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ASBMB TODAY

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

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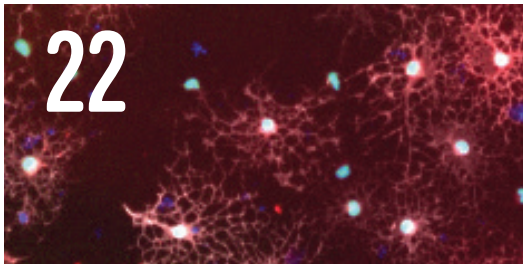

ASBMB TODAY

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

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With challenges come opportunities

By Toni M. Antalis

It is a a special honor to begin my term as president of the American Society for Biochemistry and Molecular Biology. The ASBMB is very dear to me.

I began my scientific career as an undergraduate obtaining summer research experience in a biochemistry lab and have been hooked ever since. My doctoral thesis research at Rice University focused on biophysical and kinetic analysis of electron transport in cytoahrome oxidase, which led to a first-author paper in the Journal of Biological Chemistry. Publishing that first paper in JBC and receiving those reprints with my name in print for the first time was truly exciting!

My research interests have evolved over the years into the study of proteases and protease-activated signaling pathways that affect tumor metastasis, inflammation and vascular biology. My lab studies several inflammatory mechanisms that promote blood clotting and the resolution of venous thrombosis as well as proteolytic signaling pathways used by ovarian cancers to facilitate tumor dissemination and spread.

I have continued my association with the society by serving on the Publications Committee and the Finance Committee and later as treasurer. This has allowed me to see the ASBMB grow and develop into a robust organization that strives to meet the needs of all of its members.

Thanks to the ASBMB scientific leadership, the excellent staff and the many dedicated committee volunteers, the society is in great shape. This is particularly important in the present COVID-19 environment and given the novel challenges we, as scientists, are facing. Universities have closed, and much research has been halted this year. We all cautiously are working out safe conditions for reopening and continuing laboratory research. A new paradigm is emerging at universities — virus testing systems are being put in place, and there are changes to the formal academic processes, which will undoubtedly have lasting effects. Many scientific and teaching activities are moving fully or partially online, with strict guidelines for social distancing and mask wearing.

This is unchartered territory. It has impacted our younger scientists significantly: graduate students aiming to complete their dissertations, postdoctoral fellows looking for jobs and junior faculty trying to build networks and collaborations. The ASBMB is committed to providing career-development resources for these groups, including its recently revamped online career center, the Art of Science Communication course and virtual presentation opportunities. (See asbmb.org/career-resources for those and more.)

Therewill be challenges in maintaining financial support for discovery research with increasingly competitive funds and uncertain economic conditions. The ASBMB serves as a defender of science and influencer of government policy on issues of concern to ASBMB members. The society responds rapidly to policy proposals and changes and

stands firmly against attempts to politicize science and science funding. (See asbmb.org/advocacy for recent policy statements and to learn how to participate in advocacy efforts.)

Importantly, we must ensure social justice, fairness and civility for all and in all that we do.

Our immediate past president, Jerry Hart, did a tremendous job guiding the society through some major challenges over the past two years and deserves a special thanks. Importantly, he led the careful and consultative effort by the society to make all three ASBMB journals — JBC, Molecular & Cellular Proteomics, and the Journal of Lipid Research — fully open access in 2021. This means that the final versions of the high-quality articles will be immediately available to everyone around the world, thus reducing barriers to scientific knowledge and accelerating scientific discoveries. A long history of sound financial stewardship by the society has enabled this to happen in an affordable way for authors — society members and nonmembers alike.

We are truly indebted to Herbert Tabor, who served at the helm of JBC for 40 years and who strongly supported and helped to mold the community of biochemists and molecular biologists that we have today. JBC Editor-in-Chief Lila Gierasch, MCP Editor-in-Chief Al Burlingame and JLR co-Editors-in-Chief Nicholas Davidson and Kerry-Anne Rye are doing wonderful jobs of overseeing their publications with the support of excellent associate editors and editorial board members, all of whom deserve our thanks for their dedicated service to the society and the scientific community.

With challenges come opportunities. This is an exciting time to be a molecular and biological scientist. Advances in genomics, imaging, bioengineering, CRISPR technologies, cryogenic electron microscopy, vaccine development and computational learning are advancing our understanding of biological systems significantly.

The ASBMB is devoted to advancing the science of biochemistry and molecular biology and serving the needs of the scientific community. I encourage you to visit the ASBMB website (asbmb.org) to learn about all of the resources and wonderful activities that the society provides and the impact on our scientific community.

You too can join this effort and make a difference. Let us know what will make us even better. We welcome your thoughts.

Read ASBMB Today science writer Laurel Oldach's interview with Toni Antalis on page 30.

Toni Antalis (tantalis @som.umaryland.edu) is a professor of physiology at the University of Maryland School of Medicine, where she is also the associate director for training and education and the director of the program in molecular medicine and the graduate program in life sciences. She began her term as the ASBMB's president on July 1.

Royal Society elects Clore as fellow


Clore

Marius Clore, National Institutes of Health distinguished investigator and chief of the Protein Nuclear Magnetic Resonance Section at the Laboratory of Chemical Physics in the National Institute of Diabetes and Digestive and Kidney Diseases, has been elected a fellow of the Royal Society.

Clore, a molecular biophysicist and structural biologist, is best known for pioneering characterization of the three-dimensional structures of proteins and nucleic acids using nuclear magnetic resonance spectroscopy. In addition to describing proteins from pathogens, phosphorylation-dependent structural and binding changes, and the structures of macromolecular complexes, Clore is also known for development of biophysical methods that have continually extended the range of applicability of NMR. Recently, his work has focused on development of new NMR methods to capture very short-lived conformational states, which are a small proportion of a population of macromolecules but are often critical for function. He has received numerous honors, including election to membership in the National Academy of Sciences and fellowship in the American Academy of Arts and Sciences.

The Royal Society, the U.K.'s national scientific academy, equivalent to the U.S. National Academy of Sciences, was founded in 1660. It publishes journals, makes policy recommendations and hosts scientific meetings. The Royal Society has about 1,700 fellows, with 50 elected for life each year on the basis of their scientific contributions. Americans are eligible to join the Royal Society only as foreign members; the society, however, changed its rules two years ago to allow dual citizens (not resident in the U.K. or Commonwealth) such as Clore to become full-fledged fellows.

Clore discusses his JMR article, "A common sense approach to peak picking in two-, three-, and four-dimensional spectre using automatic computer analysis of contour diagrams," in a video at youtube.com/watch?v=pmrDK_IOZKc.

Yura joins membership committee


Yura

Renee Yura is the newest member of the American Society for Biochemistry and Molecular Biology Membership Committee.

Yura is a director of diagnostics at Pfizer, Inc. where she leads implementation of companion diagnostic strategy in internal medicine, inflammation and immunity, and rare disease. She has more than ten years of experience in companion and complementary diagnostic assay development, and she previously worked at Celgene, Novartis and Ortho Clinical and Janssen Diagnostics. She received her Ph.D. in cell and molecular biology from the Pennsylvania State University College of Medicine in Hershey, Pennsylvania.

Yura will serve a three-year term on the membership committee, which focuses on the retention, growth and engagement of the ASBMB membership. The committee is charged with considering, reviewing and recommending actions to implement programs, benefits and services to advance the mission of the society and meet the needs of its members. She will also participate in the Industry Engagement subcommittee.

Ed Eisenstein, chair of the committee, said, "My colleagues on the membership committee and I are thrilled that Renee is joining our efforts. She has an ideal background and interesting ideas on how to help us develop benefits and programs of interest to society members that are interested in transitioning to a career in industry. We can't wait to start working with her."

Johnson named dean at UCLA


Johnson

Tracy Johnson, a professor of molecular, cell, and developmental biology at the University of California, Los Angeles, has been appointed dean of the division of life sciences in the UCLA College, effective Sept. 1.

Johnson, who holds the Keith and Cecilia Terasaki presidential endowed chair, has been a UCLA faculty member since 2013 and has served as associate dean for inclusive excellence in the division of life sciences since 2015. Before coming to UCLA, she was a member of the UC San Diego biological sciences faculty. She earned her bachelor's degree in biochemistry and cell biology at UC San Diego and her doctorate in biochemistry and molecular biology at UC Berkeley. She was a Jane Coffin Childs postdoctoral fellow at the California Institute of Technology.

Johnson's research focuses on un-

derstanding the mechanisms of gene regulation, particularly RNA splicing, chromatin modification and the intersection between these reactions.

A Howard Hughes Medical Institute professor, Johnson also started the UCLA-HHMI Pathways to Success program for students from diverse backgrounds in STEM fields. She is the principal investigator for an HHMI grant aimed at promoting greater access and success for students studying life sciences who transfer from community colleges.

Johnson has served as a permanent member and then chair of a National Institute of General Medical Sciences study section, is a member of the National Cancer Institute Board of Scientific Counselors, and serves on the executive board of the Society of HHMI Professors. At UCLA, she is the chair and director of the biomedical research minor and a member of the UCLA Human Pluripotent Stem Cell Research Oversight committee.

Student chapter president Evensen wins awards


Evensen

Claire Evensen, a college senior who graduated from the University of Wisconsin–Madison in May with a degree in biochemistry and mathematics, is taking a string of honors along with her.

Evensen served as president of the ASBMB Student Chapter at UW-Madison. Her research in ASBMB member Thomas Record's lab focused on the biophysics of transcription initiation by RNA polymerase.

At graduation, the university


CAROLYN LAGATTUTA

Carol Greider shared both the 2006 Lasker Award and the 2009 Nobel Prize in Physiology or Medicine.

Greider to move to UCSC

Carol Greider, a Bloomberg distinguished professor, Daniel Nathans professor and chair of the department of molecular biology and genetics at Johns Hopkins University School of Medicine, will join the faculty at the University of California, Santa Cruz, in October as a distinguished professor of molecular, cell and developmental biology.

Greider has been visiting UCSC while on sabbatical from Hopkins since September 2019. She told a UCSC press officer, "The science here in MCD Biology is fantastic … I also see opportunities to make a difference in terms of underserved populations and women in science."

Equity in STEM has long been a passion for Greider. She served on a National Institutes of Health working group that delivered recommendations to end sexual harassment, participated in a congressional briefing on the same topic that the ASBMB sponsored in 2018, and wrote a policy paper with colleagues on increasing gender diversity in the scientific workforce that appeared in Science in 2019.

Greider is best known for her discovery as a graduate student of telomerase, the enzyme that lengthens telomeres, permitting cells to continue replicating DNA without losing genetic information. She has been widely recognized for that work, sharing both the 2006 Lasker Award and the 2009 Nobel Prize in Physiology or Medicine with graduate mentor Elizabeth Blackburn and collaborator Jack Szostak.

Greider's lab at Hopkins, where she joined the faculty in 1997, has continued to explore the molecular mechanisms of telomere elongation and regulation, describing and characterizing more components of the telomerase complex in yeast while also investigating the role of telomeres in aging and degenerative diseases in humans.

CONSTANCE BRUKIN

Bruce Stillman and colleagues determined the mechanism and control of the initiation of DNA replication in eukaryotic cells.

Stillman wins Heineken Prize

Bruce Stillman, president and CEO of Cold Spring Harbor Laboratory, has been awarded the Dr. H.P. Heineken Prize for Biochemistry and Biophysics for his research on eukaryotic DNA replication.

Stillman's lab studies the process by which DNA is copied within cells before they divide. Working with yeast and human cells, his team has identified many cellular proteins that function at the DNA replication fork during the S phase, the portion of the cell-division cycle when DNA synthesis occurs. Among these are proteins that facilitate the assembly of chromatin, the protein–DNA complexes that form chromosomes. Stillman and colleagues have also determined the mechanism and control of the initiation of DNA replication in eukaryotic cells.

A native of Australia, Stillman earned a Ph.D. from the John Curtin School of Medical Research at the Australian National University and then moved to Cold Spring Harbor Laboratory as a postdoctoral fellow in 1979. He was promoted to the scientific staff in 1981 and has been at the laboratory ever since, serving as director of its cancer center from 1992 to 2016. He was appointed president in 2003.

Stillman has been elected to the Royal Society, the U.S. National Academy of Sciences, the American Academy of Arts and Sciences and the Australian Academy of Science. He has been named a fellow of the American Association for Cancer Research and his previous awards have included the 2014 Herbert Tabor Research Award and the 2019 Gairdner Award.

The Heineken Prize for Biochemistry and Biophysics, bestowed by the Royal Netherlands Academy of Arts and Sciences, honors top international researchers in biochemistry and/or biophysics whose scientific work offers new perspectives, achieves breakthroughs and opens up new avenues for others. The biennial Heineken prizes, also awarded in medicine, art, history, environmental science and cognitive science, are the Netherlands' most prestigious scientific award.

announced that Evensen had received the Teddy Kubly Award for Comprehensive Undergraduate Excellence, a $2,000 prize honoring students who have shown personal initiative, high academic achievement, leadership and communication skills, and financial self-support. This is the latest in a long series of awards for Evensen, including Goldwater, Astronaut and Marshall scholarships. She was also a finalist for a Rhodes scholarship.

Evensen's next step will be to attend the University of Oxford for a master's program in mathematical

Taylor among Diverse's top 35

Taylor

Diverse magazine has named **Erika Taylor,** an associate professor of chemistry, environmental studies and integrative sciences and faculty director of the McNair Program at Wesleyan University, one of its 2020 top 35 women in higher education.

As the faculty director of Wesleyan's Ronald E. McNair Post-Baccalaureate Program since 2018, Taylor works with students from underrepresented groups to help them succeed in postgraduate education. Women and other underrepresented students have comprised more than three-quarters of her 75 lab members to date.

Taylor's research focuses on enzyme mechanism determination, gene function assignment, transition-state and mechanism-based inhibitor design, and directed evolution of enzyme function. Her lab takes a multidisciplinary approach to investigating problems, seeking ways to exploit enzymes found in nature to perform reactions that will

advance the fields of chemistry and medicine.

Taylor holds a bachelor's degree in chemistry with honors from the University of Michigan at Ann Arbor and a Ph.D. in chemistry from the University of Illinois at Urbana–Champaign. She did her postdoctoral research at Albert Einstein College of Medicine. She joined the Wesleyan faculty in 2007.

Founded in 1984 as Black Issues In Higher Education, Diverse: Issues in High Education is a source for news and information on educating people of color and other underrepresented groups. The magazine wrote that Taylor "has been a passionate advocate for diversity, lending time and energy to provide opportunities in science for female, minority and low-income students."

Koleske appointed Ensign professor at Yale

Koleske

Neuroscientist **Anthony Koleske** has been appointed the Ensign professor of molecular biophysics and biochemistry and of neuroscience at Yale School of Medicine.

Koleske joined the Yale faculty in 1998. His lab focuses on the molecular mechanisms of dendrite and synapse development in neurons, processes that rely on cell adhesion and cytoskeletal remodeling. Using biochemistry, anatomy, advanced imaging approaches and electrophysiology, the lab investigates cell surface receptors, kinases and cytoskeleton modulators that govern brain development and its impact on cognition, learning and other behaviors. The lab is also pursuing genetic abnormalities linked to neurodevelopmental and

EMORY UNIVERSITY

Liz Enyenihi contributed to recent work that identified patients with biallelic variants in the EXOSC5 gene.

Enyenihi wins Emory chemistry award

Liz Enyenihi, a member of Emory University's American Society for Biochemistry and Molecular Biology Student Chapter, has received the school's excellence in chemistry award recognizing a senior who has excelled in chemistry throughout their Emory career.

While still in high school, Enyenihi was co-author on a published paper studying an RNA binding protein in cancer cells. She joined Anita Corbett's lab in the fall of her first year at Emory and has studied how pathogenic missense mutations in a complex required to process RNAs cause distinct, and sometimes fatal diseases. She has modeled RNA exosome malfunction in a budding yeast model system to explore how the specific amino acid changes encoded by these missense variants alter the function of this essential, evolutionarily conserved complex. She contributed to recent work published in Human Molecular Genetics that identified patients with biallelic variants in the EXOSC5 gene, and she is working on another co–first author publication. Last summer, she worked in Anton Bennett's lab at Yale University on a project that included investigating the effects of a Noonan syndrome–linked mutation on cell-signaling pathways.

A Woodruff Scholar at Emory, Enyenihi received highest honors for her senior thesis, the chemistry department's ACS Undergraduate Award for Excellence in Analytical Chemistry and a Goldwater Scholarship. She has balanced her academic interests with social justice issues on campus, volunteering with Project SHINE and as a STEM Pathways mentor.

"Working with Liz was absolutely like interacting with a graduate student," Corbett said. "On campus, she was also a role model and leader seeking to engage others in the STEM fields. I am delighted to have had this opportunity to work with such an outstanding scientist, and I greatly look forward to following her career."

She will return to the Bennett lab at Yale for the coming year while she applies to M.D./Ph.D. training programs. Her doctoral degree will ideally include a planned study of how variations in the microbiome may be linked to racial health disparities.

psychiatric disorders to understand how they disrupt normal neurodevelopment.

Koleske is the deputy dean for scientific affairs for the basic sciences at the Yale School of Medicine. Previously, he served as director of Yale's combined Ph.D. programs in the biological and biomedical sciences. He was co-founder and co-director of the university's Amgen Scholars summer research program for undergraduates pursuing research careers and has directed the China Scholarship Council/Yale World Scholars program.

The Ensign professorship is a 10-year, renewable position at the medical school, endowed by an anonymous donor in 1951 to honor Ralph Hart Ensign, a 19th century Connecticut merchant and manufacturer.

Miesenböck shares Shaw Prize


Miesenböck

Oxford professor **Gero Miesenböck** is one of three recipients of the 2020 Shaw Prize in Life Science and Medicine. Miesenböck, the Waynflete professor of physiology and director of the University of Oxford's Centre for Neural Circuits and Behavior, shares the prize with Peter Hegemenn of the Humboldt University of Berlin and Georg Nagel of the University of Würzburg in Germany for their contributions to the development of optogenetics.

Before the field of optogenetics developed, researchers could use electrophysiology to stimulate individual neurons or groups that were closely linked in space but not neurons that were members of the same functional network but dispersed throughout the brain. By genetically manipulating neurons to express the membrane photoreceptor rhodopsin and some associated signaling proteins, Miesenböck and his lab successfully activated selected neurons using light in 2002. They followed up with a demonstration that photoactivation of neurons could control behavior in fruit flies in 2005 and have continued to use optogenetic techniques — now with the easier-to-use channelrhodopsin protein — to understand how the brain organizes and processes information.

Wooldridge wins Virginia Tech award for undergraduate research

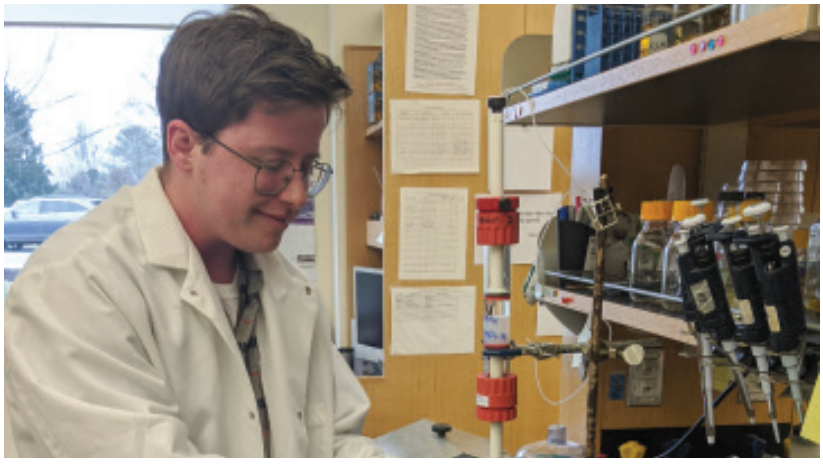
Rowan Wooldridge, an undergraduate at Virginia Polytechnic Institute and State University, won the university's inaugural Undergraduate Research Excellence Award.

Rowan Wooldridge will graduate this fall with a degree in biochemistry and will go on to graduate school.

Wooldridge, a member of Virginia Tech's American Society for Biochemistry and Molecular Biology Student Chapter, was one of three undergraduates to receive the award after the Dennis Dean Undergraduate Research and Creative Scholarship Conference, which was held virtually after the university's midsemester shift to remote learning. The daylong celebration was aimed at offering undergraduates the opportunity to gain experience communicating their research or creative scholarship while engaging faculty and other students.

During the conference, Wooldridge presented his work on molecules that bind to two uncharacterized receptors in Sinohizombium meliloti, a bacterium that fixes atmospheric nitrogen and forms a symbiotic relationship with certain legumes. His findings highlight how a better understanding of this process could lead to a reduction in chemical fertilizer use.

"This experience as an undergraduate researcher has really opened my eyes to how passionate I am about science," said Wooldridge, who is set to graduate this fall with a degree in biochemistry and plans to attend graduate school for biochemistry at Virginia Tech. "I could not have asked for a better experience to lay the groundwork for the rest of my career."


COURTESY OF ROWAN WOOLDRIDGE

Rowan Wooldridge studies a bacterium that fixes atmospheric nitrogen and forms a symbiotic relationship with certain legumes.

Optogenetics has become widespread in neuroscience and Miesenböck has received numerous awards and prizes for the work.

Miesenböck grew up in Austria, where he earned his medical degree, then went to New York to conduct postdoctoral research at Memorial Sloan Kettering. He stayed on in New York as an assistant professor at Cornell University and later joined the faculty at Yale University. He moved to his current position at Oxford in 2007.

The three annual Shaw prizes — in astronomy, life science and medicine and mathematics — each come with an award of $1.2 million. The prizes are named for the late Hong Kong entertainment mogul and philanthropist Run Run Shaw, who established them in 2002.

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 don't forget to include a photo!

Louis B. Justement is FASEB's new president. Mary-Ann Bjornsti is FASEB's new vice president-elect for science policy.

Justement, Bjornsti assume leadership positions at FASEB

Louis B. Justement, a professor of microbiology at the University of Alabama at Birmingham, took office as the new president of the Federation of American Societies for Experimental Biology on July 1. FASEB is a coalition of 29 scientific societies (including the ASBMB) that advocates for sound scientific policy and increased research funding in the biological and biomedical sciences. It also publishes rigorous and reproducible research and hosts the Science Research Conferences series.

Justement, whose studies focus on signaling pathways involved in B cell terminal differentiation, directs UAB's graduate and undergraduate programs in immunology and has published on biomedical education and training.

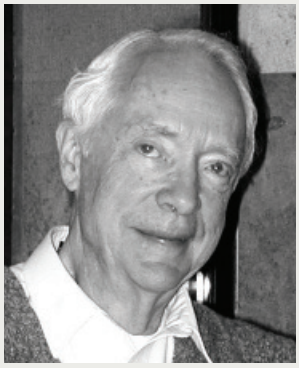
In a Q&A that FASEB published, Justement emphasized his plans to redouble the organization's advocacy efforts to promote the role of science as a source for apolitical, factual information to policymakers and legislators. He said he also intends to increase FASEB's efforts to improve diversity, equity and inclusion in science and to work diligently with the FASEB board and staff to mitigate the impacts of the COVID-19 pandemic on FASEB's finances.

Mary-Ann Bjornsti, who chairs the department of pharmacology and toxicology at UAB and is the associate director for translational research at the O'Neal Comprehensive Cancer Center, has become FASEB's vice president-elect for science policy.

Bjornsti studies the role of the small ubiquitinlike modifier, or SUMO, in response to DNA damage during replication, with particular interest in protein SUMOylation during chemotherapy and the potential for modulating the SUMO pathway as a new cancer therapy.

