentioned that I would be in England the following year and would be pleased to meet with him to discuss our data. He replied that he was intensely interested. We met on July 28 for an hour. He was impressed with our work, told me that the problem was important and urged me to publish it but agreed it would be best if we understood it better first. He conceded readily that what they had called a cofactor could well be the result of a constellation of artifacts. Also, I told him that two Spanish workers had repeated his findings using mussel hepatopancreas and that they claimed to have isolated the cofactor.

COURTESY OF RICHARD LEVY

Thinking the research following up on Krebs' work would be too risky a problem to give to a graduate student, Richard Levy asked his technician, Melody Christoff, to undertake the experiments. In this photo of the Levy lab taken in 1981, Christoff and Levy are third and fourth from the left respectively.

Upon my return to Syracuse, I sent Krebs reprints of a recent article by Birgit Vennesland, who had been my Ph.D. advisor, and one by Efraim Racker, both of which I had mentioned to him at our meeting. I also enclosed two of my recent articles, one on the simultaneous analysis of both activities of dual-nucleotide-specific dehydrogenases and another on its application to the regulation of G6PD from Leuconostoc mesenteroides. I told him I planned to do a little more work on our study and then would write it up for publication and that I would send him a copy. In his reply, dated Aug. 24, 1981, he expressed surprise at Birgit's lively and robust style of writing, stated that he was somewhat skeptical about the Racker paper and commented favorably about my papers. He also recalled our first meeting in 1954. Two months later, Krebs died unexpectedly.

Meanwhile, Melody and I wound up our research. In February 1983, I submitted the manuscript to the Biochemical Journal, the British journal in which Eggleston and Krebs' paper had appeared. In my letter to the editor, I provided some background to our work, including the interactions with Krebs, and wrote, "His death so soon after I had seen him and had witnessed his lively and vigorous intellect (seemingly undiminished from 27 years previously, when we had first met) was a great shock and I felt it inappropriate to publish at that time. In the meantime, we have reconfirmed

all our findings."

The journal responded in its editorial report: "The authors appear to have disposed convincingly of a misleading artifact. Their covering letter reveals some anxiety about challenging the work of an eminent scientist so soon after his death, but there can be little doubt that the scientist in question would have wanted to see this matter cleared up and would have been intrigued by the explanation."

The paper was accepted for publication with minor revisions and appeared that year.

A troubling footnote

When Melody Christoff came to work for me in the early 1980s, she told me she had suffered from leukemia but that it was now in remission. In the fall of 1982, she began to experience signs of a relapse. She was admitted to the Roswell Park Cancer Institute in Buffalo to receive a bone marrow transplant. While she was recovering there in an isolation unit because of her compromised immune system, we continued to correspond about the manuscript.

Early in 1983, Melody wrote that the Roswell Park doctors had found an infection in her. She finished her letter in midsentence, clearly recognizing the import of what she had written. On April 3, she died.

All the bone marrow transplant patients at Roswell Park died because the isolation ward had become contaminated with a fungus; with their drastically compromised immune systems, none of the patients were able to withstand the infection. This resulted, later, in a class-action suit against the institute.

Melody left behind a husband and two daughters. She had been a superb technician and a wonderful human being.

Thus, of the four individuals associated with this study — Eggleston, Krebs, Christoff and Levy — I was now the sole survivor. And just as the Eggleston and Krebs' paper contained a footnote about Eggleston's death, so now our paper included a footnote about Melody's death.

Spectacular fraud

Although not directly pertinent to the work on G6PD described here, the paper by Racker that I sent to Krebs, and about which he expressed skepticism, represents another, darker human dimension in scientific endeavors.

Racker, like Krebs, was one of the leading biochemists of the 20th century. Also like Krebs, he was a Jew who had escaped Nazism, leaving Austria first for Britain and then settling in the United States. (Incidentally, I too am a Jew who escaped Nazi Germany, in my case as a nine-year-old boy.)

The paper I had sent Krebs claimed to provide support for Racker's hypothesis that ATPase plays a key role in cancer. It had aroused intense discussion in the scientific community, primarily because the lead author, Racker's graduate student Mark Spector, purportedly had done the experiments so rapidly that it strained credulity. Spector was a brilliant, talented graduate student who appeared to have answers for all the criticisms levelled at him at numerous scientific meetings.

It turned out that the publication was based on completely fabricated data, one of the most spectacular cases of scientific fraud in the second half of the 20th century. Spector's deception was fabricated cleverly, fooling many, including Racker, whose reputation suffered, but the fraud was exposed. Krebs' skepticism proved prescient.

Lessons learned

The saga of this work contains several important lessons. First, it bears out the dictum that science is self-correcting. Errors occur even in peer-reviewed, published papers and can be corrected provided they are noticed and pursued.

Second, the pursuit of such errors can be dogged. Melody Christoff and I devoted a great deal of effort to solving this problem because we were convinced that something was wrong and because G6PD regulation was an important subject.

Third, even eminent scientists make mistakes, and one of the great things about the ethos of science is that it cares about the truth, not the reputation of those pursuing it.

Fourth, although science is objective, it is carried out by human beings, and thus subjective factors can impinge. The deaths of Melody Christoff and Hans Krebs will be linked forever with this work in my mind.

Finally, the kindness, graciousness and humility of Hans Krebs, as reflected in all his interactions with me and displayed in the letter mentioned above, left an indelible impression. I have met other distinguished scientists in my life, but few share these attributes with Krebs.

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