She also serves as secretary/treasurer for American Society for Pharmacology and Experimental Therapeutics, a FASEB member society, and previously was president of the Association of Medical School Pharmacology Chairs.

Earl Davie



Earl Davie was named a Legend in Hematology by the American Society of Hematology in 2008.

Earl Warren Davie, a pioneer in the study of blood clotting, died June 6.

Davie was born in Tacoma, Washington, in 1927 and earned his undergraduate and doctoral degrees from the University of Washington in the 1950s. As a graduate student, he worked with Hans Neurath on protein structure and function. (Read the Journal of Biological Chemistry's 2005 Classic article about their work, "Hans Neurath: the Difference Between Proteins That Digest and Proteins That Are Digested.")

Davie was a postdoctoral fellow at Harvard University, where he worked with Nobelist Fritz Lipmann. He then took a faculty position at Case Western Reserve University School of Medicine, where he met Oscar Ratnoff and blood research first piqued his interest. He returned to UW to join the faculty in 1962.

Davie and colleagues reported the waterfall sequence (sometimes called the waterfall cascade) in the journal Science in 1964. This sequence begins with the activation of a small amount of a factor and results in the production of large amounts of thrombin and then fibrin. (Read the JBC's 2006 Classic article on Davie's work, "The Waterfall Sequence for Blood Clotting: the Work of Earl W. Davie.") Davie's blood coagulation research informed the development of numerous clinical tests and therapeutics.

He became a member of the JBC editorial board in1968 and served two, nonconsecutive terms. By 1975, he became chair of the UW biochemistry department, serving for almost a decade. He also served as secretary of the ASBMB during that time.

He was elected to the National Academy of Sciences and named editor of the journal Biochemistry in 1980. And in 1981 he co-founded one of Seattle's first biotech companies, ZymoGenetics, which was later bought by Novo Nordisk and then Brisol–Myers Squibb.

Zena Werb

Zena Werb, a professor at the University of California, San Francisco, a renowned cell biologist, a pioneer in cancer research and an advocate for women in science died June 16. She was 75.

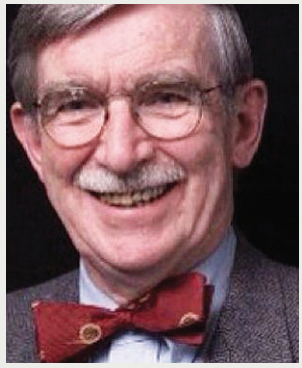
Born in a refugee camp near Bergen-Belsen during World War II, Werb moved with her family to Canada in 1948. She was educated in a one-room schoolhouse in rural Ontario before attending the University of Toronto. She earned her Ph.D. in cell biology at Rockefeller University, New York, studying with Zanvil Cohn and did postdoctoral studies with John Dingle at the Strangeways Research Laboratories in Cambridge, U.K.

Werb worked at Dartmouth Medical School before finding her academic home of more than 40 years at UCSF where she became vice chair of the anatomy department. She was also the co-leader of the cancer, immunity and microenvironment program at the Helen Diller Family Comprehensive Cancer Center and a member of the executive committee of the Sabre-Sandler Asthma Basic Research Center at UCSF.

The Werb lab studies the effects of the extracellular matrix microenvironment and its component proteases on cells, particularly in stem cell maturation and neoplasia. Werb's work in establishing the active role of the ECM in normal cell signaling and in cancer progression is widely recognized: Her lab discovered several matrix metalloproteases and characterized both the protease cascades that activate these enzymes, and the endogenous inhibitors that block them, contributing to a growing understanding of the importance of proteolysis in regulating signal transduction. The lab identified roles for cleaved fragments of ECM proteins that differed from the full-length molecules, studied integrin signaling and, in recent years, investigated protease activity in stem cell proliferation and angiogenesis.

Werb received many honors for her work, notably the E.B. Wilson Medal from the American Society for Cell Biology. She was a fellow of the American Academy of Arts and Sciences and member of the National Academy of Science with a lifetime achievement award from Women in Cell Biology and a UCSF lifetime achievement award in mentoring.

Edward L. Hogan



Edward Leo Hogan, who served as chair of the neurology department at the Medical University of South Carolina, died May 3 of complications of lung cancer. He was 87.

Hogan, an academic physician, ran a lab that studied multiple sclerosis, muscular dystrophy, spinal cord injury, Parkinson's disease and Alzheimer's disease. Narendra Bankik, who worked with Hogan in the 1970s, said in an obituary in the Post & Courier that patients from all over the region would travel to Hogan's lab to participate in his research and take advantage of his expertise.

Hogan was born in Arlington, Massachusetts, on July 26, 1932. For undergraduate and medical studies, He attended Tufts University, where he was on the cross-country team and developed a lifelong love of running.

He completed a residency at what was then the Peter Bent Brigham Hospital, which later merged with two other hospitals to form what is now known as Brigham and Women's Hospital. There he met his future wife, Gail Manning Hogan, who was a nurse. They were married for nearly 60 years and had four children.

Hogan completed a residency, specializing in neurology, at Boston City Hospital and postdoctoral training at Harvard Medical School and Tufts. He served as a captain the U.S. Army's medical corps at Fort Dix in New Jersey.

He took his first faculty position, in 1966, at the University of North Carolina School of Medicine in Chapel Hill. In 1973, he moved to join MUSC, where he was a professor and chair.

An Irish-American interested in his family's roots, Hogan bought a stone cottage in the 1990s in Leenane, a town in County Galway, and spent several months a year there with his family for 25 years. He was an adjunct professor of microbiology at the National University of Ireland.

Hogan, who had a distinct Boston brogue and a fondness for bowties and Mercedes Benzes, was an avid fan of the Red Sox, Celtics and Patriots. He ran competitively into his 80s and amassed a many race trophies. Above all, he enjoyed family time. According to a family obituary, "His love of family also involved his enlisting three generations to run the Turkey Day Run, regularly sharing a spot of superior Irish whiskey at a family gathering and cheering on his grandchildren on sports teams or in choirs."

Hogan is survived by his wife, children and many grandchildren.

A virtual high school science fair

By Anna Hoang & Patricia Melloy

The American Society for Biochemistry and Molecular Biology gave the Fairleigh Dickinson University ASBMB Student Chapter funding for an award at this spring's Nokia Bell Labs North Jersey Regional Science Fair, or NJRSF, a regional competition for high school students. Originally planned as an in-person event, NJRSF went virtual due to the COVID-19 outbreak.

A virtual science fair requires a video conferencing system. The NJRSF organizers selected a platform called BlueJeans, and they assigned each judging group to a different video conference, along with a science fair representative to help the judges stay on schedule and address any technical issues. Students entered the conference one-by-one for individual 15-minute slots to present their projects.

The two of us participated in special awards judging for biochemistry and molecular biology–related posters. All eight students in our category presented their projects via PowerPoint with little or no technical difficulty. Most gave a brief presentation and then answered our questions. We saw how well they knew the subject matter, their methods and related research questions to tackle in the future, as we would at an in-person science fair. We were amazed at their professional demeanor. According to one of the fair's judging coordinators, Diana Vengsarkar, 80% of the projects slated for the in-person fair were shared in the virtual event, for a total of 79 projects and 97 students.

Ananya Raghavan, an 11th grader at the Academy for Math, Science and Engineering at Morris Hills High School, won the FDU ASBMB Student Chapter Special Award. She studied compounds that might facilitate the reactivation of a mutant tumor protein, p53, into wild-type, specifically in glioblastoma cells. She performed a green fluorescent protein assay using two genetically engineered tumor cell lines to see how quinolines could reactivate mutant p53, with the reactivation determined by the degree of fluorescence.

"I've always been interested in cancer research, ever since two of my close family members were diagnosed with lymphoma and ovarian cancer," Ananya said, adding that she emailed about 50 professors before finding a lab at Drew University where she could work on this project.

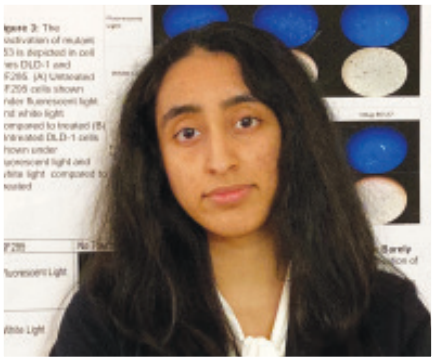
"I found it very difficult to conduct my experiments at times," she said. "I had to go to the lab during my school hours, which limited the time I could spend with the cells so that I didn't miss too many of my classes … For me, this represents a year's worth of collecting data, redoing assays and culturing cells over and over again."

Ananya's persistence earned her four more awards at the fair, including an International Science and Engineering Fair Grand Prize, the top award in the NJRSF.

We missed moving easily to different parts of a poster and having the spontaneous conversations at posters and between posters that add to the fun of an in-person fair, but the virtual fair was a success. Most students and judges were disciplined about not running over their allotted time, so students competing in more than one special award category could move on to their next video conference.

"This was my first year judging at NJRSF, and I have to say I was very impressed with all of the presentations. Since I was new to judging, I wasn't sure of what to expect. I approached the panel with an open mind and judged each student reasonably. "

—Anna Hoang



COURTESY OF ANANYA RAGHAVAN

Ananya Raghavan, who won the FDU ASBMB Student Chapter Special Award, poses with the poster she did not get to present. For the virtual fair, she presented her research as a PowerPoint.

Anna Hoang (hoang@student.fdu.edu) is the president of the Fairleigh Dickinson University ASBMB Student Chapter.

Patricia Melloy (pmelloy@fdu.edu) is the faculty advisor of the Fairleigh Dickinson University ASBMB Student Chapter. She is an associate professor of biological sciences.

ASBMB launches industry advisory group

Aim is to link industry and academic scientists effectively

By Laurel Oldach

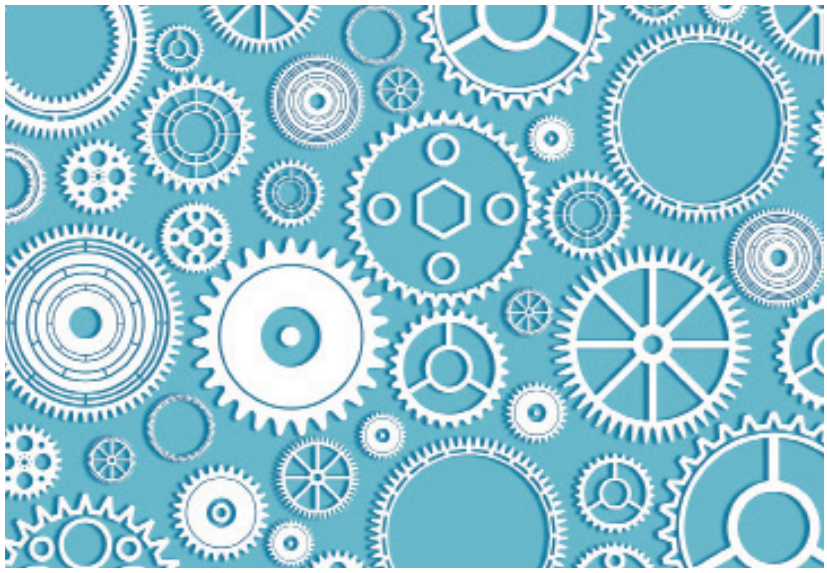
Young researchers in the life sciences who want to chart a career path in industry often feel cast adrift, according to Ed Eisenstein, because many professors have little experience with business hiring practices and professional norms.

Eisenstein, a professor of bioengineering at the University of Maryland and chair of the American Society for Biochemistry and Molecular Biology Membership Committee, is leading a new advisory group convened by the committee and society staff to help both in the society's outreach to scientists in industry and in educating ASBMB members about possible industry careers and how to prepare for them.

"I ran a biotech center for Maryland for a dozen years," Eisenstein said. "I discovered very quickly … that there was exciting science being done everywhere, not just in academia." However, he said, that appreciation for industrial research is not widespread among his peers.

Eisenstein and other members of the Membership Committee see a role for scientific societies such as the ASBMB in connecting scientists who work within and outside of the ivory tower. But before launching such efforts, he said, the society needs expert feedback.

"Rather than get a group of academics in the room" to discuss outreach to industry, Eisenstein said, "we decided we needed some better inside information. … We tried to convene a diverse group of people: large industry and small; early career and later career — even retired; men and women; (from) different geographic areas of the country."



Six ASBMB members who work at companies such as Genentech and PepsiCo signed on to help. Over the next year, Shyretha Brown, Mark Harpel, Lana Saleh, Melissa Starovasnik, Douglas Storts and Paul Wright will work to determine how the ASBMB can offer programs and resources of value to scientists working in, and contemplating, nonacademic research careers.

The group is considering several preliminary ideas. The first is to offer professional skills development for trainees in academia who hope to transition to industry: for example, offering training in science communication to potential investors, rather than fellow scientists. The society might also match student members with internship programs and work to highlight the career paths of successful scientists in industry.

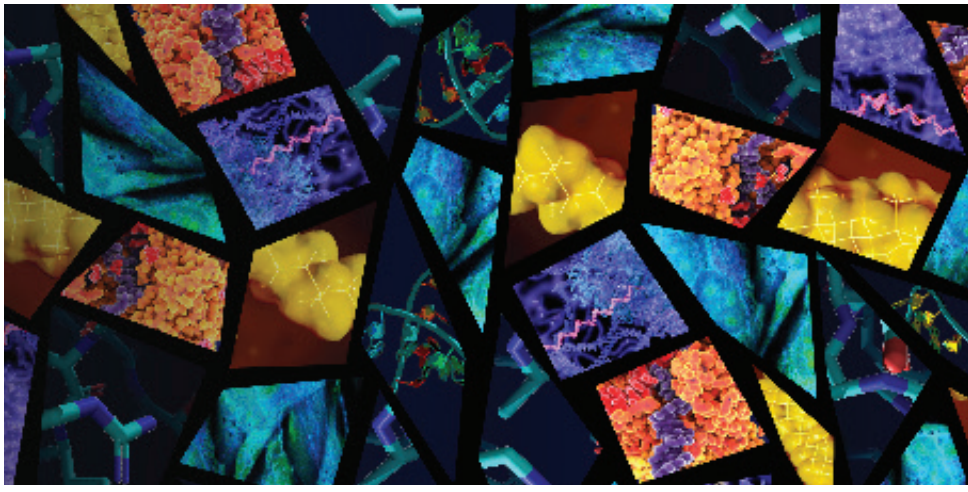
Finally, Eisenstein said, he would like to see the society recognize some of the research he didn't see until he began working with biotech companies: work that may become part of the patent literature instead of appearing in journals. The ASBMB could highlight this work with new awards or invited lectures at the annual meeting, and by inviting members who work in industry to share stories about their careers and research. If you would have advice or ideas for the new working group, please contact Jennifer Dean at jdean@asbmb.org.

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

ASBMB receives NIH grant to promote faculty diversity

MOSAIC program will provide individualized coaching and networking and presentation opportunities tailored to scholars' needs

By Angela Hopp



The American Society for Biochemistry and Molecular Biology has received a cooperative agreement with the National Institutes of Health's National Institute of General Medical Sciences to develop and execute a program that will support postdoctoral fellows and new investigators from diverse backgrounds embarking on careers at research-intensive institutions.

The ASBMB will receive almost $1.27 million over five years to serve as one of three inaugural host organizations for the Maximizing Opportunities for Scientific and Academic Independent Careers, or MOSAIC, program. The American Society for Cell Biology and the Association of American Medical Colleges are the other two host organizations.

"The ASBMB has a long history of supporting underrepresented scientists. We established what is now known as the Minority Affairs Committee in the 1970s. Over the past almost five decades, it has engaged in a number of effective activities," said Barbara Gordon, the ASBMB's executive director and MOSAIC principal investigator. "I am very pleased that we have received this grant, as it will allow us to take our support to a new level."

The MOSAIC Postdoctoral Career Transition Award to Promote Diversity (K99/R00) aims to enhance workforce diversity by facilitating a timely transition of promising postdoctoral researchers from diverse backgrounds from their mentored, postdoctoral research positions to independent, tenure-track or equivalent faculty positions at research-intensive institutions.

The NIGMS began accepting applications from postdoctoral researchers for MOSAIC K99/R00 awards in 2020. Once it makes the awards, the institute will assign awardees to participating host organizations that align with their scientific interests.

The ASBMB's MOSAIC program will leverage its established professional development, mentoring and networking activities and offer new ones.

"The society's IMAGE grant writing workshop, for example, has been very impactful, and our Journal of Biological Chemistry recently launched an early-career reviewer program. We will extend these programs to our MOSAIC scholars," said Ruma Banerjee of the University of Michigan, the co-investigator for the ASBMB's MOSAIC grant. "In addition, we will create opportunities for our scholars to present their work at the national meeting, network cross-institutionally with peers, and receive culturally aware coaching in a setting that is non-evaluative."

Barbara Gordon

Ruma Banerjee

Each participant will be paired with a coach at a different institution. In addition, each year's scholar cohort will be anchored by a coach, building a community of practice. Importantly, all coaches will be trained to discuss and respond appropriately to issues relating to gender, race and culture, including, for example, stereotype threat and

Other ASBMB programs and awards for minority scientists

IMAGE grant writing workshop: This annual program, funded in part by the National Science Foundation, trains about 35 new faculty members in best practices for securing federal research funding.

Marion B. Sewer Distinguished Scholarship for Undergraduates: This annual program provides up to $2,000 to help cover the tuition costs of up to five undergraduates committed to enhancing diversity in the biomedical workforce.

Graduate student travel awards: This program provides up to $1,000 in travel expenses for underrepresented graduate students presenting their work at the society's annual meeting. Recipients of the travel awards also are paired with mentors at the meeting.

Ruth L. Kirschstein Diversity in Science Award: This annual award recognizes an outstanding scientist who has shown a strong commitment to diversity. The winner receives a cash prize of $3,000 and a plaque and gives an invited lecture at the society's annual meeting.

Promoting Research Opportunities for Latin American Biochemists: This annual travel-award program allows Latin American graduate students and postdoctoral fellows to spend up to six months in U.S. or Canadian laboratories. Participants get access to technologies and expertise that may not be readily available in their home countries, allowing them to grow their skills and contribute to building capacity in the life sciences at home.

microaggressions.

"A major goal for the coaches will be to engender a culture of effective communication and openness that invites frank discussions of concerns without anxieties about repercussions," Banerjee said. In addition, each cohort will have regular virtual meetings to establish "a safe space for open discussions of sensitive issues that they might not discuss with colleagues and mentors at their institutions."

What the ASBMB participants will do

The ASBMB's component of the MOSAIC program will offer a professional-development curriculum to help awardees prepare for and navigate the transition to professorship.

In the first year, when all participants will be engaged in postdoctoral research, participants will focus on network building and science communication. Their activities will include, for example, taking the ASBMB's online course The Art of Science Communication to develop their public speaking skills.

In the second year, they will put those skills to the test by giving short talks at the society's annual meeting, and they will engage in a number of other skill-building workshops and webinars, such as training on preparing scientific figures for publication and reproducibility.

A highlight of the third year will be the society's grant writing workshop. That workshop is assessed regularly and, by the last count, 85% of participants had won grants within three years.

The final two years of the MOSAIC program, which will coincide with participants' first years as professors, will be carefully tailored to individual scholars' goals and needs but could include, for example, editorial training, additional public speaking opportunities, pedagogical training and mentoring training.

Institutional change

Though the society aims to serve each scholar's needs, Banerjee emphasized that the ASBMB rejects looking at the need to diversify the biomedical workforce through a deficit lens.

"To achieve what has been an elusive goal of diversification, it is imperative that we assess and address the restrictions that continue to challenge inclusive participation and help perpetuate a demographic imbalance," she said. "We will introduce new programming to engage administrators at the MOSAIC scholars' home institutions in discussions on barriers to sustainable change and evidence-based approaches to improving outcomes."

For more information about the ASBMB MOSAIC program, visit www.asbmb.org/diversity/MOSAIC.

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

Organizing fat: Mechanisms of creating and organizing cellular lipid stores

By W. Mike Henne

Life is unpredictable, so cells create nutrient reservoirs that enable them to subsist during prolonged starvation. Cells generate lipid droplets, or LDs, the primary nutrient reservoirs of eukaryotes. These lipid storage organelles, composed of a phospholipid monolayer surrounding a neutral lipid core, form on the surface of the endoplasmic reticulum, or ER, which generates almost all the lipids within LDs.

In many cells, LDs maintain contact with the ER for extended periods, so ER–LD interorganelle crosstalk is essential for cellular lipid homeostasis. We know that LDs play important roles in energy and cellular homeostasis, but recent studies also highlight noncanonical roles for LDs in lipotoxicity control, development, cell signaling and even reservoirs for hydrophobic metabolites.

LDs can remain in cells for extended periods before metabolic cues mobilize them. They often are mobilized in periods of energetic crisis, prompting the question: How do cells organize their LD stores to maximize storage and harvesting efficiency?

Uncontrolled LD mobilization can spill toxic fatty acids into the cell interior. Fatty acids act as biological detergents that can dissolve membranes, so cells must regulate LD production, storage and mobilization.

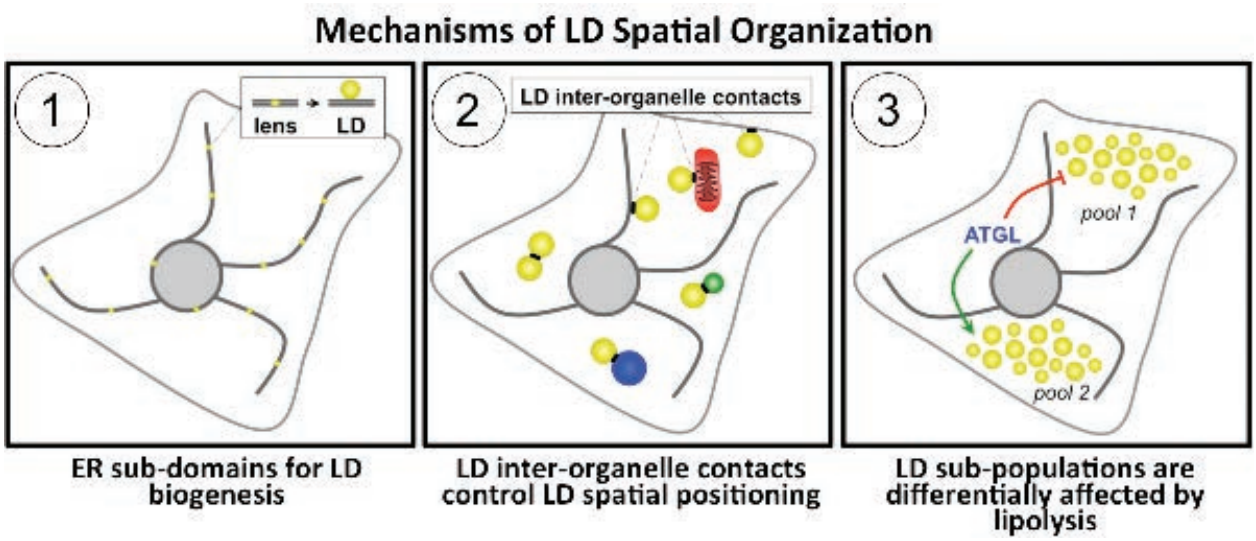
Studies have found that LD production and turnover are highly regulated, establishing the existence of spatial determinants that govern not only where LDs form within the ER network but also where they accumulate within the cytoplasm. Here, I briefly summarize some of these findings and how they reveal a remarkable spatial organization in lipid metabolism and LD biogenesis.

Lipid droplets can be organized by these three mechanisms within a cell. 1) The endoplasmic reticulum contains nascent LD lenses that are subdomains for LD biogenesis. 2) LDs establish contacts with other organelles, and this affects their spatial positioning as well as their ability to exchange lipids with those organelles. 3) LD subpopulations can be segregated spatially in the cytoplasm and are affected differentially by lipases such as ATGL.

1. The ER network contains lipogenic hot spots that organize lipid processing reactions and LD biogenesis: Many recent studies of LD formation and emergence from the ER network focus on seipin, an ER-resident protein linked to a severe form of congenital generalized lipodystrophy, or abnormal fat storage. Studies show that seipin accumulates at neutral lipid lenses within the ER network where seipin oligomers support the growth of nascent LDs. Researchers now view nascent LD lenses as lipogenic ER subdomains containing structural factors and enzymes that drive lipid synthesis reactions. In addition to seipin, our group has identified Snx14, a member of the sorting nexin protein family, as a tether that promotes LD biogenesis at ER–LD contact sites. Snx14 is highly conserved, and orthologs in yeast and Drosophila play similar roles in ER–LD crosstalk, underscoring the functional conservation of LD tethers across evolution.

2. Protein tethers connect LDs to other organelles, regulating LD positioning and use in the cell: In addition to being tethered to the ER as they mature, LDs are connected to other organelles, and this provides an intuitive mechanism to arrange them spatially in the cell. Elegant studies have found proteins that enrich at interfaces between LDs and mitochondria, LD–peroxisomal contacts, LD–plasma membrane contacts, LD–lysosome contacts, and even contacts between LDs. Many of these studies show that LD interorganelle junctions are sites of lipid exchange between the LDs and recipient organelles.

3. LD mobilization is highly regulated, and cells appear to contain pools of LDs that are created and mobilized under specific nutrient cues: During fasting or in response to cellular cues, cytoplasmic lipases mobilize LDs to liberate free fatty acids and glycerol into the cytoplasm. Hyperactive lipolysis can disrupt cellular homeostasis, so regulatory mechanisms fine-tune LD synthesis and breakdown. Some regulate the recruitment and activity of lipases on the LD surface, and others control the creation of LD subpopulations that are mobilized



W. MIKE HENNE

Lipid droplets can be organized by these three mechanisms within a cell. 1) The endoplasmic reticulum contains nascent LD lenses that are subdomains for LD biogenesis. 2) LDs establish contacts with other organelles, and this affects their spatial positioning as well as their ability to exchange lipids with those organelles. 3) LD subpopulations can be segregated spatially in the cytoplasm and are affected differentially by lipases such as ATGL.

differentially by lipolysis.

Our lab uses Drosophila tissue to study how adipocytes control LD storage and mobilization. We have found that larval adipocytes contain spatially distinct LD subpopulations that respond differentially to LD mobilization. A pool of small LDs near the cell surface are mobilized when the organism fasts and multiply during high-nutrient feeding. This indicates that LD positioning in the cytoplasm may dictate lipolysis. Similar mechanisms are present in yeast and mammalian tissues. In yeast entering into stationary phase growth, LDs tend to grow and accumulate near the cell's digestive vacuole, where some LDs are delivered to be broken down during low-nutrient subsistence. In mouse enterocytes, pools of LDs derived from lipid absorption at the basolateral side of the cell are mobilized by intestinal adipose triglyceride lipase, or ATGL, activity, but lipids absorbed on the enterocyte apical surface appear to resist ATGL lipolysis and are instead shunted into chylomicron synthesis for export. This all implies that distinct lipid pools are maintained within cells and are exposed selectively to lipolysis. It suggests that positioning of LDs and lipid pools determines lipid storage and mobilization.

Many questions remain. How are distinct lipid pools and LD subpopulations maintained and demarcated by the cell? How do cells decide where to create hot spots in the ER network where nascent LDs are created and emerge? Is LD biogenesis a protein-driven event, or are proteins mere facilitators of lipid-driven LD biogenesis?

We hope to address these and other questions as new tools and technologies emerge.

W. Mike Henne (mike.henne@UTsouthwestern.edu) is an assistant professor in the department of cell biology at the University of Texas Southwestern Medical Center in Dallas. His lab studies lipid droplets and the organization of metabolism in cells.

How lipid droplets stay in shape

By Martin J. Spiering

Lipid droplets, or LDs, are key lipid storage structures in cells. One might think that they simply result from lipid molecules separating out within the aqueous intracellular environment. However, LDs are well-organized organelles surrounded by proteins that act as gatekeepers that tightly control lipid entry and exit.

One LD-associated protein is perilipin 1, or PLIN1. Andrew Greenberg, his late mentor Constantine Londos and colleagues at the National Institute of Diabetes and Digestive and Kidney Diseases discovered PLIN1, an abundant protein in fat cells and the first protein identified on the LD surface. They reported this in a 1991 Journal of Biological Chemistry paper now recognized as a JBC Classic.

JBC technical editor Martin Spiering asked Greenberg about the discovery of PLIN1 and how it spurred further investigations into fat storage and metabolism. The conversation has been edited for length and clarity.

How did you become interested in studying LDs?

When we started this work, LDs had been identified, but their roles in regulating lipid metabolism were unclear. We knew little about the intracellular architecture of neutral lipid metabolism and the nature and localization of the proteins that regulate LD assembly and maintenance.

In earlier studies, LDs were found only in fatty liver and in the foam cells of atherogenic plaques. But as we studied the literature, we saw that they are present in almost all cell types. So we hypothesized that LDs serve as active centers for the storage and breakdown of neutral lipids.

These metabolic processes are critical for maintaining energy homeostasis in the body. For example, during feeding, the adipocyte stores food energy that exceeds the body's current energy needs; during fasting, adipocytes release fatty acids into circulation.

We wanted to study these fundamental processes and identify the adipocyte proteins that regulate neutral lipid metabolism in response to fasting and feeding.

What prompted your study?

In 1990, we became interested in investigating the role of a phosphatase that dephosphorylates hormone-sensitive lipase, or HSL, and contributes to insulin actions that inhibit lipid breakdown in adipocytes. To home in on the phosphorylation/dephosphorylation mechanisms, we loaded rat adipocytes with phosphorus-32–labeled inorganic phosphate and incubated them with varying concentrations of the beta-adrenoreceptor agonist isoproterenol in the absence and presence of insulin.

We previously had seen that after cAMP-dependent protein kinase A, or PKA, activation, a major hyperphosphorylated protein migrates as a 65–67 kDa protein on SDS-PAGE. When we fractionated the phosphate-loaded adipocytes, this phosphoprotein localized exclusively to the fat cake, sparking our interest in learning more about its potential role in adipocyte metabolism.

Andrew Greenberg and colleagues identified perilipin as a major protein associated with lipid droplets.

What did you find in your 1991 paper?

More than 95% of all radiolabeled phosphate that was incorporated into cellular proteins after the PKA stimulation went into PLIN1, making it the predominant PKA substrate in adipocytes. In immunocytochemical studies in differentiated adipocytes, we saw anti-perilipin immunoreactivity in well-defined ringlike patterns around both large and small intracellular lipid droplets.

PLIN1 was the first protein we found that localized specifically to the LD surface, suggesting that it regulates triglyceride metabolism in LDs, and PLIN1 was expressed most robustly in adipocytes

What's the main function of perilipin in LD maintenance?

PLIN1 mainly acts as a dynamic scaffold for proteins involved in the storage and hydrolysis of neutral lipids in LDs. It's a dynamic interplay; PKA-mediated hyperphosphorylation of PLIN1 enhances lipolysis by activating adipose tissue triglycer-

ide lipase, or ATGL, and localizes PKA-phosphorylated HSL to the LD surface.

Without PKA activation, PLIN1 binds and sequesters the LD-binding protein CGI-58. With PKA activation and ensuing PLIN1 phosphorylation, CGI-58 is released from PLIN1 and then binds to and increases the activity of ATGL.

Is PLIN1 the only LD-associated protein?

Since our 1991 paper, researchers have identified four more proteins that resemble PLIN1 in both sequence and conserved motifs. Among these, PLIN2 and PLIN3 are expressed ubiquitously. PLIN1 and PLIN2 are present exclusively on LDs, whereas PLIN3, PLIN4 and PLIN5 have been found on the LD surface, the cytoplasm and, in some cases, the nucleus.

PLINs have distinct roles in different cell types. Depending on cell type, PLIN3 or PLIN 4 binds initially to the nascent LD. In non-adipocytes, PLIN2 then binds to and displaces PLIN3 on the mature LDs. In adipocytes, after PLIN2 associates with developing LDs, PLIN1 binds to and displaces PLIN2 from the mature LD.

Other proteins at the LD surface include the cell death–inducing DFFA-like effector proteins, which inhibit the hydrolysis of stored triglycerides.

What's the main focus of current research into PLINs?

We want to understand better how PLINs are involved in regulating the activities of ATGL and autophagy that hydrolyze stored triglycerides and to delineate the functions of the PLIN isoforms.

Research has expanded into LD biogenesis, the role of phospholipids associated with the LD surface, identification and function of other proteins that associate with and traffic to LDs, and interactions of LDs with other intracellular organelles such as mitochondria.

A growing body of work is investigating how PLINs and other LD proteins may act as nutrient and lipid sensors to link changes in LD metabolism to downstream signaling pathways.

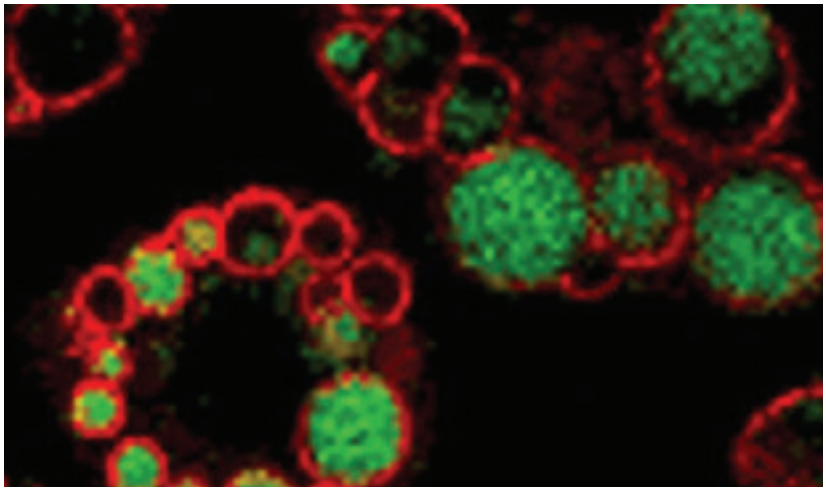
Does PLIN1 have a role in metabolic disorders such as obesity and diabetes?

In obesity, inflammation in adipose tissues is marked by elevated levels of cytokines, such as tumor necrosis factor alpha, that reduce the expression of both the PLIN1 gene and protein, resulting in increased adipocyte lipolysis and release of fatty acids into circulation. These fatty acids are taken up by the liver and can cause nonalcoholic fatty liver disease and elevate triglyceride levels.

These fatty acids also can alter insulin signaling pathways and result in insulin resistance in hepatocytes and skeletal muscle cells, which may lead to diabetes. In steatotic human livers, PLIN1 expression is increased, and PLIN1 is localized around hepatocyte lipid droplets, likely promoting triglyceride accumulation.

Have any therapeutic strategies or agents emerged that target PLIN?

One class of anti-diabetic drugs, the thiazolidinediones, bind to and activate a transcription factor that binds the PLIN1 gene promoter and increases its activity. This can increase the levels of PLIN1 mRNA and protein and block TNF-alpha's effects on PLIN1 expression and rates of lipolysis. So, both PLIN1 and cytokines represent potential targets for ameliorating inflammation caused by fatty acid release from adipocyte LDs.



COURTESY OF ANDREW GREENBERG

Perilipin (stained red) binds to the surface of lipid droplets (green) and functions as a dynamic scaffolding protein that controls entry and exit of lipids from the droplets.

Martin J. Spiering was the technical editor at the Journal of Biological Chemistry. Follow him on Twitter @spieringmj.

Sorting and secreting insulin by expiration date

The age of insulin parcels may matter, researchers say, when it comes to diagnosing and treating diabetes

By Anand Rao

A study in the **Journal of Biological Chemistry** describes a new way to determine the age of insulin-storage parcels, known as granules, and sheds light on how their age affects their release into the bloodstream. The findings could help experts better understand diabetes and fine-tune therapies for it.

Insulin is a hormone that manages the level of sugar, or glucose, in the bloodstream. It is secreted by the pancreas into the bloodstream when blood sugar levels rise. When insulin circulates in the bloodstream, muscle and other cells absorb glucose to use it as fuel, and so blood sugar levels decline. In Type 2 diabetes, formerly known as adult-onset diabetes, this process fails. Glucose builds up in the blood, either because the pancreas cannot produce enough insulin to keep up with dietary sugar intake or because the gland simply isn't working as it should.

About one in 10 Americans and more than 415 million people worldwide have diabetes, according to the Centers for Disease Control and Prevention. Up to 95% of them have Type 2. Treatment often requires painful and frequent insulin injections or the use of mechanical insulin pumps. There is no cure.

The researchers noted in their paper that existing therapies for diabetes increase insulin secretion without regard for insulin granule age. "Accordingly," they wrote, "these approaches are effective only for a short period."

Insulin is produced by beta cells of the pancreas and stored in insulin granules, which are then organized into pools and finally secreted into the bloodstream. Pools of young insulin granules are preferred for secretion over pools of old ones, for reasons that remain unclear.

About one in 10 Americans and more than 415 million people worldwide have diabetes, according to the Centers for Disease Control and Prevention.

The scientists whose work was published in JBC wanted to learn more about how pancreatic cells can distinguish between pools with young or old insulin granules.

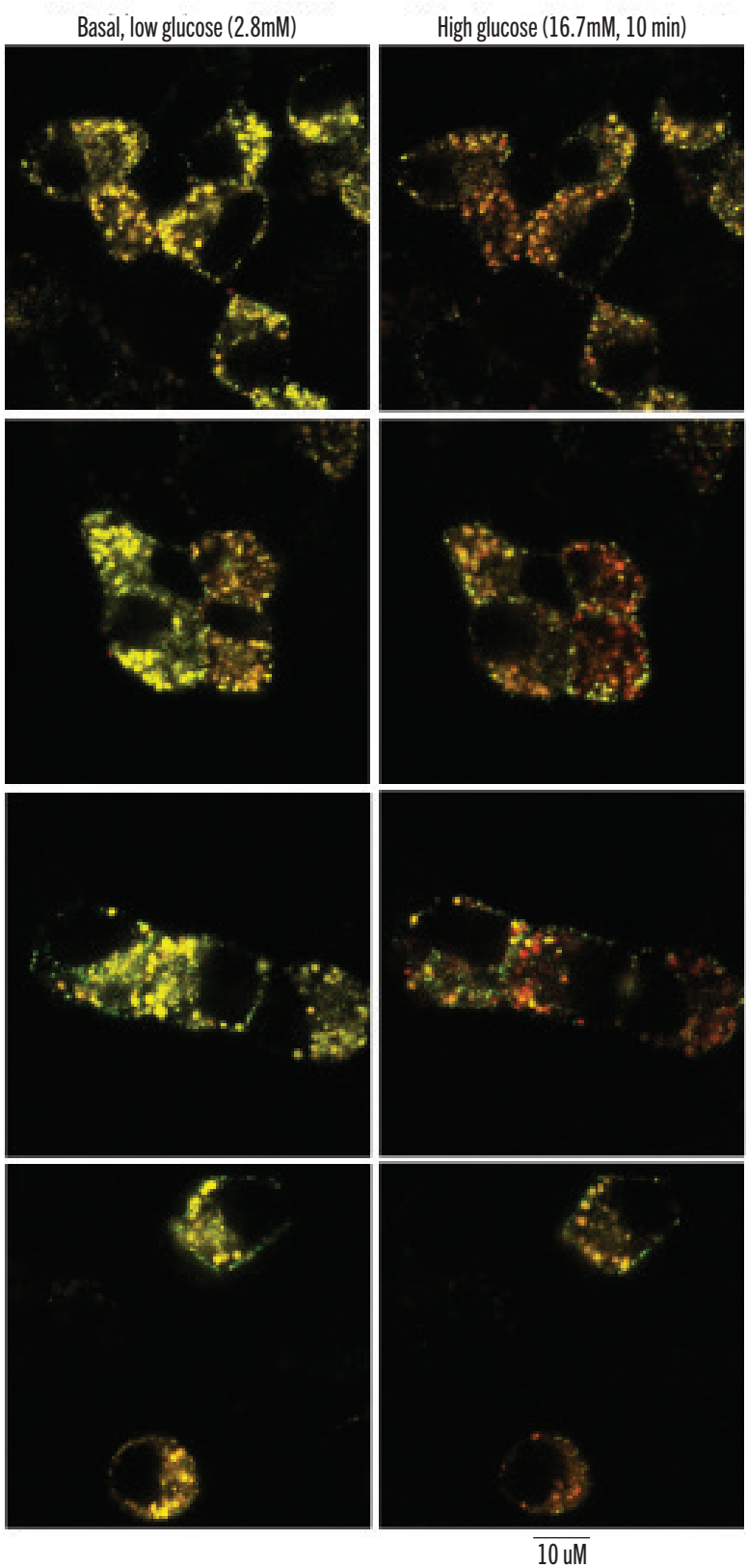
"Current therapeutics do not take the existence of pools into consideration," said Melkam Kebede, an assistant professor at the University of Sydney who oversaw sthe study. "By evolution, the (pancreatic) cells have determined what to secrete and what not. Understanding the mechanism and molecular differences between the pools definitely is going to lead us into something meaningful."

In their paper, the researchers describe a technique they developed to distinguish younger insulin granules from older ones. The scientists placed a fluorescent protein, called Syncollin-dsRedE5TIMER, into newly created insulin granules and used a laser and detector to visualize that marker. In younger granules, the marker emits a green fluorescent light; as granules get older, the marker begins to emit a red fluorescence.

The authors monitored the movements of and other changes in insulin granule pools and saw that, as predicted, both mouse and human cells preferentially release younger insulin granule pools into the bloodstream in response to glucose.

The researchers then set out to learn more about how pancreatic cells sort insulin granules into pools and release them when they are experiencing metabolic stress. The concern is that, when under stress, beta cells "could potentially lose their ability to distinguish young (granules) from old," they wrote in their paper.

The team isolated beta cells from mice and simulated chronic low, high and normal blood sugar levels and found different glucose levels determine which pools of insulin granules, young or old, are secreted.



BELINDA YAU

This series of live cell images represents insulin granule secretion. Syncollin-dsRedE5TIMER was used to visualize the age of secretory granules in beta cells subjected to low or high glucose conditions.

They saw similar results when they used a common mouse model for Type 2 diabetes known as the db/db mouse.

These findings are important, Kebede said, because "all the drugs that affect insulin secretion…just push any granule within the cell and eventually fail."

Older insulin granules are naturally degraded in normally functioning beta cells, noted lead author Belinda Yau of the University of Sydney, but, in diabetes, a greater percentage of insulin granule pools are secreted, and there's a mismatch in how they're released.

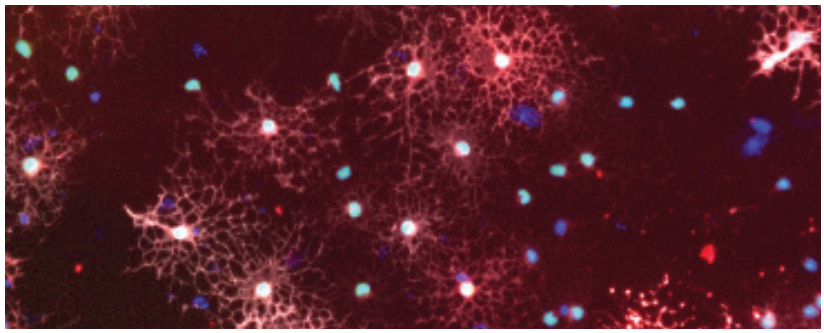
Being able to visualize insulin granules as they age and understanding better how their age affects their secretion may lead to the discovery of new biomarkers capable of indicating the development of diabetes and could help in the creation of therapies for Type 2 diabetes.

"If we can understand what makes up the granules and makes them do what they do, we can figure out a way to target the things that slow down or speed up their secretion," Yau said.

Anand Rao
(arao@asbmb.org) is a science communicator for the ASBMB. Follow him on Twitter @AnandRaoPhD.

Proteomics reveals hallmarks of aging in brain stem cells

By Laurel Oldach



ALERIE GUZMAN DE LA FUENTE

A cell culture mixture grown in the lab includes oligodendrocyte progenitor cells (green dots) and differentiated oligodendrocytes (white and red, with branches). Guzman de la Fuente conducted the cell culture and microscopy.

Myelin, a fatty substance akin to wire insulation, allows fast neuronal signaling both within the brain and to the rest of the body. When myelin in the brain or spinal cord is damaged, adult stem cells called oligodendrocyte progenitor cells, or OPCs, respond by developing into new, fully fledged oligodendrocytes that wrap new myelin around neurons, protecting them and restoring their ability to carry fast electrical messages.

The human body's ability to regenerate lost myelin declines with age. Patients with multiple sclerosis are intimately familiar with this shift. The disease, usually diagnosed in a patient's twenties, arises when a person develops an immune response to myelin proteins. It starts out as a series of flare-ups of symptoms such as muscle weakness and numbness, followed by months or even years in remission as new oligodendrocytes provide fresh myelin. The disease shifts to a progressively worsening disability in middle age.

Neuroscientist Alerie Guzman de la Fuente is interested in developing a better understanding of oligodendrocyte progenitor cells to determine why remyelination falters with age. The answer could inform scientists who hope someday to treat MS with pro-remyelinating therapies.

"Most labs studying oligodendrocyte progenitor biology use neonatal OPCs to test drugs," Guzman de la Fuente said. "These cells are incredibly powerful at forming myelin." That makes them an imperfect system for studying how myelin formation goes awry with age, she said. "We think that studying adult OPCs … is more relevant to what will happen in the progressive phases of MS, in patients over 50."

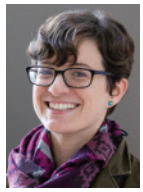
In a recent paper in the journal **Molecular & Cellular Proteomics**, Guzman de la Fuente and her colleagues in Robin Franklin's lab at the University of Cambridge reported a comparison of the proteomes of OPCs from neonatal, young adult and mature mice. Franklin's lab and others previously have studied the transcriptome of these cells. However, Guzman de la Fuente emphasized, RNA and protein levels are not always perfectly correlated.

Some protein features were quite stable through a mouse's lifetime. Others changed dramatically. The team focused on the proteins that changed most between young and mature adulthood, and they identified a few patterns.

As with many aging cells, the stem cells from older mice showed some gene-expression drift, acting as if they had begun to differentiate but without gaining the ability to make myelin. The team noticed that as animals aged, their stem cells were more likely to have difficulty metabolizing cholesterol, an important component of myelin; older OPCs were more apt to express proteins involved in other neurodegenerative disorders such as Alzheimer's and Parkinson's disease, although what these changes mean remains to be elucidated . Finally, as with many aging cells, the OPCs from older mice also showed changes in protein homeostasis.

It will take time and further experiments to determine which of these changes cause the remyelination decline that appears with age. But, Guzman de la Fuente said, having a clearer picture of how the brain changes with aging can only help future efforts to treat multiple sclerosis.

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



Estrogen receptor antagonist shows promise for treatment of gallstone disease

By Guananí Gómez–Van Cortright

Women are twice as likely as men to suffer from gallstone disease, due to estrogen's role in triggering cholesterol gallstone formation. While small gallstones are common, in some people cholesterol forms crystals that build up and become too large for the gallbladder to expel. The resulting gallstone disease causes excruciating pain and sometimes sepsis. The standard treatment is surgical removal of the entire organ.

Christopher Arnatt, a researcher in the department of chemistry at St. Louis University, has been working to address the role of estrogen in gallstone disease. "Having a preventative cure out there for all at-risk people would be amazing," he said.

Arnatt's lab collaborated with David Q.H. Wang's lab at the Marion Bessin Liver Research Center at the Albert Einstein College of Medicine in New York on a recent paper published in the **Journal of Lipid Research**.

Arnatt's lab, which specializes in synthesizing compounds that target G protein–coupled receptors, created an array of drugs and tested their affinity for the G protein–coupled estrogen receptor, or GPER, which previously had been associated with gallstone formation.

"It took almost four years to nail down how to test for whether these compounds were binding to and antagonizing the G–coupled estrogen receptor," Arnatt said. "No one had done any true medical chemistry on this, and now we have over one hundred compounds that bind to this receptor that can be used to study it further."

Arnatt's team showed that one of those compounds, 2-cyclohexyl-4-isopropyl-N-(4-methoxybenzyl) aniline — referred to as CIMBA — was selective for GPER, making it a strong candidate for further testing.

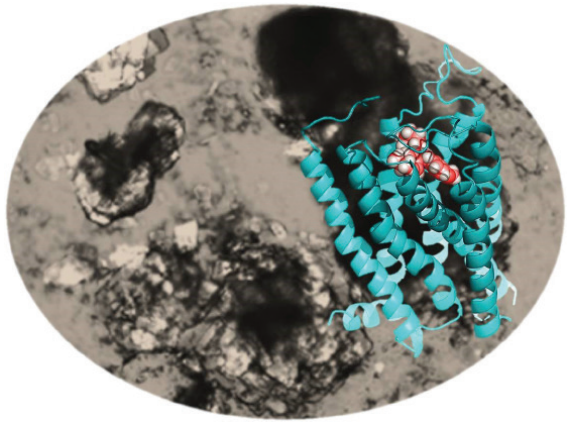
The second phase of the project put CIMBA to the test in mice. Wang's lab, one of very few labs in the world that research gallstones, put ovariectomized female mice on a high-cholesterol diet and gave them doses of estradiol to induce gallstone formation. After eight weeks, the mice were injected with various doses of CIMBA, and then researchers removed their gallbladders.

These gallbladders, each about the size of a grain of rice, had to be cut open under a microscope to count and analyze their gallstones. Wang's lab found that treatment with CIMBA reduced the formation of estrogen-induced gallstones in some mice and also found a dosage at which no gallstones formed. While the mouse model results are promising, making this compound available for human use would require safety testing and clinical trials.

Arnatt is optimistic about the potential of CIMBA and the other GPER antagonists. "These new compounds will provide researchers with a lot of new tools," he said. "Having new drugs out there will expand people's ability to test this receptor and its pharmacology."

Arnatt plans to investigate how to make CIMBA more bioavailable and less toxic for gallstone prevention treatment, and he hopes to use these GPER-binding compounds to understand better the receptor's role in the body.

DOI: 10.1194/jlr.RA119000592



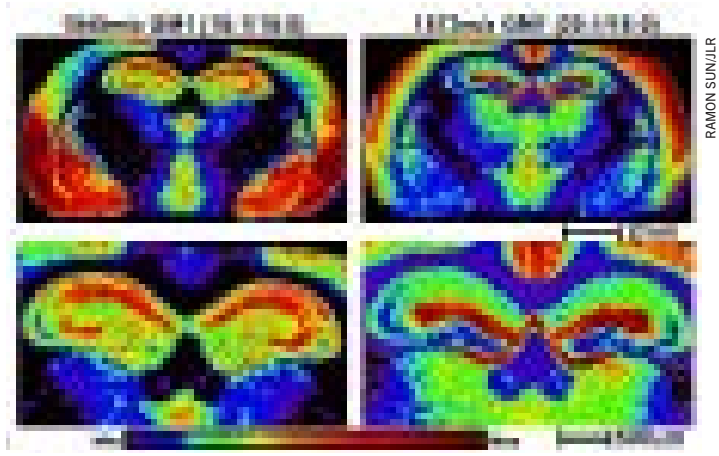
CHRISTOPHER ARNATT

G protein-coupled estrogen receptor with new selective antagonist, CIMBA, bound reduces estrogen-induced gallstones (background image) in female mice.

Guananí Gómez–Van Cortright (guananigvc@gmail.com) is an outdoor educator and science writer.

Celebrating the images scientists create

By Courtney Chandler


RAMON SUN/JLR

In his "Images in Lipid Research" paper, researcher Ramon Sun included these MALDI-mass spectrometry images of gangliosides in a wild-type mouse brain, which show distinctive distribution of two very similar ganglioside species in different regions of the brain.

If an image is worth a thousand words, then images of lipid research are worth their own series. The **Journal of Lipid Research** has started just that with a new article format, "Images in Lipid Research," launched earlier this year.

These articles are one-page, peer-reviewed publications with a single image and caption that highlight current topics in lipid physiology and biochemistry.

The idea stemmed from a suggestion made by Stephen Young, associate editor at the JLR and a professor at University of California, Los Angeles, during an editors' meeting. Kerry-Anne Rye, co-editor-in-chief of the JLR and professor at the University of New South Wales in Sydney, Australia, said the idea resonated with the group. After that, the American Society for Biochemistry and Molecular Biology staff took the reins and turned the concept into reality.

In his editorial about the series, Young wrote that he hopes to "celebrate scientists and the images they create" in a format that is also "effective in communicating discoveries of lipid research."

So far, the Images in Lipid Research series has been popular with authors. Rye said submissions took off right from the start.

"The series may resonate so strongly with authors because many of them have wonderful pictures that end up not being a good fit in the final manuscript," Rye said. The series "provides a forum for these pictures to be shared with a community of like-minded, interested colleagues."

The published images are citable, which also may appeal to authors. With their compressed format, the articles give authors the opportunity to make a single point clearly and concisely.

Ramon Sun, an assistant professor in the department of neuroscience at the University of Kentucky, decided to submit to the series to highlight one of the many images he's been able to collect using an advanced mass spectrometry technique. With his image of differential ganglioside localization patterns in the brain, he hoped both to highlight the technique his group used and to tell a short story that spatial differences should be taken into consideration during interrogation of lipid metabolism.

"Images can convey an otherwise complex paradigm in a simple and easy to understand format," Sun said.

In addition to highlighting new lipid research with the series, the editors hope to generate interest within a broader audience. The JLR is sharing most of the images through social media outlets such as Facebook and Twitter as well as publishing them in the journal.

Rye said the editors hope that a visually appealing image with a simple, targeted message will catch the attention of a broad scientific audience beyond those who regularly read the JLR. The images and their stories might then prompt this new audience to read the JLR, thus expanding the footprint of the journal.

"Who knows? We may even end up helping some nonscientists recognize that science is fun and exciting and not limited to the domain of the stereotypical, white-coated and bespectacled test-tube holders of comic book fame," Rye said.

Check out the JLR's Images in Lipid Research page for more stunning images. If you're interested in submitting an image of your own, all the information can be found on the JLR website.

Courtney Chandler (courtneyec19@gmail.com) is a postdoctoral researcher at Johns Hopkins University and a careers columnist for the ASBMB. Follow her on Twitter @CourtneyCPhD.

From the journals

By Jack Lee, Amrita Mandal & Anand Rao

We summarize a selection of recent papers from the **Journal of Biological Chemistry**, the **Journal of Lipid Research** and **Molecular & Cellular Proteomics**.sion. Future investigation will help delineate the exact pathways and molecules involved.

Analyzing the lipid profile in atherogenic dyslipidemia

Low-density lipoprotein, or LDL, often has been called the "bad cholesterol." Excess LDL accumulates in the walls of arteries, progressively leading to atherosclerotic plaque formation. The rupture of such plaques triggers a thrombotic reaction that can block blood flow to the heart or brain, causing a heart attack or stroke. Factors such as genetics, a high-fat diet, lack of physical activity, obesity and diabetes can contribute to high LDL. To lower LDL, many physicians prescribe statin drugs, which block the function of a key enzyme in liver for cholesterol synthesis.

Atherogenic dyslipidemia is a clinical condition in which patients have high levels of both LDL and triglycerides with low "good cholesterol," or high-density lipoprotein. In a study published in the J**ournal of Lipid Research**, M. John Chapman and a team of international researchers analyzed the effect of statin treatment on 12 obese, hypertriglyceridemic hypercholesterolemic men for 180 days. They report that the treatment reduced absolute plasma concentration of all 23 lipid classes in LDL except the lipotoxic ceramides.

The authors also observed specific enrichment of bioactive lipids — LPC, LPC (0) and LPI — in the small dense LDL subclass, which is highly atherogenic. These three bioactive phospholipids are known to drive inflammation and could therefore favor fatty plaque formation in blood vessels. These data suggest that the bioactive lipid signature in highly atherogenic LDL could be a potential biomarker for atherogenicity in cardiovascular disease.
DOI: 10.1194/jlr.P119000543

A new target to tackle hard-to-treat cancers

Treatment of patients with triple-negative breast cancer, or TNBC, is hindered by a dearth of therapeutic options. This is because TNBC cells lack estrogen receptors, progesterone receptors and excess human epidermal growth factor receptor 2, better known as HER2 receptors, and thus do not respond to traditional hormonal therapies or interventions targeting HER2 receptors.

In recent work published in the **Journal of Biological Chemistry**, Renee Geck of Beth Israel Deaconess Medical Center and collaborators used metabolomics profiling to show that TNBC cells grown in culture dishes, when exposed to cytotoxic chemotherapy drugs, display alterations to arginine and polyamine metabolites, suggesting changes to polyamine metabolism. The authors demonstrate that this occurs through a reduction of the polyamine biosynthetic enzyme ornithine decarboxylase, or ODC, and that ODC inhibitors sensitize TNBC cells to existing therapies.

These results suggest that by targeting ODC, TNBC cells might become responsive to cancer therapeutics that are effective in other cancer subtypes.
DOI: 10.1074/jbc.RA119.012376"

Identifying acetylation sites in a coronavirus

Like the virus that causes COVID-19, MERS-CoV is a coronavirus that can cause severe respiratory illness. A better understanding of how host cells respond to MERS-CoV infection could help prevent a future pandemic.

Some other viruses require protein acetylation for viral replication; in a recent paper published in **Molecular & Cellular Proteomics**, Lin Zhu of Hong Kong Baptist University and a team of Hong Kong researchers explored whether MERS-CoV proteins also are acetylated by host factors.

After obtaining viral proteins from infected cells, the researchers enriched for peptides with acetylated lysine residues. All the acetylated peptides corresponded to pp1ab, a polyprotein that forms 15 different proteins involved in MERS-CoV replication. Bioinformatic analysis suggested that proteins in the SIRT1, HDAC and TIP60 families could be upstream regulators of these acetylation sites. Experiments are needed to confirm the actual role of the acetylated proteins during viral replication, but the study's findings hint at possible therapeutic targets to explore.
DOI: 10.1074/mcp.RA119.001897

Zinc triggers a tau transformation

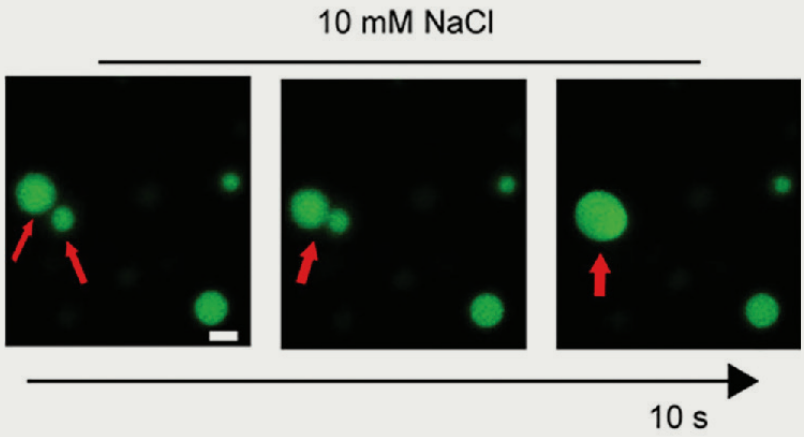
Alzheimer's disease is characterized by brain cells that wither and die, resulting in loss of memory and other mental faculties. Tau is a soluble microtubule-associated protein that, under pathological conditions, accumulates and aggregates, causing intracellular inclusions known as neurofibrillary tangles, a hallmark of Alzheimer's. Recent studies have indicated that tau is capable of forming liquid droplets after undergoing liquid–liquid phase separation, or LLPS. This process can induce the formation of pathological tau, which then propagates from neuron to neuron, inducing tau aggregation. However, how LLPS of tau is stimulated remains unknown.

Growing evidence indicates that the level of zinc ions is elevated in vulnerable regions of brains with Alzheimer's disease. In a recent paper published in the **Journal of Biological Chemistry**, Virender Singh and colleagues at Case Western Reserve University sought to determine whether abnormal zinc homeostasis plays a role in the origination of Alzheimer's. Using recombinantly expressed tau proteins, turbidimetry — the measurement of particle concentration by light scattering — and fluorescent microscopy, the researchers observed that zinc strongly promotes LLPS of tau. Once formed, the highly dynamic tau droplets retain their liquidlike characteristics for several hours, and they are abolished by the addition of a metal chelating agent. The authors demonstrated that replacing select amino acid residues from tau protein eliminated zinc's ability to induce LLPS. Exposure of tau to other divalent metal ions such as magnesium, cobalt, nickel and iron did not induce the same response.

The researchers suggest that zinc could accelerate tau's propensity to aggregate. Moreover, in contexts of cellular stress, zinc may influence the abnormal interaction of tau with other proteins, thereby disrupting normal cellular function. These findings provide new insights into the link between abnormal zinc homeostasis and the pathogenic process in Alzheimer's disease and other tauopathies.

DOI: 10.1074/jbc.AC120.013166

—Anand Rao



VIRENDER SINGH ET AL./JBC

A panel of representative images depicting fusion events of tau droplets induced by the addition of zinc.

New insights into the consequences of a retina protein mutation

Retinal degeneration is a leading cause of incurable low vision and blindness worldwide. Mutations in the retinaldehyde-binding protein 1, or RLBP1, gene, which encodes for the visual cycle protein cellular retinaldehyde-binding protein, better known as CRALBP, cause an autosomal recessive form of retinal degeneration. However, the functional consequences of these mutations have not been well studied.

Jose Ronaldo Lima de Carvalho Jr. and colleagues at Columbia University investigated the significance of RLBP1 mutations through an analysis of siblings with RLBP1 mutations, their asymptomatic carrier parents and Rlbp1/Cralbp–/– knockout mice, which do not produce RLBP1 or CRALBP. Using a range of functional assays, the authors observed that the mutant mice and human siblings with RLBP1 mutations had retinal pigment epithelium and photoreceptor abnormalities and reduced levels of 11-cis-retinal, a vitamin A derivative critical for light detection. The authors found that mutation carrier parents show a reduction in 11-cis-retinal, demonstrating visual cycle deficiencies though they reported no symptoms.

These findings, reported in a recent paper in the **Journal of Biological Chemistry**, expand the defined

CEP5 helps plants tolerate droughts

Environmental stresses, such as drought, affect plant growth, development and reproduction. In a recent paper published in **Molecular & Cellular Proteomics**, Stephanie Smith of the University of Nottingham in the UK and Shanshuo Zhu of VIB/University of Ghent in Belgium, together with an international team reported a previously unknown role for the CEP5 peptide in osmotic and drought stress tolerance in Arabidopsis. They propose that the peptide stabilizes auxin transcriptional repressors and fine-tunes the level of auxin signaling.

CEP5 previously was shown to play a role in shoot and root growth. To better understand activity downstream of the peptide, the researchers quantified differences between the proteomes and phosphoproteomes of normal shoots and those of shoots overexpressing CEP5. Based on gene ontology annotations, they write that 30% of the proteins that were upregulated or downregulated were involved in "response to stress" while 17% were involved in "response to abiotic stimulus."

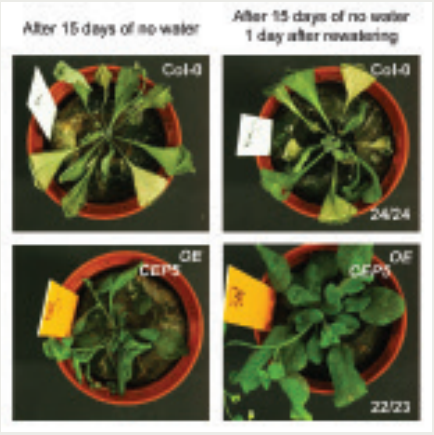
Consistent with these findings, CEP5-overexpressing plants withstood drought stress tolerance tests better than normal plants. After 15 days without water, normal plants were pale and wilted, but nearly all the overexpressing plants still had green leaves. The researchers saw similar tolerance to osmotic stress. They observed elevated expression of stress-related transcription factors in CEP5-overexpressing plants even under unstressed conditions; they propose that this readies plants for future stress conditions.

Auxin is a plant hormone involved in growth and developmental processes. Auxin-responsive markers had reduced activity in plants overexpressing CEP5. Additional CEP5 also led to quick stabilization or accumulation of transcriptional repressors of auxin signaling. Seedlings overexpressing the peptide were more sensitive to chemical or genetic interference of proteasome activity than normal seedlings.

These results indicate that CEP5 affects auxin-mediated processes, including drought and osmotic stress tolerance. Future work is needed to identify all the proteins involved, but the results support a new model for regulating auxin transcription repressors.

DOI: 10.1074/mcp.RA119.001826

—Jack Lee



STEPHANIE SMITH ET AL./MCP

After 15 days without water, normal Arabidopsis plants appear pale and wilted (top panels). In contrast, plants overexpressing CEP5 remain green (bottom left panel). Additionally, these plants can recover quickly from drought (bottom right panel).

phenotype of affected individuals, uncover a previously unreported phenotype in carriers of RLBP1 mutations and show consistencies between affected humans and R lbp1/Cralbp–/– mutant mice.
DOI: 10.1074/jbc.RA120.012695

Ether lipids and fatty acids in disease

Ether lipids, or ELs, are a special class of phospholipid in which the sn-1 position of the glycerol backbone has a lipid attached by an ether or vinyl–ether bond and the sn-2 position is enriched for polyunsaturated fatty acid, or PUFA. ELs play important roles in cell signaling, cellular differentiation and membrane trafficking. Some cellular effects of ELs could be downstream of their role in regulating ion channels, which are embedded in lipid membrane.

In a recent review published in the **Journal of Lipid Research**, Delphine Fontaine and colleagues at the Université de Tours, France, summarized the role of ELs and associated fatty acids, or FAs, in neurological diseases, cardiac abnormalities and cancer biology. The review emphasizes the role of ELs in ion channel regulation because both are involved in human disorders.

FAs derived from ELs are a major component of neuronal membranes and regulate membrane ion channels important for neurotransmissions.

Plant stanol shows promise for rare disorder

Niemann-Pick type C disease, or NPC, is a rare inherited lipid metabolism disorder caused by mutation in NPC1 or NPC2 genes responsible for the transport of cholesterol in lysosomes, membrane-bound organelles that contain digestive enzymes. When transport out of the organelles is impaired, cholesterol builds up inside. Common symptoms of NPC include nerve disorders, liver damage, weight loss and inflammation. No cure exists, and the disease can be fatal.

Plant stanol ester supplements have been beneficial against cholesterol accumulation and inflammation in nonalcoholic steatohepatitis, or NASH, and atherosclerosis. Plant stanol esters look a lot like cholesterol at a molecular level and help to block cholesterol absorption in the body. They are found naturally in nuts, seeds and legumes as well as in stanol-fortified margarine spreads, cereals and other foods that are widely available.

In a paper published in the **Journal of Lipid Research**, Inês Magro dos Reis of Maastricht University and a team of European researchers describe their recent work on the effects of stanols on mice with dysfunctional NPC1 protein. After feeding the mice a plant stanol–enriched diet for five weeks, the researchers observed a significant lowering of liver damage, cholesterol accumulation and inflammation, as well as a shift toward an anti-inflammatory blood profile. This improvement was more pronounced at higher stanol doses.

The study indicates that dietary supplements of plant stanol esters could be an effective way to reduce damage related to cholesterol storage. Researchers now need to investigate the appropriate doses and side effects of plant stanol for use in humans with NPC.
DOI: 10.1194/jlr.RA120000632

—Amrita Mandal

PETER FEGHALI/UNSPLASH

Nuts are natural sources of plant stanol esters.

FA deficiency is involved in neurological disorders. Diets rich in n-3 PUFAs are beneficial for heart disease patients. EL-derived PUFA helps regulate ion channels in the heart to prevent arrhythmia. EL-derived FAs are also involved in cancer cell proliferation, metastasis and apoptosis, and FAs are used as a biomarker in breast, prostate and lung cancer. The authors propose that EL-regulated ion channels could have an important role in cancer progression. Future investigation will help delineate the exact pathways and molecules involved.
DOI: 10.1194/jlr.RA120000634

An energy-regulating enzyme needs nutrients

AMP-activated protein kinase, or AMPK, is a sensor that helps cells adapt to changes in nutrition to maintain cellular energy states in the liver, but what exactly AMPK is sensing has not been clear.

In recent work published in the **Journal of Biological Chemistry**, Camille Huet of the University of Paris and the National Institute of Health and Medical Research in France, along with collaborators, sought to uncover the factors responsible for AMPK activation. Using mouse liver cells grown in culture dishes, the researchers showed that glucose availability activates AMPK, while changes in levels of the hormones glucagon and insulin had no effect on AMPK. Furthermore, they showed that glucose deprivation and the deficiency in AMPK activity exacerbate the reduction of cellular ATP.

These results suggest that nutritional changes rather than hormonal variation sensitize AMPK to the energetic strain associated with fasting and that this effect is critical for regulating energy in liver cells.
DOI: 10.1074/jbc.RA119.010244

Enzymes, TB and allostery

Allostery, the process by which proteins transmit effects from one site to a separate, often distant functional site, can help enzymes meet the metabolic demands for their end products. Better understanding of this phenomenon helps researchers understand biological processes and catalyzes the design of new drug treatments.

In a paper published in the **Journal of Biological Chemistry**, Wanting Jiao of the University of Canterbury and collaborators examined 3-deoxy-D-arabino-heptulosonate 7 phosphate synthase, or DAH7PS, an enzyme central to amino acid synthesis in Mycobacterium tuberculosis, the bacteria that causes tuberculosis in humans. The authors showed that a single amino acid substitution abolished the allosteric communication in DAH7PS, but it did not affect its catalyzing abilities.

These results provide insights into the delicate dynamics of enzyme regulation and may lead to the discovery of new treatment options for TB.
DOI: 10.1074/jbc.RA120.012605

Deamidation is rife in the immunopeptidome

T cells target infected and damaged cells by recognizing peptides presented on cell surfaces by human leukocyte antigen. Post-translational modification of these peptides expands the variety of possible signals displayed by cells. But few systematic studies have explored modifications across the entire immunopeptidome.

In a recent paper published in **Molecular & Cellular Proteomics**, Shutao Mei of Monash University and a team of Australian researchers found that 2.5% to 7% of associated peptides are deamidated, with the amide group removed from asparagine and glutamine residues.

The researchers analyzed the amino acids flanking the deamidated residues to identify possible motifs. They found a pattern for asparagine: a preference for threonine or serine two positions following the affected residue. This motif, NX(S/T), is canonical for N-linked glycosylation.

The researchers tested a possible role of peptide:N-glycanase, or PNGase; this enzyme removes N-linked glycans from misfolded glycoproteins and is known to deamidate asparagine. In the presence of a PNGase inhibitor, the immunopeptidome contained significantly fewer NX(S/T)-containing peptides. The researchers propose asparagine deamidation as a means for the immune system to identify cells with perturbed N-glycosylation for elimination.
DOI: 10.1074/mcp.RA119.001846

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Leadership on the Cutting Edge

Toni Antalis, a physiologist who discovered membrane-anchored proteases, takes on the ASBMB's presidency

By Laurel Oldach

COURTESY OF TONI ANTALIS

Toni Antalis became the 87th president of the ASBMB on July 1. She will serve for two years.

New American Society for Biochemistry and Molecular Biology president Toni Antalis and the ASBMB go way back. Her first first-author paper as a Ph.D. student was published in the Journal of Biological Chemistry, as was a paper she co-authored with a Ph.D. student of her own that set her on her current research path studying membrane-anchored serine proteases.

Antalis, a professor of physiology at the University of Maryland School of Medicine in Baltimore, directs the school's Ph.D. training program in molecular medicine and is the associate director for training and education at the Marlene and Stewart Greenebaum Comprehensive Cancer Center. On the day that Antalis' lab began gingerly to reopen after four months closed due to COVID-19, ASBMB writer Laurel Oldach spoke to the society's new leader about her research and the challenging times ahead. Their conversation has been edited for length and clarity.

How has it been for you leading a lab during the pandemic?

For me as a PI, it has not been as bad as it has been for my students and postdocs and for others in research training. I enjoy reading and writing and catching up with the scientific literature. The story of SARS-CoV-2 has been fascinating. However, I have students who really had to put their whole theses on hold for three or four months because they could not get into the lab to start new experiments. I find that young scientists love to be in the lab doing experiments and discovering, but they don't like to write so much. In some ways, this has been an opportunity for them to gather their thoughts, put all of their data together and think about what their research findings mean in the context of the scientific field. But they probably didn't need this long to do that.

As for me, I seem to be busier with virtual meetings from home than when I was in my office. It is hard to say why, but there are always student proposals and exams, as well as organizing how teaching is to become more virtual in this new COVID-19 environment. Virtual meetings can be quite tiring — although it is good to see faces and expressions as well as have conversation. I think it calms everybody down.

We're looking forward to being in person in the lab, though this will take time. The University of Maryland is reopening very cautiously, and there are lots of changes around the buildings to mitigate spread of the virus.

LAURIE RELUZCO/ASBMB

Antalis (sixth from right) joined an excursion to Great Falls National Park during the 2019 Serine Proteases small meeting. She cofounded the biannual meeting in 2015.

We've set up a social distancing regimen for the lab so that everybody maintains six feet of distance, wears gloves and masks when appropriate, and has access to plenty of sanitizers. In our building, a special antiviral adhesive has been put on all the door handles and frequently used push buttons — this seems a neat invention.

As you get back into the lab, what research questions are you most excited about working on?

My research interests are in proteases and protease-activated signaling pathways that affect tumor metastasis, inflammation and vascular biology. We are studying several inflammatory mechanisms that promote the resolution of venous thrombosis, in order to accelerate the process and potentially avoid surgical intervention.

We also study how membrane-anchored serine proteases function to promote the dissemination and spread of ovarian cancers and affect their responses to chemotherapy. While chemotherapy will kill tumor cells, tumors can become resistant to these treatments, and this is a problem because alternative effective therapeutic options are limited. We use pre-clinical mouse models of human ovarian cancer dissemination and spread to better understand molecular mechanisms that we might be able to exploit for alternative treatments. As we are always looking for ways to translate our basic research findings to the clinic, we are working on a potential prodrug therapy using a mutated anthrax toxin to target and kill ovarian tumor cells.

How does the anthrax toxin work?

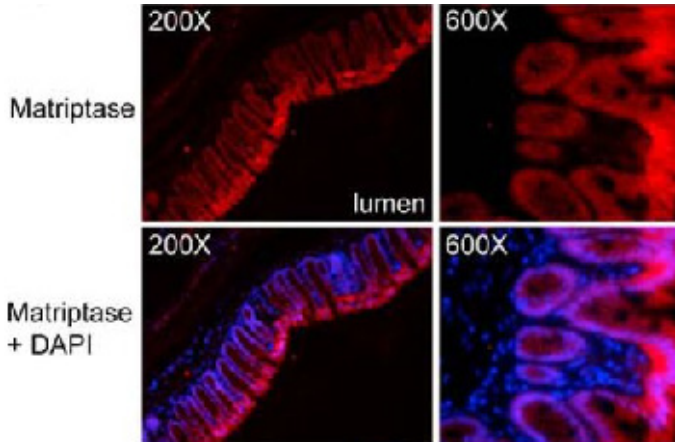
One of the anthrax toxin proteins binds to specific receptors on human cells where it is proteolytically processed by human proteases, allowing it to form a pore that enables toxic peptides to enter and kill cells. We have engineered a toxin that takes advantage of the overactivity of membrane-anchored serine proteases on the surface of ovarian tumor cells and limits the growth of the cancer cells in ovarian cancer and likely many other cancers.

How did you first get interested in serine proteases?

As a postdoctoral fellow. I cloned a serine protease inhibitor of the plasminogen activation cascade, known as PAI-2/SerpinB2, and that began my interest in fibrinolysis, the process of blood clot dissolution.

When the genome was sequenced at the turn of the century, I was working at Queensland Institute of Medical Research in Brisbane, Australia. My graduate student John Hooper and I noticed that there was a family of serine proteases that anchor directly on cell membranes. We published a review on this protein family in JBC in 2001, and we've been trying to better understand what these proteases do ever since. In fact, one of these, TMPRSS2, is an activator of the SARS-CoV-2 virus, and inhibitors of this protease are in clinical trials. The growth in this field led to a 2015 ASBMB Special Symposium on Membrane Anchored Serine Proteases, which is now held every two to three years.

“I’ve been involved with the ASBMB for a long time, and



BUZZA ET AL. / JBC 2017

The membrane-anchored serine protease matriptase is involved in epithelial barrier formation and maintenance. In this micrograph of the mouse intestinal epithelium, from an Antalis lab study investigating how the enzyme is changed in a model of irritable bowel disease, matriptase is shown in red and nuclei (stained with DAPI) are in blue.

ASBMB

Tony Antalis, past president Jerry Hart (left) and ASBMB chief financial officer Steve Miller (right) pose at a meeting of the ASBMB Council.

JBC was key to how you got involved in ASBMB leadership, right?

I have had a longstanding relationship with the journal and the society. I was invited to join the editorial board of JBC in 2003 by Dr. Judy Bond, an associate editor, and was elected to serve as a member of the ASBMB Publications Committee in 2006. I was chair of the committee from 2008 to 2011, and in 2011, I was elected treasurer of the society; I served in that capacity for six years. So, yes, I’ve been involved with the ASBMB for a long time, and I’ve watched it progress and evolve over the years. It’s a really impressive society. I am proud of the ways in which the ASBMB serves the needs of the scientific community by promoting science advocacy, communication, education and outreach and how it invests in the careers of junior scientists.

As president, what do you see as the way forward for the society?

I believe a number of challenges are facing not only this society but all scientific societies in the next few years. The ASBMB is remarkably well positioned to meet these head-on. I look forward to working with the society leadership, the membership and all of the staff to help keep the society moving forward and continuing to innovate.

One major change this year is the transition of the ASBMB journals to gold open access. This is an important step. As scientists, we all want scientific literature openly accessible to all members of the scientific community, but at the same time it is important to develop a workable finance structure that maintains the quality, transparency and rigor that are the hallmark of the ASBMB journals.

Another challenge we face these days is the importance of not politicizing science. Scientific societies play an important role in trying to prevent politicization of science funding and of scientific results. In the next few years, given the persistence of COVID-19 and the uncertain economy, maintaining financial support for scientific research and supporting funding agencies like the National Institutes of Health is going to be critical.

Years of basic research in diverse fields have made it possible to move fast in developing a vaccine for SARS-

I've watched it progress and evolve over the years."

ASBMB

Antalis and her graduate students Tierra Johnson (left) and Nisha Pawar having some fun at the 2019 ASBMB annual meeting in Orlando, Florida.

COURTESY OF TONI ANTALIS

During the 2019 Serine Proteases meeting, Antalis posed with organizers Bob Lazarus of Genentech (left) and Eric Camerer of INSERM.

CoV-2. For example, we know about TMPRSS2 because of cancer research, ACE2 because of research in vascular biology, the SARS-CoV-2 protein structures and genomics because of biochemistry and molecular biology — all research is important in the middle of a pandemic. We need to support our society members so they can continue to do important groundbreaking research.

In these times, scientific advocacy is crucial. We want to maintain support, stability, fairness and good practices in science and throughout the community. Supporting young people so they can progress in their science careers is important, and the more we can advocate for the next generation, the better it will be for the scientific community and for research as a whole.

This is also a crucial time for facing America's legacy of racism. Scientific societies can play a pivotal role in advocating for broader access to and equity in STEM. Communication is key. I want to hear from all members of the society and make sure that all ASBMB leaders are aware of their issues and perspectives so we can move forward in the best possible and most strategic way.

What do you enjoy doing in your time outside of working hours? What do you do to recharge?

I can highly recommend yoga; it's so good for relieving stress. I try to do other exercise too, but yoga is my favorite. My family includes two rescue cats that keep me busy — they're about 2 years old now. I do a fair bit of reading of news stories and analyses, and I also belong to a book club, which allows for interesting discussions and many different perspectives. We recently read "Bad Blood: Secrets and Lies in a Silicon Valley Startup," the bizarre story about the rise and fall of the biotech company Theranos — and a lesson in the importance of ethics.

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

Job seekers feel the effects of the pandemic and politics

Grant-funded postdoc positions seem secure, but hiring freezes and the Trump administration's attempts to curb immigration worry researchers ready to start new labs and PIs and committees courting talent.

By John Arnst

Deepika Vasudevan

Daniela Cimini

In mid-March, Deepika Vasudevan was in the middle of negotiating faculty position offers with two public universities in the Northeast. Then campuses across the U.S. shuttered to help stem the COVID-19 pandemic. And then came the hiring freezes.

Just like that, the positions favored by Vasudevan, a sixth-year postdoctoral research fellow at New York University's Langone Medical Center, disappeared.

"We finalized the start date and the start-up package. And the chair of the department emailed me saying that they were waiting to hear from the dean," she said. "But then, a week later, he emailed me saying, 'the dean has asked me to withdraw your offer citing financial uncertainties the school of medicine is facing due to COVID-19.' That was really tough."

Vasudevan quickly reached out to the department chair at the second university, who shared her concern about the rapid uptick in hiring freezes. On April 2, that university also announced a freeze — leaving Vasudevan with few options once her K-99 funding runs out in September.

She is not alone. Since April, hiring freezes have halted faculty searches and some postdoctoral hiring at more than 400 universities. At the same time, recent restrictions on H-1B visas have constrained recruitment of international postdoctoral fellows.

Vasudevan, who investigates regulation of mRNA translation in ophthalmological disorders, is one of more than 350 members of the "Future PI" Slack channel, where academic researchers discuss job applications, interviews and offers, along with other aspects of preparing to become a principal investigator.

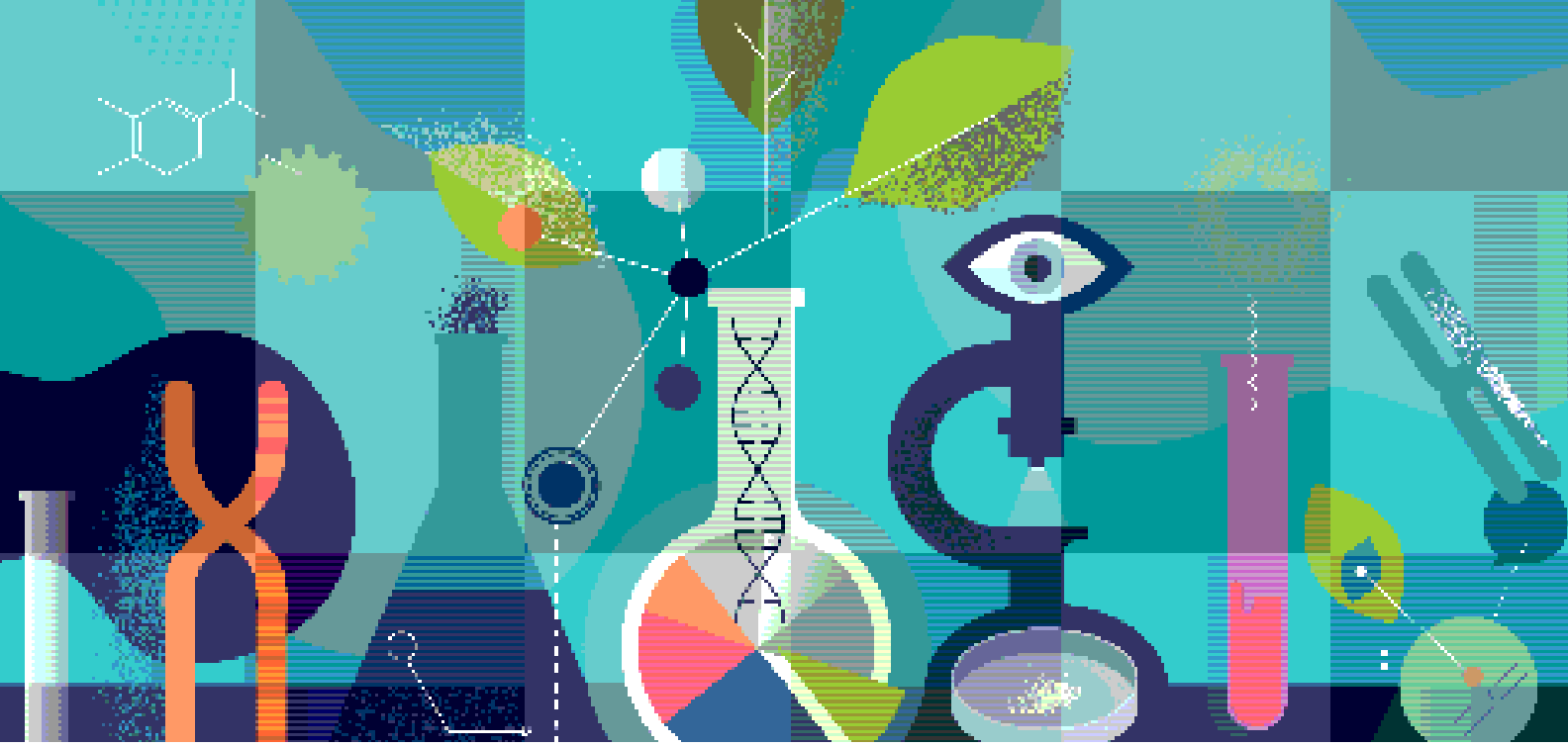
"There are at least a dozen people who are in limbo. They've had second visits canceled or soft verbal offers withdrawn. At least from what I read, I seem to be the only unlucky one who had a written offer rescinded," she said. "A couple of people talk about search chairs really going to bat for them and making sure the offers have been signed even with hiring chills in place. There are also many for whom second visits were canceled due to the search being suspended."

Uneven thaw

For every aspiring PI frozen out of a faculty search, there are frustrated hiring committee members whose efforts to fill their departments have been derailed.

Daniela Cimini is one of them. A professor at Virginia Polytechnic Institute and State University, Cimini thought she had found the perfect candidate back in March for a tenure-track systems biology position at the university.

"We had a great candidate, but the hiring freeze went into effect before we could get a



contract signed," she said. "That freeze will not be lifted for the next recruiting cycle, so it is quite uncertain when or if we will be able to get this candidate."

However, some universities, such as Oklahoma State, have continued filling faculty positions deemed essential while funds for other positions remain frozen.

Charles Sanny chairs the department of biochemistry and microbiology at the OSU Center for Health Sciences and has been involved in its ongoing search for a new faculty member.

"It's not like there's been a whole bunch of recruiting going on throughout the Center for Health Sciences during the COVID-19 crisis. It's just that we started about a year ago, and the process was allowed to continue and come to a conclusion," Sanny said. "We had some candidates that actually were able to come to the interviews before the lockdown happened."

A more recent candidate, he added, had to be interviewed on Zoom.

Despite hiring freezes for faculty positions, many primary investigators still are hiring recent Ph.D. recipients to work in their labs.

Patricia Phelps, director of professional and career development at the Johns Hopkins School of Medicine, has been tracking how universities have changed their postdoctoral hiring policies in response to the pandemic.

Phelps and her staff conducted a survey of postdoctoral affairs offices and found that 67% of the institutions that responded have granted one-year extensions to their postdoctoral term limits. They also found that many universities have granted exceptions to hiring freezes for PIs who will fund postdoctoral positions with their grants.

"It seems like most institutions are still hiring if the positions are externally funded, which is most of the positions," she said.

This was the case for **Michael Johnson**, a bacteriologist at the University of Arizona seeking a postdoctoral fellow for his lab. "I needed to get a waiver to even be able to have the job opening," Johnson said. "I think there's a lot that people can do remotely in terms of training, and then we can get them into the laboratory once things are, I guess, back to normal, whenever that might be."

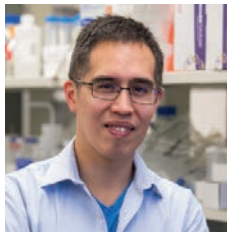
Carlos Castañeda, a biophysicist at Syracuse University, also is seeking two postdoctoral fellows for his lab despite the university's hiring freeze and distancing requirements in lab settings.

"These positions are supported entirely by my federal grants, and that has been extremely helpful in convincing the university that these are positions that I'm entirely taking care of," he said. "So, in some ways, the fact that there is a hiring freeze throughout the university

Charles Sanny

Michael Johnson

Patricia Phelps



Carlos Castañeda

> "Our state-supported public institutions are taking a huge financial hit because of the pandemic."
>
> —Paula Stephan

Paula Stephan

April Rodd

hasn't affected my ability to hire."

Castañeda is, however, concerned about increasing difficulties in hiring both international and domestic candidates.

"Many strong candidates have been international, and the ability to hire them is definitely a big question mark right now, partially because of the pandemic and partially for other reasons," he said. "Currently, it is certainly easier to hire domestic than it is to hire international. However, many domestic candidates have had their Ph.D. defenses pushed back due to prolonged lab closures."

Phelps noted a similar shift in policies at universities that responded to her survey, saying, "The key change I see is the focus on U.S. candidates, which could create a whole separate issue for research."

Beleaguered budget

In July, U.S. Immigration and Customs Enforcement announced that international students would have to take some in-person classes in the fall or leave the country, spurring Harvard University and the Massachusetts Institute of Technology immediately to sue the government. As amicus briefs from other universities piled up, the government backed down.

International students are a major source of revenue for both public and private universities, and mounting costs related to COVID-19 are already punishing large public universities, many of which are in states that cannot run budget deficits.

Worse, an analysis provided by Moody's Investors Services to the Washington Post in 2016 found that the University of Virginia, University of Michigan, Ohio State University, the University of North Carolina at Chapel Hill and the University of Texas system, among many others, had less than one year's worth of cash in their financial reserves. Earlier this year, millions of dollars from the federal government's coronavirus relief package, known as the Coronavirus Aid, Relief and Economic Security (CARES) Act, went to universities that were close to closing.

So, as universities are freezing hiring, they're also slashing other parts of their budgets.

Ohio University, which boasts an on-campus student body of 20,000 undergraduates and an endowment of nearly $600 million, recently announced that it was planning to eliminate 58 nonfaculty staff positions in its College of Arts and Sciences. In May, Ohio Gov. Mark DeWine announced a nearly $800 million cut in state spending, $110m of which was from college and university funding. And in July, the University of North Carolina Board of Governors told chancellors at all 17 campuses to prepare plans to cut their budgets by up to 50%.

According to Paula Stephan, a labor economist at Georgia State University who focuses on the careers of scientists and the economics of science, that pain is being felt at most public universities and institutions.

"Our state-supported public institutions are taking a huge financial hit because of the pandemic. In my own state, institutions are going to have to take an 11% to 14% cut next year," she said. "And, if you talk to people and ask how they're going to cover those, one of them is through canceling positions they were seeking to fill. So I think that says that the market for new hires is definitely not going to be very strong."

Postdoc prospects

April Rodd, an environmental toxicologist in the fourth year of her postdoctoral fellowship at Brown University, in March began looking at her options for academic jobs in the fall, only to watch faculty searches get canceled.

"It worked out. I wouldn't have gotten maternity leave if I had ended up taking any of those positions. But it's put me in a nervous position," said Rodd, who recently became pregnant after years of trying to

start her family. While Rodd and her PI had discussed the possibility of her staying in her lab until the beginning of the 2021 academic year, limited resources and funding rendered that untenable.

"No matter what, I'm going to lose that window of time between the spring and the beginning of the next academic year," she said. "And I just don't know what the fall is going to look like. I don't think any of us do, including the universities."

(Read April Rodd's essay about her postdoc experience on page 51.)

Ryo Higuchi–Sanabria, a fifth-year postdoctoral fellow at the University of California, Berkeley, and his peers are also dismayed.

"Usually things would start to open up now. That was my experience last year," he said. Last fall, Higuchi–Sanabria applied and interviewed for tenure-track positions at universities in the greater Bay Area, more or less as practice, and then he started applying again in earnest this summer.

"There's absolutely nothing open. And some universities are saying that they're planning to open applications in September if they didn't fill positions from last year."

Because many of the postdocs who would have filled those tenure-track positions are still on the job market, Higuchi–Sanabria is worried that the pool of applicants will only become more competitive next year.

"Essentially all the people who couldn't get a job from the 2020/2021 cycle because of the hiring freeze will be applying in the 2021/2022 cycle," he said. "A lot of my colleagues who were planning to apply are saying they're going to wait till next year, or they're just going to start applying for industry now."

Industry's appeal

Ashley Frakes, a research fellow in the same lab as Higuchi–Sanabria whose research involves how astrocytes and microglia regulate aging, is considering positions both within and outside of the academy.

"I've always thought that industry sounded appealing; it's somewhere you can still do research but also have the infrastructure to contribute to a pipeline to impact a disease," she said.

According to Kerry Boehner, an executive recruiter at KOB Solutions who has been recruiting scientists for the pharmaceutical and biotech industries for two decades, certain industry sectors have remained mostly unfazed by the economic downturn.

"When the recession hit in 2008, things definitely slowed down," Boehner said. "So, when the pandemic hit, I expected the same, because everything else slowed down, so why wouldn't biotech and pharma? And, the exact opposite has happened. It really depends on the kind of research that someone was doing in their postdoc or in their Ph.D."

According to Beth Keeler, associate vice president of global talent acquisition at Merck, the pharma giant has not seen a notable increase or decrease in the number of applicants for positions that require postdoctoral or other levels of experience.

"I think it's been steady and it's been consistent, and if you looked at it year over year, you would not see this year standing out as being all that different," Keeler said. "I think in pharmaceuticals, you always have a little bit of a shift, whether it's to a therapeutic area or toward particular functional expertise, like oncology or vaccines. But there has not been a dramatic uptick or a downtick in terms of volume … when you look at our overall hiring volume for this year versus last year, it's almost exactly the same."

For scientists like Frakes, whose research is readily translatable to industry, that means a path out of academia may be available. But for postdocs like Rodd and Vasudevan, who hope for careers as independent investigators, the future is less clear.

While Vasudevan waits for the freezes at the universities she'd been negotiating with

Ryo Higuchi–Sanabria

Ashley Frakes

Kerry Boehner

Beth Keeler

"I think the fact that so many New Yorkers have it worse really gives me pause to say, 'Well, I guess it could be worse.'"

—Deepika Vasudevan

to thaw, her PI, Hyung Don Ryoo, is piecing together funding so she can continue working in his lab.

"Moving forward in the fall, I think I'm going to be doing all the preliminary experiments that I would have been doing in my new lab, except at my postdoc lab," Vasudevan said. "That's kind of the thread to my sanity. I think it also gives me a little bit of perspective that New York has just taken such a big hit … I still mope from time to time, but I think the fact that so many New Yorkers have it worse really gives me pause to say, 'Well, I guess it could be worse.'"

A long arc

Some universities are making changes in policies to reflect how disruptions from COVID-19 have affected researchers' productivity.

According to Johnson, the University of Arizona has allowed professors who were up for tenure, including him, to delay turning in their packets for one year. But he's worried about how hiring committees will evaluate the overflowing pool of applicants for tenure-track positions next year, some of whom had less access to their labs and research materials than their peers.

"Hopefully they will be erring on the side of grace, saying, 'We know you didn't get a chance to do this (experiment) because of COVID, so we can't in good faith or good conscience hold that against you,'" he said. "But, at the same time, here's this other person that might have been working throughout this entire thing and got some great results. How do you treat that?"

John Arnst (jarnst@asbmb.org) is an ASBMB Today science writer. Follow him on Twitter @arnstjohn.

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VIRTUAL ISSUE

Coronaviruses

jbc.org/site/vi/coronaviruses/

ASBMB PUBLICATIONS

THE Careers ISSUE

How a research tech can work from home in the time of COVID-19

By Scott Aoki

Kara, my research technician, asked what she should be working on from home during the coronavirus outbreak, and I didn't know how to respond.

I just started my research lab last August, and she was my first hire, a recent college graduate with two years' work experience in biotech. I have big plans for Kara. In two years, I will encourage her to apply for graduate programs in biochemistry. It will be a challenging next step, but with her intelligence and diligent work ethic, I know she will do well. I don't know what she'll do with her degree, but I not-so-secretly hope that she comes back to Indiana to be near family and improve the community she loves.

This is all whimsical daydreaming. Right now, I need to figure out what a research technician should be doing while physically away from the job she was hired to do. Graduate students and postdocs have their to-do list built into the job. They can start work on a grant, catch up on reading or finish writing that thesis, manuscript or review. We typically hire lab technicians to do tasks at the bench. What can they do if they no longer have access to a laboratory bench? Kara and I came up with these three general categories.

1. Personal and professional development

This category includes tasks that improve a research technician's knowledge base. Graduate students are not the only people who need to catch up on their reading. We all benefit from reading further into laboratory projects, and this time away from the lab allows techs to study the origins of their work. Kara now is investigating the expression profile of a Caenorhabditis elegans gut-specific promoter and when it turns on during larval development.

This category also includes deeper investigation into the methods,

COURTESY OF SCOTT AOKI

Lab technician Kara Osburn and researcher Scott Aoki keep in touch with Zoom calls while Aoki's lab at Indiana University is closed due to the COVID-19 pandemic.

equipment and programs we use in the lab. We are still novices using the departmental confocal microscope, and part of Kara's work from home is to become acquainted with the microscope software. The knowledge she gains about using the imaging software for quantitation and generation of publication-quality images will be a great help to the lab once we get back up and running.

2. Lab organization

Working from home provides time to catch up on lab organizational projects. Kara has helped me update our lab inventory in an electronic database, including primer and plasmid lists that were months behind. Organization also can mean developing new protocols for the lab. As Kara learns the microscope software, she will draft new cheat sheets to help novice users.

3. Creative opportunities

Creative tasks often go on the back burner when we have work that needs to be done right away. Working remotely forces us to slow down and provides time to work on creative lab-related endeavors. Much to the chagrin of my friends and mentors, I've been dragging my feet on developing a lab website. Kara now has time to help me with this project; she's looking into user-friendly software and helping to plan and develop content. With this work, she is developing new skills in website design and programming. I've also asked her for help with my writing, such as editing the essay you are currently reading.

When I became a professor, the first thing other professors told me was that nothing I'd done previously in science would prepare me for the position's demands. I'm certain no one was referring to the challenge of starting a lab in the face of a pandemic. It was hard enough trying to figure out the correct next steps to recruit talent, develop a laboratory culture and obtain extramural funding. What is my role as a supervisor during a catastrophic event that is completely out of my hands?

My conclusion is to strive for normalcy. I may not have the training to work in a hospital emergency room or develop a potent virus vaccine, but I can adjust our work to make my team feel needed and productive. By continuing to contribute as a lab member, Kara will, I hope, return to the bench feeling that she never left her position.

Scott Aoki (staoki@iu.edu) grew up in Hawaii, earned a veterinary degree from the University of California, Davis, obtained a Ph.D. at Harvard University and did his postdoc work at the University of Wisconsin–Madison. He is an assistant professor of biochemistry and molecular biology at the Indiana University School of Medicine.

Grant writing tips for beginners

By Bill Sullivan

Grant writing is a daunting task, especially if you've never written a grant before. I've been writing grants for 20 years, and I've served on multiple study sections for a variety of granting agencies. Here are some of the lessons I learned along the way.

1. Define the key question your research will address.

If you cannot state your research hypothesis or goal in a succinct manner, you are not ready to write a grant. You need to refine your thoughts and ideas, and identify a distinct gap in the knowledge that you are qualified to fill. You may need to read more literature, brainstorm with others or gather more experimental data before you write. It is much easier to write (and review) a grant that has a highly focused question. After you formulate that research question, develop two or three specific aims that address different aspects of it. Aims cannot overlap, and one aim should not be dependent on the results of another.

2. Identify multiple funding agencies.

Once you've defined a question to study, you are in position to market your solution to a variety of granting agencies. Note the plural. It is permissible to pitch your idea to multiple funding agencies and foundations, although you cannot accept money for the same project from more than one. For example, if you submitted a grant to the National Institutes of Health to study cardiovascular disease, why not submit it (or a portion of it) to the American Heart Association as well? If there is an aspect of your project that does not have a clear clinical application, then investigate the possibility of sending it to the National Science Foundation.

Many private foundations fund research proposals. At some universities, grants administration offices circulate calls for proposals from a variety of these foundations. If yours does not, do some hunting online and compile a list of granting agencies you can target. When you read research papers in your field, take note of who funded the work — maybe you can submit your grant to them. Be sure to tailor your application appropriately to each funding agency. An application that has been repackaged without care is spotted easily and typically suffers in the review process.

3. Target the correct funding mechanisms and review panel.

Granting agencies usually have multiple types of applications. Some of the most common at the NIH are the R01, R21 and R03.

R01 grants fund three- to five-year research projects that require substantial preliminary data to convince reviewers of their significance and feasibility. Projects of this kind include detailed studies that address mechanisms underlying biological phenomena or clinical problems.

R21 grants are for shorter two-year research projects that are defined as high risk, high reward. R21s can fund exploratory projects that take a chance on an unorthodox idea.

R03s are for smaller two-year projects designed to address simpler questions, gather data or make reagents for a larger project in the future.

Be sure the scope of your aims fits with the correct funding mechanism.

Large funding institutions such as the NIH house multiple agencies and study sections. Talk to your colleagues and the program officers at the funding agencies; they can help you gauge whether your research topic is appropriate for submission there.

4. The significance of your work should not be limited to the medical problem.

Significance is not limited to the epidemiology of a disease or disorder; everyone knows that cancer, diabetes and malaria are major clinical problems. Your significance section must include why your particular approach to these health problems is unique or important. What makes the particular signaling pathway you chose to investigate worthy of intense interrogation? What is it about your experimental compound that makes it more promising than others? How will the results from your work represent a sustained impact on the field and not just an incremental advance? If you fail to convince a reviewer that your specific approach to the stated biological problem or disease is novel and groundbreaking, your grant is likely to fall through the cracks.

It is useful to spell out clearly the deliverables of your project. After

GREEN CHAMELEON/UNSPLASH

the aims are completed, state exactly how the results will advance the field. In addition, if you are generating key reagents, data sets, compounds or methods that the field can use for years to come, be sure to mention them.

5. Watch your language!

Do not take it for granted that everyone knows the importance of your subject area. More often than not, at least one of your reviewers will be outside of your field. It is critical that you make your application understandable and exciting to those reviewers. Nothing loses a reviewer faster than excessive jargon; if you must use jargon, clearly define the terms. Remember that a picture speaks 1,000 words — a simple diagram that clearly spells out the overarching question and how each aim will address it is an effective way to depict your research plan.

Action words such as "determine," "define" and "identify" are better than nebulous or incremental words like "characterize," "validate" and "explore." You also want to avoid proposing to test "if" something will happen because it raises the question, What will be done if that something doesn't happen? For example, rephrase "We will test if protein x interacts with protein y" to "We will determine the proteins that interact with protein x."

Remember, reviewers have a large stack of grant applications to review. It helps to make yours easy on those tired eyes. Make your application readable and inviting so it is clear and understandable. A convoluted grant application is frustrating to review and often works against you. The best applications I've reviewed are elegant, simple and clear.

Take advantage of grant-writing seminars or pre-review panels at your university. Check out society resources such as the American Society for Biochemistry and Molecular Biology's IMAGE workshop. If no such resources are available or feasible, form your own group to critique your research plan prior to submission. Be

No one enjoys negative reviews, especially when you were misunderstood or when the reviewer was flat-out wrong. A trusted colleague once gave me some great advice: After getting your reviews, write the rebuttal you want to write; delete it the next day, and then write the rebuttal you have to write.

sure to include people who are not in your field.

6. Learn what a successful research proposal looks like.

Study grant applications that have been funded. You can ask your colleagues or campus grants office if they have applications that you could examine for guidance in crafting your own. Examples of successful grant applications are also available online (the National Institute of Allergy and Infectious Diseases has a page devoted to sample applications at niaid.nih.gov/grants-contracts-/sample-applications).

One of the best ways to learn what sort of application works and what doesn't is to serve on or sit in on grant review panels. You probably will not be asked to serve on a study section until you are a funded investigator, but some agencies and universities may allow you to sit in and observe. It is incredibly valuable to learn what reviewers like and dislike in an application. Even if you are successful in securing a grant, serving on a study section is highly recommended to help improve your future grant writing.

7. Timing can be important.

It may behoove you to make a big splash with the work supporting the application just prior to its review. Try to target publication of this study a month or so before your grant is reviewed (that is when reviewers will be reading proposals). Arrange a press release from your university to help promote said publication, and share the news on social media. You and your exciting new findings will be fresh in the minds of reviewers, and your productivity will be noted. Alternatively, preprint servers can be a useful way to showcase your work prior to study section, and most agencies allow you to cite preprints in your research plan. On a related note, take care not to publish anything that completes any part of the research plan, or you will be dinged for already having finished a part of your proposal.

8. Respond appropriately to reviewer comments.

No one enjoys negative reviews, especially when you were misunderstood or when the reviewer was flat-out wrong. A trusted colleague once gave me some great advice: After getting your reviews, write the rebuttal you want to write; delete it the next day, and then write the rebuttal you have to write. In other words, get your frustrations out but do so in private. The response to reviewers that you have to write must exude a respectful tone and showcase your objectivity regarding the science you are proposing.

More often than not, reviewers try very hard to critique your grant fairly and weigh its merit objectively against the other competitive applications in their steep pile. Many reviewers offer helpful comments that will, in fact, improve your application and the quality of your science. On occasion, however, a reviewer may have been unqualified or unfair, and you can bring this to the attention of the study section officer in a professional manner.

I hope these tips help you craft winning grant proposals. Good luck!

Bill Sullivan (wjsulliv@iu.edu) is a professor at Indiana University School of Medicine and the author of several books. He is a member of the ASBMB Today editorial advisory board. Follow him on Twitter @wjsullivan.

F(i/u)nding your next hypothesis

By Audrey L. Lamb & Graham R. Moran

One of the most daunting moments in anyone's career is realizing that you need a new idea. For a research scientist, this realization typically coincides with the assembly of a grant proposal.

If your ideas seem derivative, pedestrian or uninspired, you will have a hard time depicting them as anything else. In the early brainstorming period, you need to develop a genuine fascination. Scientific funding has an unintended validating effect for researchers, but history only reports discoveries; no textbook ever lauded the career funding associated with a foundational idea. Inquiry and analysis remain the bases of scientific achievement.

In recent history, there was a period when senior faculty would, with some pride, quote the number of years "their" grant had been funded. The current generation of researchers does not expect such funding continuity as the norm. Nor do they expect that one area of accomplishment will be sufficient to sustain the four decades of their career.

Arguments can be made for and against merit-based funding, for which the researcher's reputation and past research successes are the primary review criteria. In recent years, we have seen the reinstatement of this idea in the form of the National Institutes of Health's Maximizing Investigators' Research Award and Method to Extend Research in Time mechanisms, known as MIRA and MERIT. However, these grants only equal about 6% of all those funded via the R01 mechanism. Most researchers must seek funding based on their current ideas.

The current generation of researchers is drawn necessarily into cycles of renewal and reinvention. New ideas can come in a variety of forms: They can be a branch of a path you are already on or a new path altogether. Either way, new ideas require courage, a willingness to be inspired, and an investment of time for literature research and the development of preliminary evidence.

How might you identify and develop a new idea?

- **Listening:** Attend seminars and be open to ideas of colleagues in your field (enzymology for us) or more broadly (biology/chemistry). Audrey developed a new idea after receiving an email from a trusted friend and colleague who sent a recently published and rather overstated article that claimed the focus of both of their labs was out-of-date. While not accurate, it was certainly a spur.
- **Lists:** We have a shared drive titled "grant ideas." It contains nine project folders, two of which we have gotten funded. More than half of the projects remain in the gestational stage. When we hear or see something that sparks our interest, we drop the idea into a folder for future evaluation and maturation.
- **Digging:** Spend some time digging up new ideas in the literature. For example, review articles frequently have "unanswered questions" sections, which provide a foundation of prior work and a solid premise for future investigation. In contrast, articles from high-impact journals often have leading-edge, high-risk, high-reward results that can serve as the basis for projects that will elaborate knowledge in a new field. This is especially useful for developing cross-disciplinary projects in which you apply your skills to expand on the work of someone from a disparate field.
- **Teamwork:** Sometimes, to stay afloat while new ideas are hatching, it is wise to contribute

your expertise to other people's projects. A strong collaboration frequently leads to a new inspiration.

- **Life:** Paying attention to major life events can be a source of invention. For example, one of Graham's current projects evolved when a childhood friend succumbed to brain cancer. After reading about the treatment plan, Graham chose to initiate a new project about an enzyme that is implicated in the disease's progression. Similarly, we are all aware of the potential of contributions to the worldwide effort to thwart the march of COVID-19.

A new project is only viable if it is intrinsically interesting to the researcher, feasible at the bench and inspiring to other researchers. Possibly the most difficult skill to develop is the ability to recognize which ideas satisfy all three criteria.

Many of us have fallen into the trap of chasing grant dollars, writing aims for a grant in response to a call for applications that does not inspire us (ask Audrey about high-throughput screening). Few aspects of research are more demoralizing than having grant funding that compels you to complete aims that do not fascinate you.

Some ideas have an easy path to demonstrating feasibility. For others, persistence is key, and some never pan out. Avoid being drawn into areas that do not readily adapt or scale to your skill set (ask Graham about RNA modifying enzymes and observations made on the micromolar scale).

Lastly, when developing your ideas for the broader scientific community, remain aware that they must be framed in a way that inspires others, including grant review panels. You need a receptive audience for your new idea, and targeting the wrong audience is futile (for example, we originally targeted our riboflavin biosynthesis grant to the wrong panel).

Being nimble has advantages for researchers at all levels, from primary investigators to trainees, and expands the discipline to which they contribute. They acquire versatility by maintaining an opportunistic and willing stance toward new problems. As researchers tackle multiple projects during their careers, this provides opportunities for continued learning and growth. In addition, the scientific community benefits from improved inclusivity of perspectives, which in turn more efficiently drives discovery.

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Illuminating leadership during crisis

By Melissa Vaught

Crisis has a way of revealing things about leaders, from the lab manager to the top of the institution. In times of uncertainty, the spotlight is on them. How they react and communicate decisions (or don't), while influenced by organizational policy and culture, tells us something about their values.

The charismatic, confident leader might make for a good business profile or biography, but contrary to popular caricatures, these characteristics don't make an excellent leader. Literally volumes have been written to describe styles, types and characteristics of leaders good, bad and great. In this moment, I find myself looking most for the following three traits.

Transparency

Knowledge is power, yet sometimes managers hoard it, claiming that it protects employees. They don't want an employee thinking about budget constraints or the stability of their position. In the lab, this is framed as allowing members to focus on the science. At other times, managers lack information or clarity and, worried that transparency will undermine their authority, say something with certainty they cannot possibly have or say nothing at all.

These situations readily can backfire: In the absence of a compelling narrative, people will create their own. Leaders recognize the importance of transparency, especially in times of crisis. That's not to say leaders disclose everything to everyone. No work ever would get done that way, and there's some information that a leader cannot or should not disclose (examples include legal proceedings and confidential matters). Transparency is more than a data dump. It includes contextualization: how we got the information, what it means for us, what assumptions have been made, how the organization is responding. Sharing the what and why of the things that affect your team builds trust, which can help your team grow.

Humility

In my own experience, the culture of academic science often pushes for an appearance of confidence, even to the point of arrogance. We are taught to pick apart every result presented to us, to question every claim and to defend vociferously our own work and point of view. As our scientific training advances, a tension builds between the joy of learning and openness and the demand to be self-assured and right. We are pushed to promote the importance and impact of our work and field and, implicitly or explicitly, to elevate its value — or at least the perception of its value — above others.

It should come as no surprise, then, that transparency can feel risky or at the very least uncomfortable, in part because it may require admitting weaknesses, deficiencies, even mistakes. Humility requires that we recognize failures and flaws. But it also frees us from perfection. Humility empowers us to say, "I don't know." It keeps us from buying into our own hype. We can accept and embrace a dependence on others. They may even help us with those questions we don't have answers for yet. It comes easier to some than others, but just

Compassionate leaders can transform organizations for their employees. Kim Scott suggests, from her experience and review of research, that individuals and organizations excel when managers directly challenge their employees while also caring deeply — or practicing "radical candor."

like any other skill, humility can be cultivated through honestly assessing what we don't know, genuinely listening to weird ideas and nourishing our curiosity.

Compassion

Leadership requires connection, and we often turn to empathy to relate to others. But empathy has its limits. It is short-lived and exhausting and can even be paralyzing. It can keep us from being honest with critical feedback (Kim Scott in "Radical Candor" refers to this as "ruinous empathy"). Perhaps most importantly, we tend to empathize most with those who look like us, so empathy can disrupt equity and diversity.

That doesn't remove a place for care in leadership. Now more than ever, the folks we work with need compassion. Care does not diminish the effectiveness of leadership. Compassionate leaders can transform organizations for their employees. Kim Scott suggests, from her experience and review of research, that individuals and organizations excel when managers directly challenge their employees while also caring deeply — or practicing "radical candor." Imagining how someone must be feeling doesn't spur action, but compassionate leaders work to remove barriers for their teams. They make space for others and seek to lead through influence rather than authority.

Maybe these aren't the top characteristics that come to mind when you think of leaders. Yet these elements represent grounding principles from which other powerful qualities flow — clarity, flexibility, mindful presence, accountability and thoughtful delegation, among others. Crisis shines a light on the difference between management and leadership, and it's time to broaden our vision of what leadership can be.

Melissa Vaught (vaughtmd@gmail.com) is the director of research development for the Institute of Translational Health Science at the University of Washington. (Views expressed here are her own.) In Seattle, you might spot her running on the roads or the trails. You can also find her on Twitter @biochembelle.

My postdoc road was rocky — then the pandemic hit

By April Rodd

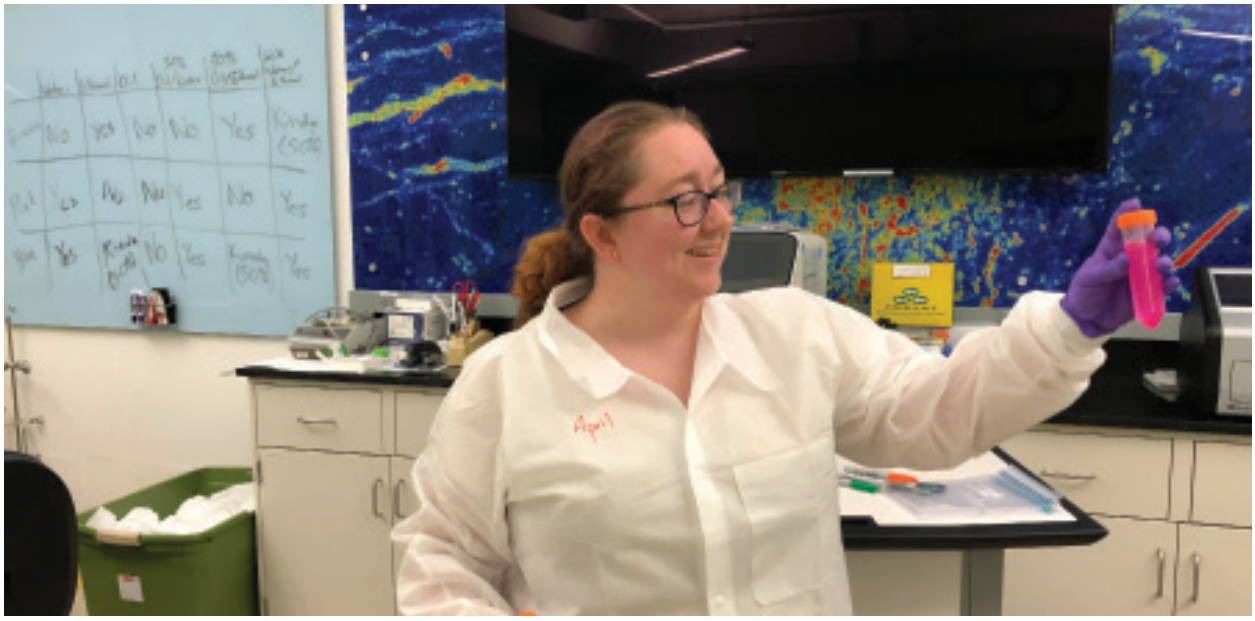
This should have been a year of big transitions and exciting changes. It's the final year of my three-year postdoc, and I planned carefully since the start. I took advantage of every opportunity to expand my skills in the lab and the classroom, and I even created some opportunities of my own.

Stepping outside the lab, I designed and taught two short pre-college classes, I founded a monthly writing group to improve science communication skills in departmental trainees, and I attended local scientific meetings to expand my understanding and network. I had projects in motion for publications and future independent work, and I was ready to jump into the next phase of my career as an independent scientist.

Like all researchers, I hit stumbling blocks along the way, and I worked hard to adapt and stay on track. The lab animals for one project took an unexpectedly long time to reach breeding size, so I pivoted to focus on another cell type while they caught up. When a large funding application didn't succeed, I worked on expanding other projects for future opportunities. I tried to view these challenges as exercises in flexibility and persistence, traits I knew would help me succeed as a principal investigator.

Last fall I had my worst challenge yet when mental health issues I was struggling with hit the breaking point. After years of pushing through graduate school and my time as an early postdoc, I had to accept an immovable truth: I needed to find new ways to do my work, or I could not do it anymore. I was in denial until I found myself in the hospital, and then it was something I could no longer ignore.

In science, we often feel that there is no such thing as good enough — we can always do more work. My mental health crisis forced me to value my time and life outside of work. I poured my efforts into building new habits and managing my illness. As the fall of 2019 came to a close, I was doing better than I had in a long time. With a new set of coping skills, my baseline health improved. In addition to seeking help from doctors and clinicians, I found success using a skills-based approach that taught



MICHELLE KOSSACK

April Rodd teaches her one-week summer course "Factory to Faucet: Environmental Toxicology and Chemistry" to precollege and high school students at Brown University last summer. In this lab activity, the students were learning how contaminants move in the environment.

me how to cope with my feelings in the moment and achieve healthier behaviors. I focused on establishing specific short-term goals and connecting them to realistic timelines. Perhaps most importantly, I accepted that I can't control every aspect of a research project and that burning myself out trying only would make me less successful.

I felt more on top of my future than ever, and 2020 looked like a bright new year to take the next big step forward. Then the pandemic hit, and suddenly my year looked very different.

I had planned to begin my job search this year, but that became unexpectedly difficult. An application for a nonresearch university job ended with a canceled search, and several others were canceled while I was finalizing my application materials. Planning ahead for faculty applications, I had a specific idea of how to present my research goals as a future principal investigator with projects independent of my postdoctoral lab. My university began a phased-in approach to research in early summer, so I will be able to finish one publication, but I won't have time to build more data toward that independent research. To finish the publication in progress, I must devote my time to that and will have a weaker proposal for future funding opportunities and job applications.

A year before my contract was set to end in February 2021, I started discussing with my PI how to move into applying for positions as an independent investigator and what funding opportunities would allow me to do research through the summer until I could start at a new position in the 2021 academic year. However, with changes in lab resources and the reduced time post-quarantine to develop new applications, the ideas generated by these planning sessions became unrealistic. Now there will be a gap between my postdoc and the start of the next academic year, leaving me at a disadvantage for the next application cycle and out of the running for funding applications.

In a last unexpected wrinkle, right at the beginning of the COVID-19 quarantine here in the U.S., I found out I was pregnant after years of trying to start my family. As is common, my pregnancy required changes to my mental health management tactics, and it has brought back challenges I previously had controlled. My medications had to be adjusted to stay at safe and effective levels, and the physical and emotional stress of pregnancy makes it difficult to maintain a healthy mental state. The skills and tactics I developed for maintaining a healthy balance do not always succeed. On top of that, because I am a toxicologist, I will need to rely on others to handle the dangerous materials that are essential to my research, and the timing of my due date will cost me the last two months of this postdoc.

I am facing a snarl of problems, and I have no answers. Any one of these difficulties would be a challenge — my mental health issues, the pandemic, my job transition, the pregnancy. Facing them all, I feel overwhelmed as I try to navigate the crosscurrents and start the next phase of my career. My transition to independence is looking more like another leak from the academic pipeline.

I always have kept an open mind about the direction my career takes, but it's frustrating to feel my options shrink. I am grateful to have a job and a paycheck when so many others have lost theirs, and I am lucky to have a partner in a similar position. But the path forward is murky, and my goals for 2020 seem unreachable. Instead of an exciting move to a new level of academic independence, this stage feels fragile and the obstacles insurmountable.

I focus on what I can do today and take the changes as they arrive. Rather than dwell on what is delayed, I've used my time at home to get through more data analysis and to begin writing manuscripts. The more flexible schedule has given me the space to incorporate more mental health skills and strategies into my daily routine, keeping me healthy in a difficult time. As the university opens up, I focus on what I can do day to day and week to week.

Though it may not be what I had planned, I hold on to hope for my next step forward, and I do what I can each day to be as successful as possible in this evolving environment. That hope inspires me to reevaluate why I have chosen to be a researcher and why I have these career goals: my love of science.

Whatever I do next, whether it's staying on the path of academic research or something else, if I stay focused on that love of science, I know I can achieve the goals that matter most to me.

April Rodd (april_rodd@brown.edu) is an environmental toxicologist, developmental biologist and overall science enthusiast. She earned a Ph.D. in pathobiology from Brown University.

How can labs reopen safely?

Critical thinking and the courage to speak up are essential as we navigate this uncharted territory

By Elizabeth Stivison

Labs are trying to reopen and get back to research while not spreading COVID-19. Great goal, but how do we do that? For this article, I'm taking a look at best practices for reopening labs and what we who spend our days at the lab bench need to be asking ourselves as we move forward.

Many universities and research institutes have published guidelines on their websites. When in doubt, follow your institution's guidelines.

Make sure the guidelines that your lab or institution has decided on are communicated clearly and often. It's important that everyone is on the same page, and having the rules in writing will help achieve that.

However, this is uncharted territory, so we should all think critically about what to do and work together (from a distance) to make sure we're doing what's best. To this end, I looked at the Centers for Disease Control and Prevention guide for reopening, which states, "All employers should implement and update as necessary a plan that is specific to your workplace." I then asked how this applies to labs.

Just as labs are different from offices, every lab is different from every other lab. Everything varies, from the number of people to the building's ventilation system. A lab with two people is going to make different decisions and rules than a lab with 20 people, and a wet lab is going to make different decisions than a dry lab, and so on. Because of this variability, I've included guidelines and lab-specific info, but I've also included questions to ask about your lab and institution.

Students, postdocs and technicians don't set institutional policies, but we can talk to our principal investigators about how to work things in our own labs and advocate for policies if we need to. I suggest talking to your PI first about any reopening questions; that way if any big issues come up, you're on the same page and can work things out together.

Here are the three main points from the CDC guidelines and what each might look like in lab.

1. Stay home if you are (at all) sick, or if someone you live with is sick.

By now, everyone knows this. After staying home, follow CDC guidelines for returning to work. These guidelines state that if someone had COVID-19, they should stay home at least 10 days from first symptoms or three days from the last day of fever, or, if testing is available, they should get tested (again) and test negative (though sometimes tests stay positive after the virus is gone).

What should you do if you've had symptoms but couldn't get tested and don't think it was COVID 19? What I've seen: People with mild symptoms stay home just in case, and, if it turns out to be nothing, they stay home another three days after recovering.

Since people likely will be staying home more than usual, it is important that employers are generous with sick leave. People who typically would come to work with a mild cold now are staying home to protect their co-workers and shouldn't be penalized for missing work. Sick days might be more flexible for students on stipend than technicians who are paid hourly, so you should talk to your PI about these rules or perhaps contact the people in charge at your institution to get clarity. Advocate for leniency with sick time, especially for hourly workers.

2. Perform daily health checks. (This often ends up being temperature checks.)

This one is tricky because it's important to maintain social distancing while doing these checks. It does less good, and possibly does harm, to funnel every employee into one entrance and have them stand around in a crowd waiting to be screened, and then have everyone take off their masks and stand less than an arm's length from a person sticking a thermometer in their mouth.

Another potential risky spot is the case of labs that are associated with hospitals. It might seem to make sense to set up one station to screen all employees in a hospital system, but if this site is in the hospital, people are forced to go into the hospital when they might normally just go to the lab and not see anyone. This seems like a risk since a hospital is the one place where people with coronavirus are guaranteed to be.

If your institution seems to be making risky choices about screening employees, it might be worth suggesting ways to do so more safely. Infrared no-contact thermometers or sneeze guard–like barriers that people can reach around without breathing

MORNING BREW/UNSPLASH

Make sure the guidelines that your lab or institution has decided on are communicated clearly and often. It's important that everyone is on the same page, and having the rules in writing will help achieve that.

on each other are potential solutions. You might ask if multiple screening locations can be set up to reduce the chance of crowds. If you're at a hospital, ask if these could include sites outside the hospital.

If you think screening processes could be safer, go to your PI first. If your institution has a webpage dedicated to COVID-19 policies, you can look there for contact info for the people registering concerns and answering questions. Consider getting in touch with the occupational health office, the dean, or even the head of your program. All these people have more clout than a student or postdoc and are more likely to be able to effect changes.

It's possible, especially in big institutions, that the way it's being done is just the way it will continue to be done. In that case, try to work out hours with your PI so you can avoid rush times and crowds at the screening sites.

3. Think about how and where exposure can happen, identify hazards in your workplace, and reduce them.

This can include wearing personal protective equipment (PPE) and cloth masks, practicing social distancing and making hygiene central, including handwashing and frequently cleaning high-touch surfaces like doorknobs. This last one is easy for labs. We wipe stuff down with ethanol all the time.

But this is also where the real decision-making comes into play, and we have to decide what it looks like in the lab. First, find out if your institution has guidelines for labs. Research centers and universities seem to vary widely. Some have every detail covered on a website. Others just say to be careful. Some leave it up to departments or individual labs.

Even those of us who have clear guidelines from the top are still learning as we go. Some guidelines might turn out to be wrong; more might be added. Some might become useless, while others become essential. As we go through the trial-and-error process of returning to lab, making a list of questions and factors influencing your own lab's practices is helpful. You then can talk to your PI or lab mates about them and make plans together.

Questions to consider

Masks: Should we be wearing masks everywhere? Are they provided or are employees bringing their own? Do any exceptions to mask-wearing make sense? Possibly at one's personal desk (not bench)?

Space: How spacious are the bays? How many people can work in a bay while easily maintaining distance? One person per kneehole? One person per bay? One person every other bay? Most of the labs I know of have decided one person per bay makes the most sense.

Staffing: How many people work in the lab space? Do we need staggered hours to allow for the distancing described above? Again, most labs I know are staggering their hours so some people work in the morning and others in the afternoon.

Gloves: Are typical lab rules, such as no gloves on elevator buttons or doorknobs, still in place? Can we allow people to wear gloves to open doors while still avoiding contamination from dirty lab gloves?

Food: Where can people eat lunch? The bays might be spaced out nicely, but lab lunchrooms are often tiny. Where is food safe? In labs associated with hospitals, is the hospital cafeteria safe?

Meetings: Will lab meetings be by Zoom?

Equipment: Will scheduling use of shared equipment change? For example, training on equipment use might be canceled, or Zoom training may be possible. Facilities with multiple pieces of equipment may have to block off time slots to minimize crowding.

Other tips and pointers such as making hallways one-way and considering space around desks can be found on Labmanager.com.

Questions for your PI or department head

What if you can't come back to lab? While some people are coming back to work, many can't because they are at high risk or because they are not allowed (including undergrads). What will your lab do if you can't come back yet? What will happen to your projects? Are there data that you can analyze at home? Papers or grants you can help write? If not, will your salary and health insurance be protected? For how long?

Lastly, where can we read rules? Help make sure the guidelines that your lab or institution has decided on are communicated clearly and often. My PI sent out an email to all lab members with the current schedule of who comes in during what hours, along with mask and distance rules. If your PI is more hands-off and doesn't do that, you might consider sending an email of your own with the rules and guidelines as you understand them, even if it's just, "I think these are the rules. Is this correct?" That way, it's written down somewhere and people can reference it if they need to. It's important that everyone is on the same page, and having the rules in writing will help achieve that.

What will your lab do if you can't come back yet? What will happen to your projects? Are there data that you can analyze at home? Papers or grants you can help write? If not, will your salary and health insurance be protected? For how long?

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A year of unrest and grace — reflections on my journey to tenure

By Kelly N. Chacón

After five years in my tenure-track appointment, I am now preparing my tenure packet. What does this entail? It is a synthesis of all of my course teaching, a chronological account of my research program progress, and a recounting of my service to college and community into a very long document.

The readers of this document will be colleagues, select former students and external reviewers, who I may or may not know personally, at other comparable academic institutions. Likely for the first time, my busy peers will have a chance to not only see what I have been up to as an assistant professor at beautiful Reed College but also, by way of letters of support or impartial reviews of the tenure packet, to give their measured opinion as to whether I should be granted tenure this fall.

These letters and reviews will be weighed carefully by a panel of Reed professors who were elected to our institution's Committee for Advancement and Tenure. Late this coming fall, the committee will send a decision to our college president and me. Getting a negative tenure decision isn't the end of the world — often, it just means that a professor would be happier at another institution, and it can open exciting new doors. But that doesn't make the process any less stressful, and of course, I would be thrilled to get a positive decision.

So I am writing The Packet. But aside from writing, and doing personal and activist work surrounding the Black Lives Matter movement, I have been a little … lazy. Bright summer days spent hitting the "next episode" button on my remote until the light wanes outside my window. Sleeping in late. Playing Candy Crush until my eyes hurt. Eating my latchkey kid comfort foods like SpaghettiOs (with meatballs), barritas de piña and Kraft Mac & Cheese. I am lucky that my wife has an understanding and loving nature.

I think this laziness is part of *just letting go* for a minute. An unconscious stepping away from the constant productivity, investment, planning and achieving that has been my life for the past 17 years, since getting that GED and embarking on the academic scientist track. As I write this painstakingly organized biography of my professional life, so many feelings bubble up and demand to be processed. It is hard to believe this moment has arrived. I have felt joy, but also plenty of anxiety and hurt as I struggled to understand an academic world that many of my more privileged colleagues seem to navigate intuitively.

More than anything, I find myself making notes of what I would want to tell a new assistant professor starting on the tenure track — particularly a person from a marginalized group. So I'll take a moment here to share some hard-earned techniques and tips that helped me find balance as a nontraditional person in academia embarking on the tenure journey.

The broadest bit of advice for a new hire is to practice self-compassion. *Would we talk to a dear friend in the same way that we often negatively talk to ourselves?* No! Incorporating self-compassion into my day-to-day life has dramatically reduced my feelings of inadequacy and anxiety and has allowed me to forgive myself in deep ways. I have just divulged to the entire ASBMB Today readership that I sometimes waste full days on Netflix and mega-refined carbohydrates. Most of us would cheer on a generally hard-working friend for doing the same thing and would encourage them in well-deserved indulgence. Why are we not as kind to ourselves?

The add-on to that is to consider employing vulnerability. When I speak my weaknesses and fears out loud to peers and students, the monster of self-doubt and fear is often vanquished. I have also become comfortable with inducing slight discomfort in more privileged colleagues when I point out something that I was not brought up with or a

difference in how I see the academic world based on my ethnic, socioeconomic and cultural differences.

Many of my intelligent and talented colleagues attended prestigious high schools and universities. Many were automatically enrolled in college preparation workshops and SAT prep courses in high school and were introduced to social networks that helped guide them to success. This was not my academic experience, and I sometimes have to point that out gently, because I can feel isolated when my colleagues are relating to one another in my presence. This is uncomfortable to do, but as a light-skinned Mexican American, I can and do use the problematic privilege of my lighter skin color to more easily and vulnerably speak truth to power. This allows folks that may not have that particular privilege to do more important things with their time. It also allows me to feel truly seen in the academy as an intersectional, multifaceted human.

The above suggestions are broad. But no one told me about the day-to-day, often emotionally overwhelming grind of being a new underrepresented minority assistant professor on the tenure track.

When I began my professional appointment, I was completely unprepared for teaching: how to structure a course; how to write tests (it's so hard); how to know if what I was doing engaged students and worked as it should. It seemed like everyone else had been a great teacher since birth. What I've learned since is just how personal teaching is and that a course doesn't gel until around the third time you teach it.

So my advice for beginners is to stick to the main things you think a person taking your course should come away with and to believe in yourself. Trying to mimic a more-experienced teacher will add hours to your workweek and may not engage students in the way that your own vision will. That said, if someone shares their amazing materials and says you can do whatever you want with them? Save your energy and shamelessly use those materials all you want. There is no reason to reinvent an introductory chemistry or biology course if you don't want to.

The above goes for establishing your research lab. Keep things simple, and do it your way. You are an experimentalist, so use that same approach in managing your lab members and your projects. My only other suggestion is to walk through your lab once a day, even if only to water a plant or dust your own lab bench. Why? Because it reminds you that even if you aren't making all the research progress you'd like, you are still doing this. You finally have your very own research lab. Be proud. Also, it doesn't hurt for your students to know you might pop in at any time.

Next is the unspoken norm that you should always be available and always say "yes," particularly if you are an underrepresented minority. Many of us have learned that the occasional "I regretfully decline" response is important. So why don't you reclaim some of that "no" time just for you? You deserve and have earned the right to have lunch or an afternoon cup of coffee alone for 20 or 30 minutes in your office with the door closed. Every single day. Do not apologize or explain. Just close the door, and eat your reheated pasta. Maybe even click Buzzfeed open or watch a short episode of your current favorite show. If the knocking of students or colleagues persists, put a note on your door, or you can escape to a less-used building or a pleasant spot outside.

Finally, it is essential to have a constantly maintained, your-own-eyes-only CV (academic resumé) that documents every single little bit of outreach, service, informal talks, minor honors or awards, and in-person or virtual panels that you have done. Look at it when you feel you aren't doing all that you could. You are doing so much, and it adds up. And the magical part is that when it is finally time to write up your tenure packet, you have everything in one place, and you won't forget anything of value. I am grateful that I started and kept up such a document

In this journey toward applying for tenure, it became clear to me that there is no one true way to accomplish anything in this world. It's not OK for anyone to make us feel weird or wrong for doing what comes most easily to us — being ourselves and doing things in our own unique way. As underrepresented minorities, we can be all of the things, and we enrich our academic environment with our unique lens and approach.

I hope you will be faithful to your own light — and in the meantime, allow yourself a few lazy, snack-filled days.

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Think you'd like to move away from the bench?

Consider jobs in medical affairs or medical writing

By Isha Dey

While performing experiments in the lab, have you ever thought, "I don't see myself still doing this in five years"? But if you don't want to do bench work, what steps can you take to move out of the lab? Many graduate students have this question. We know off-bench career options exist, but we don't know how to prepare for them or what to expect. Why not learn about beyond-the-bench options in the life sciences from people who have transitioned to such roles?

Subhashri Kundu has been the Asia Pacific lead for medical affairs at GlaxoSmithKline, or GSK, for a year and a half. She earned her bachelor's degree in microbiology from St. Xavier's College and a master's in medical microbiology from Kasturba Medical College, followed by Ph.D. in molecular bacteriology from the National University of Singapore.

Jiaju Wang has been a medical science liaison at Takeda Pharmaceutical Co. for almost a year. After earning a bachelor's degree in pharmaceutical sciences from China Pharmaceutical University, he earned a Ph.D. in physiology and biophysics at Rosalind Franklin University of Medicine and Science in Illinois.

Arunava Ghosh has been the scientific writing manager at Cactus Communications for three years. He earned his bachelor's degree in microbiology, then went on to earn a master's and a Ph.D. in biochemistry from the University of Calcutta and Rush University in Chicago, respectively.

I talked to these three science professionals about what their job titles mean and what skills and qualities are required for such roles. They also shared a few pearls of wisdom and advice.

What does medical affairs mean?

A pharmaceutical company's medical affairs team serves as a buffer between external key opinion leaders (often called KOLs for short), such as healthcare professionals, and the company's research and development division. Medical affairs professionals also work closely with the company's commercial team or business unit. They help healthcare providers learn about drugs in a certain therapeutic area by sharing data from clinical trials, real-world evidence and meta-analysis.

Broadly, a medical affairs team consists of medical science liaisons, or MSLs, medical advisers, medical managers and medical directors. MSLs, such as Wang, have the most direct communication with the KOLs. They need a sound scientific understanding of the relevant disease and its therapeutics. They work closely with medical advisers and share the external KOLs' feedback with their team and their partners in the business unit so the company can direct research to address unmet patient needs.

As a regional lead of a medical affairs team, Kundu trains her region's MSLs and medical advisers on a specific disease area.

What is medical writing?

Medical writers create various types of clinical content. They prepare regulatory and research-related documents for drug regulatory authorities and healthcare providers. They create disease- and drug-related educational and promotional slide presentations, and they write journal manuscripts and abstracts for doctors and medical researchers. They also write content for healthcare websites or health-related magazines or news articles to share information about diseases and medicines with the public.

What skills are important for these jobs?

All three of these jobs require two related skills: communication and presentation.

Wang said that a strong scientific understanding of a therapy area, critical thinking, and the ability to simplify complex scientific problems for better communication are skills that have helped him as an MSL.

Strong data-analysis skills are extremely important in medical affairs, Kundu said. Both she and Ghosh said the ability to do a thorough literature search and extract necessary information is a useful skill in their respective roles. Ghosh said his adaptability to new


Jiaju Wang


Subhashri Kundu


Arunava Ghosh

challenges helped him switch from doing bench work to a desk job.

How did they land the job?

As a postdoctoral fellow and then a publication manager at Takeda, Wang collaborated with the company's MSL team on a few projects, including training, resource development and covering talks and poster session at scientific conferences, which strengthened his résumé. He was a strong internal candidate when the MSL position opened. His willingness to travel for work helped in his application; 40% to 50% of the job involves traveling, he said.

Ghosh was looking for nonacademic jobs on job portals during the final year of his Ph.D. when he came across the listing for a medical writer at Cactus Communications. He polished his résumé and applied for the position. Six months later, the company contacted him. He went through interviews and a few rounds of writing tests and was finally selected. "I learned almost everything on the job," he said. "It's doable."

Kundu said extensive networking landed her a job outside academia. She participated in career events hosted by her university. During one, she initiated a good scientific conversation with a representative from a pharmaceutical company who later directly referred her for an MSL position at the company. She thinks her extroverted nature has helped her adapt to a role that involves a lot of communication.

What do they like about their jobs?

Office-based medical affairs and medical writing jobs can involve communication with clients around the globe, and medical science liaisons usually travel extensively, so these are not 9-to-5 jobs.

However, because these are not on-bench, experiment-oriented jobs, Kundu, Ghosh and Wang all said the work schedule is flexible, which reduces stress and helps them maintain a good work–life balance.

"I tend to have a mental shutdown from work in the evening," Wang said. "I refrain from checking emails and prepare myself for a good sleep to kick off another exciting day as an MSL."

Kundu is an avid traveler. She plans her work so she can take breaks to travel and rejuvenate herself. As a new mother, she said, her job flexibility makes parenting easier to handle.

Ghosh said his job allows him to be very creative; he caters to audiences involved in different spheres of activity and prepares scientific content accordingly. He also gets to learn about the latest research and clinical trials in various disease areas.

Any advice for others aspiring to such careers?

"Network, network, network," Kundu repeated. Now on the other side of the transition, she said that 90% of moving away from the bench happens through networking. "Make sure your LinkedIn profile is up to date," she added.

Graduate students should work on their presentation skills, Wang advised. "Embrace opportunities to help the community and get experience in soft skills," he said. "The right opportunity only presents itself when you are ready."

Ghosh advises job seekers to tweak their résumés for each application to fit the role. "Use keywords mentioned in the job requirements to make it easy for the human resources department to screen," he said. For a writing job, "put more stress on achievements on the writing front, such as publications, posters and presentations. Also, make sure your résumé is editorially correct."

Isha Dey (ishaadey@gmail.com) is a scientist at Thermo Fisher Scientific in India.

Supporting Ph.D. students in the time of COVID-19

By Marina K. Holz

In the best of times, pursuing a Ph.D. in biomedical sciences takes incredible grit, as students are tested not only intellectually but also mentally, emotionally and sometimes physically as they spend long hours at the bench or computer. The COVID-19 pandemic amplified all of the challenges and created new ones.

Mentors and advisers must be aware of the unique hardships imposed on graduate students by the pandemic and by the gradual return to campus and labs.

Separation from family

Many graduate students attend institutions in locations away from their families and partners. Now, with mandatory quarantines and self-isolation, even traveling short distances is risky. Visiting family abroad is in most cases impossible. In addition to many state-mandated quarantines, such as the one in the New York region, nations around the world are barring entry, including return of their own citizens. Meanwhile, visa restrictions by the U.S. add to the confusion and uncertainty about the feasibility of traveling home. Experiencing this separation without a clear end in sight is difficult and painful.

Sick family members

Some students have family members and friends sickened or even killed by COVID-19. Sadly, they've been unable to attend funerals or be near family to grieve. We also must be aware that students are often the main caregivers to sick and vulnerable family members, responsible for running errands, taking care of family businesses, looking after younger siblings and putting food on the table. These challenges and health disparities are even more pronounced in the Black and Latino communities, as they continue to struggle with discrimination and racism.

Students with children

Staying productive while also taking care of children is a difficult task for every working parent. While some universities and research labs are reopening, students are required to resume work. In the meantime, many summer camps are severely restricted, and safe childcare options are scarce, making return to work difficult for parents. The challenges are glaring for students who are parents, especially women, who shoulder the majority of the domestic responsibilities.

Students with health conditions

Graduate students may suffer from physical and mental illnesses that (due to privacy concerns) they have not disclosed. It is vital for mentors and advisers to keep in mind that students may be affected by conditions that are exacerbated by the pandemic or that make them feel unsafe to come to campus.

Mental exhaustion

Advisers need to realize that not everyone easily can cope with difficult circumstances and maintain the same level of productivity. Graduate students suffer from anxiety and depression at higher rates than the general population, and those challenges are amplified during the pandemic.

Access to resources

Students may not have dedicated home offices, reliable internet access or even updated laptops. Without the ability to work in libraries and coffee shops, some students are confined to their homes, which may lack many amenities, such as air conditioning. Some live in unsafe homes and share apartments with many roommates, making work from home challenging. Living in confined conditions during the pandemic has been shown to lead to increased instances of domestic violence, to which graduate students are not immune.

What can you do to support your graduate students?

Keep open lines of communication, but do not demand that students divulge specific information or details — they may not be ready to share the particulars of their personal struggles.

Be flexible when it comes to scheduling, workload or the timeline for deliverables. Students' priorities at this time may be different than your own.

Be mindful about the ability of students to be productive at home, and be vigilant about signs of

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domestic abuse.

Provide support, but be prepared to take a step back, and don't be intrusive. Your well-intentioned offer of help may be more of a burden than a solution at this time.

Most importantly, remember that this crisis will end, but your students always will remember your kindness and support during this time.

Marina K. Holz (mholz@nymc.edu) is the dean of the Graduate School of Basic Medical Sciences and professor of cell biology and anatomy at New York Medical College and a member of the Women in Biochemistry and Molecular Biology Committee of the American Society for Biochemistry and Molecular Biology. Follow her on Twitter @Holz_lab.

In my first real U.S. winter, I got snow; in my second, I got a pandemic

By René Fuanta

I grew up in the tropical climate of Cameroon and later moved to Auburn, Alabama, which has similar weather patterns. I never dealt with feet of snow until the winter of 2018–2019, which I joked was my first real winter in the U.S.; 2019–2020 was my second.

Heading into the spring 2020 semester at East Stroudsburg University of Pennsylvania, I anticipated snow days with canceled classes and makeup lectures. As a second-year tenure-track assistant professor, I am still adjusting to this. To my surprise, the winter was relatively warm, with very little snow. Nearing the end of February, the university had not canceled any classes. I thought this semester was going to give me an opportunity to reevaluate my course content and delivery and make some needed changes and updates. The threat of COVID-19 appeared distant, with about 60 cases in the U.S. and none in Cameroon. I hoped this coronavirus would be contained before long.

Pennsylvania confirmed its first case of COVID-19 on March 6, a few days before our students went on spring break. Given that part of my educational background is in microbiology and infectious disease, I should have anticipated an unusual semester — but I was adamantly optimistic. I was certain that, given the relatively low number of cases at the time, they could be traced and quarantined and normalcy hopefully restored. A few days into spring break, I received an email from our provost saying the university would close and all classes would go online after the break.

I had to adjust posthaste to a new mode of course content delivery, something I did not want to be doing at a point in my career after having taught the course only once. I had to convert all my quizzes and exams for online delivery by changing the format and style of the questions. I took into account that students who suddenly found themselves stuck at home might not have the appropriate tools to draw or answer some questions online. In the late hours of the night, I made lecture videos. Sometimes I failed to hit the record button and had to start all over. I was thankful that the university gave us an extra week to convert our course material to a suitable online format. The ESU information technology and communications team offered training on online tools like Zoom and D2L, making for a relatively smooth transition and navigation.

This well-managed move to online classes, though the safest option, was a bitter pill. My students felt that they had lost their connections with the faculty. They were not used to learning from home. Immediately, as we transitioned to distance learning, grades dropped. I shared a few tips to help them adjust or avoid distractions; I suggested they try to study late at night when their homes would be quiet and calm.

As I talked with my students, I realized that learning from home was not their only new challenge. Many had to bear extra responsibilities in their households. Some had to take a job (or two) to help support their families after their parents or sponsors lost their jobs or had to stop working because underlying health conditions put them at high risk. Other students became teachers and caregivers to their younger siblings and other children at home. With these added duties, most had little time to attend an online class or even study. I addressed this by sending them links to my prerecorded videos. They could watch these at any time of the day and email me questions or meet me during online office hours. This improved student performance as it helped them to attain more work–life balance.

Teaching from home was also a challenge. As a faculty member, I am far more productive when I am on campus. Sitting at home in front of a computer all day for lectures, research and office hours is not what I envisioned for my second year. I had to make several cushion adjustments to stay comfortable in my home office setup. I take occasional walks around the living room and do stretches, pushups and other exercises between lectures and meetings to keep my mind sharp and improve blood circulation. That has become my new normal, but I miss the aroma of coffee in the university building and the hum of students chatting about how they're looking forward to graduation or panicking about their next exam or experiment.

COURTESY OF RENÉ FUANTA

Left: A native of Cameroon, René Fuanta is more accustomed to warm weather than Pennsylvania's snowy winters. This year, instead of snow, he experienced a pandemic. Below: A building on the campus of East Stroudsburg University of Pennsylvania where Fuanta is a second-year assistant professor.

My family has always been a great support. With about 15,000 confirmed cases of COVID-19 as of early July (in a population of close to 27 million), Cameroon is also on lockdown. My family calls me every single day to make sure I am doing OK. With four brothers and a sister, four nephews, and two nieces, my ears are buzzing every day. They all want to talk to me, yelling and screaming at the same time. My mom (aka the General) gets especially frantic if I don't respond immediately to her call. Thankfully, my dad (Pa Steve) is always there to calm her down. Being so far but yet feeling so close to them, and knowing they are all doing their very best to stay healthy, is to me a great blessing.

COVID-19 has given me a new perspective on all my interactions. It is a challenge to know the difficult situations my students find themselves in during this period and to be of so little help to them. I have a deeper appreciation for online teaching and communication tools such as Zoom and WebEx, though I quickly "zoom out" from attending so many virtual meetings. This has been a period of many unexpected adjustments, but each one has shown me how much I value my interactions with my students and family.

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There and back again

5 questions with Grant Blouse of Catalyst Biosciences

By Laurel Oldach

Protease expert Grant Blouse has spent two separate stints working at Catalyst Biosciences. When the protease-engineering firm first launched, Blouse worked there as a senior scientist. Today, he's the senior vice president of research and development.

"They went through the standard biotech wind-down of research and ramping up of development," Blouse said. He took a job at the large pharmaceutical company Novo Nordisk. Six years later, Nassim Usman, the CEO of Catalyst, offered him a role as vice president of research.

"It was an opportunity to come back as part of the executive team and rebuild the science aspect of Catalyst," Blouse said.

While he was gone, one of Catalyst's drug candidates had hit a snag in development: Patients in a clinical trial developed antibodies that threatened to reduce its effect. The company paused clinical trials while determining what this meant for the molecule's future. After returning, Blouse led follow-up analyses showing that the compound in question was no more immunogenic than competing treatments, and the molecule is now ready to enter late-stage clinical trials. Blouse and his team also have worked on targeting other proteases, such as the immune-signaling complement system.

ASBMB Today spoke to Blouse, who is now Catalyst's senior vice president of translational research, after he presented at last year's Membrane Serine Proteases meeting. The conversation has been edited for length and clarity.

1 As senior vice president of translational research at Catalyst, what does your day-to-day look like?

I wear many hats because we're a small company now. I mix my day between interacting with my team and the projects they're running and interacting with all the other functional areas.

I wear the hat of a project lead on one of our clinical programs. I keep up to date with what everybody's doing in nonclinical development and toxicology. My team and I interact with the consultants and contract research organizations that run these studies for us. We don't have any research labs in house, so a fair amount of time is working with contract research organizations and building relationships with academic groups.

2 What skills do you need that you didn't learn in graduate school?

These days, I'm starting to give presentations to investors. When you're giving a great scientific talk, that's one thing, but it's different to present that same exciting work to the investor community. I'm learning how to have business development interactions and how to move a company's different programs forward strategically.

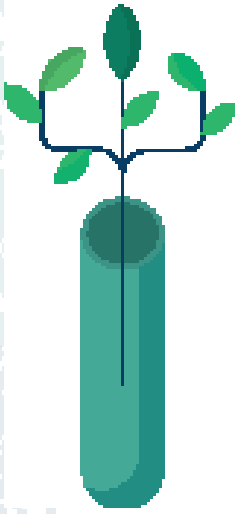
3 You've worked at Catalyst and also a big multinational pharma company. How do those compare?

I went from working with 65 people at Catalyst to 40,000 worldwide at Novo Nordisk. It was definitely an eye-opener.

Many of the roles I took on in the larger company were as a project leader, making sure that all the scientists were cohesive about the project. In the big company — we call it a mixed matrix organization — there was a protein sciences team, a biology team, an in vivo pharmacology team. I had to make sure everybody was on the same page. Communications are very important in that role.

It's been fun to come back to a small company. I can have a broad view over all the programs and players. And coming in as part of the executive team was a great opportunity — the kind you don't turn down.

Smaller companies offer more growth potential, especially if you've just started out; they give you opportunity to do different things, which gives you more options when you



"One bit of advice about networking: Sometimes when you're at a table talking with a bunch of PIs, you're excited and you want to tell your own story about everything you're doing. But sometimes it's good just to listen, to hear what everybody else is doing."
—Grant Blouse

want to make a move. Big companies are, typically, more stable, but you're not guaranteed to have no volatility in big pharma. I tell students they have a runway of a few years about anywhere they go, and beyond that, (job security) can never be guaranteed.

4 Any other advice for students who'd like to do what you're doing someday?

One bit of advice about networking: Sometimes when you're at a table talking with a bunch of PIs, you're excited and you want to tell your own story about everything you're doing. But sometimes it's good just to listen, to hear what everybody else is doing. You learn a lot that way.

5 How important has networking been for your career?

Everything has come through relationships I've built in the field. I went to do a postdoc in Denmark because of an academic collaboration during my Ph.D. I ended up at Catalyst the first time because, from my academic work, I knew the chief science officer.

When I go to conferences, I catch up with everybody I've known throughout my journey to see how they're doing and how their research is going. Things seem to grow organically out of those relationships. You just say, "Let's touch base and connect at the conference." Sometimes people bring out opportunities and say, "Hey, we're looking for somebody."

I've been a strong proponent of networking all through my career. I think it's important. And it's good to make sure you leave each job on good terms with everyone and keep those relationships strong.

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

GRANT BLOUSE

CURRENT POSITION
Senior vice president of translational research, Catalyst Biosciences

CAREER PATH
Ph.D., Wayne State University School of Medicine, 2003

POSTDOCTORAL RESEARCH
Adjunct assistant professor, Aarhus University in Denmark

FIRST INDUSTRY JOB
Catalyst Biosciences

FAVORITE MOLECULE:
"Obviously a protease — they are the quintessential signaling molecules and necessary for all walks of life."

After the longest March, science marches on

By Emilia (Emily) Arturo

March 2020 was the longest March. It started for me with the sweetness of budding trees and a trip to an excellent five-day workshop on cryo-electron microscopy in New York City. I was aware of concerns about aged people in faraway Italy and nagging reminders that coronaviruses don't just cause colds, but I still juggled an impossible number of deadlines, travel plans with family, travel plans for work and the usual failed experiments, along with occasional musings on carbon footprints, political candidates and how I should read more about everything — ordinary chronic stuff for any scientist.

In its second week, March roared to a time-warping bang — a worldwide sonic boom of industry shutdowns, social isolation, school closures and pending personal and global economic collapse. We'd known that a pandemic of a virus novel to all humans was possible, but we hadn't fathomed that it literally would play out as it does in all the bad pandemic movies.

A few months later, if you still receive a salary, you probably are still working, even if you suddenly have cats and kids and enduring deadlines in an enormous makeshift pile of priorities in the middle of your living room with no practical way of sorting them all out. If you don't still receive a salary, and some scientists now don't, the optimism is wearing thin. The prospects of recovering lost research prowess are scary.

For anyone working on viruses, drug discovery, immune therapies and vaccines, however, the call to action now is as tremendous and conflicting as the call to stay home.

A structural virologist at home

I am a mathematician turned structural biologist who didn't take a straightforward path to becoming a scientist. I am a postdoctoral research associate and structural virologist in the Ollmann Saphire lab at the La Jolla Institute for Immunology Division of Structural Biology and Infectious Diseases. My children are in my living room, isolated from their school and friends, and from the same living room I continue my research into structural features of immunogenic viral glycoproteins.

As virologists, my colleagues and I in the Saphire lab now enjoy an uncommon job security. For more than 15 years, our lab has been rooted in the structural biology and design of immunotherapeutics against some of the world's most deadly viruses, including Ebola, Lassa and rabies. We are home to the Viral Hemorrhagic Fever Immunotherapeutic Consortium, or VIC, and now also to the Bill & Melinda Gates Foundation–sponsored CoVIC — the Coronavirus Immunotherapeutics Consortium.

And many of us are just ... home. The irony of virologists sheltering in place during a viral pandemic is unsettling. While we knew it before, we own it now: Our work on understanding viruses, viral proteins and immune responses that tackle them is of paramount importance. Whatever we manage to do now in the lab or via telework will affect how the world fares in coming years.

Fortunately, many of us are armed at home with piles of literature and piles of cryo-EM data that can all be analyzed remotely, though sometimes only with considerable effort. The literature we're finally getting around to reading provides new insight into some of our experimental rationale, while the data analysis is critical to designing and improving therapies that target viral infectious diseases, COVID-19 included.

Distance learning

As social and physical distancing restraints have shut down in-person workshops and meetings, data processing now means learning at a distance from experts and colleagues and teaching ourselves. Teaching ourselves is not atypical in a field that's evolving as rapidly as EM, but now the urgency to learn and apply is unprecedented.

Cryo-EM data analysis is a trying process for beginners and intermediate users alike. The researcher must navigate a multitude of possible processing workflows. The process requires remote data connections, a lot of data storage and a dozen different file extensions, and the researcher must be at ease with mathematical concepts (or with the fact that they don't know them), individual software peculiarities, and the potential to introduce bias at multiple steps. Making the protein sample may have

EMILIA ARTURO

The author denoises her EM particle data at home with Fred, her irreverent cat, in March.

taken months, but getting the density map from the data and making the map into a model takes the average EM scientist anywhere from a few weeks to many, many months. The same can be said for any structural biology data, including that from X-ray diffraction, mass spectrometry and nuclear magnetic resonance.

Before COVID-19, junior scientists learning to process data often hesitated to interrupt their more experienced colleagues with questions. We wouldn't dare contact the software or EM experts to ask for one-on-one help by email, Zoom or phone. We turned to Google, YouTube, Twitter and online bulletin boards in a valiant effort to be self-taught or to preserve confidentiality. And if our Google-fu failed us or no one had posted a solution, we returned to wallowing in the inefficiency of self-teaching. There is no time for that now; in our lab, we need to see these viral proteins and the antibodies that bind and lock them, and we need to do it ASAP. So now we Zoom, Slack and dial with abandon.

Ordinarily introverted and self-isolating, many scientists are changing our behavior, perhaps in part because our passion to help one another now trumps these personality traits, and also because virtual meetings and workshops are increasingly available.

One particular cryo-EM center, perhaps realizing that scientists don't always reach out for the help they need, has been especially forward-thinking about distance learning. The National Center for CryoEM Access and Training, or NCCAT, in New York City is one of the National Institutes of Health Common Fund's three cryo-EM national centers. These centers train us in the technical aspects of EM and give us access to the pinnacle of equipment. Now that the centers'

scientists are themselves at home sheltering in place, many of their microscopes are warmed, and their electron detectors are off. In addition to making past workshop course material freely available online, NCCAT now offers virtual office hours and virtual live roundtable discussions related to sample preparation, data collection, data processing and model building.

Our field of structural virology using cryo-EM is so small and so rapidly growing that this opportunity bears repeating: We are being offered free time to discuss difficult data with world-renowned experts one-on-one. This creative generosity is available because we need the knowledge and they have it — as simple as that. I hope these connections will continue and other institutions will emulate them, even when a pandemic no longer drives us.

Future Marches

A sign from the first organized March for Science on April 22, 2017, stated what scientists are now experiencing: "The oceans are rising and so are we." In one form or another, the viral pandemic caused by SARS-CoV-2 has swamped our psyches, our labs and our time.

We are seeing versions of scientists we never noticed before. Experts share their time and knowledge. Principal investigators allot portions of their own salaries to support research associates who otherwise would be furloughed. More researchers use and cite preprint servers to share information and credit rather than shield it. We are taking time to expand our understanding by reading outside of our fields, and we all recognize and tolerate personal struggles better because we feel them collectively. The feats of accommodation and caring go on and on.

What March 2021 will look like is anyone's guess. From my cluttered living room corner to yours, I wish you well. I hope you can learn more broadly and more deeply. Most importantly, I hope you will, when you can, reach out to give and to ask for help.

Emilia (Emily) Arturo (earturo@lji.org) is a postdoctoral research associate and structural virologist in the Ollmann Saphire lab at the La Jolla Institute for Immunology Division of Structural Biology and Infectious Diseases. She earned her Ph.D. at Drexel University College of Medicine. Follow her on Twitter @moonlightterturo.

EMILIA ARTURO

The author computes at home in April with her son, who is in the fourth grade.

Being Black in the ivory tower

My journey through the criminal justice system and academia

By Kayunta Johnson–Winters

When the video of George Floyd's killing first surfaced, my heart sank, and I immediately tuned out. As the mother of an African American male, I simply could not watch because it was too emotional. Every time a Black male dies at the hands of a police officer or vigilante, a wound opens, and it feels like it is happening directly to me.

There is a part of me that has not recovered from my own trauma two years ago, when my 14-year-old son was the victim of a shooting incident. Whenever a child utters "Mom," every mother within earshot turns toward that voice. A mother knows the cry of her child, especially when that child is in distress. When I was finally able to watch the video, I saw that George Floyd in his last moments cried for his mother, and I had an anxiety attack. In that moment, I understood those words, "I can't breathe."

I was able to relate to George Floyd because, like him, my son, Kailand, is also a gentle giant. Fortunately for me, my son survived his attacker's pursuit, and I was able to hug him again. However, that doesn't take away the trauma that my son and I experienced. The events that followed the shooting involving my son taught us many lessons about who we were and how the justice system views Black males.

Kailand was spending the summer of 2018 with my mother in Wisconsin. He and a 12-year-old friend were out taking a walk when a woman fired her gun at them from the other side of her fence. The children were not trespassing and had done nothing wrong, and when they heard the shots, they ran. The woman moved from behind the fence, walked into the middle of the street and continued to shoot at them.

After my mother called me, I went to teach my biochemistry class, because I was committed and didn't want to let my students down. However, I struggled to teach effectively. My mind was in turmoil because I could do nothing to help my son. I needed to see with my own eyes that Kailand and his friend were OK. I told my students what had happened to my son and immediately booked a flight, not bothering to inform my department, until I was settled, that I was on my way to Wisconsin.

> **"The only thing necessary for the triumph of evil is for good men to do nothing."**
> **— Edmund Burke**

After my son and his friend endured the trauma of having bullets fired at them, the police doubted their account of what had happened despite multiple witnesses, bullet casings and an immediate 911 call from a passerby. Ultimately, the police arrested the woman who shot at them. My son and his friend identified her in a lineup, and she was jailed for four months, pending trial.

I went through the proper channels so the district attorney and the judge would know that we took the situation seriously and that the mother of the other child and I wanted justice for our children. We attended every pre-trial court date; my son and I had to travel frequently from Texas to Wisconsin, using personal funds, while my son missed about 20 days of school over several months.

I mailed several letters to the judge, which the district attorney's office added to my son's case file because I wanted to be sure the judge would read them. The judge did not respond to my letters. To our surprise, when we attended court, the judge didn't even look in our direction, never acknowledging our presence. When the district attorney argued his case, my Ph.D. in chemistry, my position as a professor, all the papers that I have published and the grants that I received were irrelevant. The same applied to my son, who is a role model for many STEM-oriented students. While I recognize that our status should not matter, highly educated white people often receive disproportionate sympathy. The system does see color (and money), and that matters more than anything else.

The shooter was a convicted felon with a long history of breaking the law, but the judge granted her an obtainable bail amount. The district attorney pleaded unsuccessfully that the bail needed to be higher because the shooter had the resources to make the bail. To add insult to injury, the judge returned a portion of the bail money to the shooter, because she wanted to have a nice Christmas with her children. My son and I were not

TROY GARDNER/TG PHOTOGRAPHY

Kayunta Johnson–Winters and her son, Kailand, celebrate his high school graduation earlier this year.

able to spend the holidays with our family, because we had spent our resources traveling to court.

The woman who shot at my son died before the case went to trial, the victim of a terrible act of domestic violence. I was devastated for her family but still outraged at the disparities in the way the police and court treated my son and his friend.

In the eyes of the judicial system, my son — this sweet honor roll student who attended an elite STEM academy at his school, who had never been in trouble — was still a Black boy who didn't deserve justice. The systemic racism that has plagued this country from its inception made us feel invisible. This is the message that our country sends to Black America all too often. We felt tired and defeated. As his mother, I could do nothing to comfort Kailand, and he lost some of his innocence in the harsh reality of how dismissive the legal system was of him. The entire experience, from being shot at to his treatment by the police and the judge, taught him that his Black life did not matter.

The story of George Floyd is all too familiar — we have seen these stories play out time and time again in this country. Trayvon Martin was a 17-year-old boy who was murdered when he went to the store for Skittles and a drink; Tamir Rice was a 12-year-old boy who was killed by police while playing with an Airsoft gun but viewed as a threat. The Central Park Five were innocent boys framed for a rape and denied access to proper counsel, which sealed their fate for many years. These are only a few of the many stories.

In conversations with Black friends and relatives, we all wonder the same thing: At what point did our Black children lose their humanity, their right to justice and their right to live? When do our children start looking like suspects, compelled to prove that they did nothing wrong, rather than being innocent until proven guilty?

In 2020, Black Americans continue to live in fear. Every time a death occurs at the hands of a police officer, we are reminded that our lives do not count.

I am a proud American citizen. I am a scientist. I take pride in my research and in championing underrepresented students through my work on the American Society for Biochemistry and Molecular Biology's Minority Affairs Committee, as director of the Louis Stokes Alliance for Minority Participation Bridge to the Doctorate program, and as organizer of the College of Science Black Graduate Student Association through my home institution. However, despite my doctoral degree, my credentials and my status as a tenured professor, I am still an African American woman with a Black son, and neither of us is given the benefit of the doubt at school, at work or within the justice system.

Just last year, when I tried to enter our new state-of-the-art research building with several students from my large biochemistry course, a university police officer stopped me and would not allow me to access my office and laboratory until I provided credentials that showed that I belonged there. After I produced my identification and swiped myself and students in, the officer proceeded to lecture me in order to justify his actions. My response to him was, "I have students who need my assistance. Now that you have done your job, I need to do mine. Please excuse me." I simply walked away. I didn't want to engage. Initially, I didn't

say anything to my students about what they had witnessed. However, I noticed that the Black students treated the incident as normal and had no reaction. Other students were emotional and needed a moment to discuss what had happened. They were shocked and appalled. Although the experience was demeaning and diminished my authority in front of my students, my goal was to be diplomatic and comfort them with my words. Here is the message I shared with them:

One of the things I love most about being a university STEM professor is that I don't fit the typical profile. I am always happy to teach the larger undergraduate classes, because I get to break the perceived stereotypes. However, this doesn't change how I am viewed by people who don't know me. That's the downside.

As an African American professor in STEM and higher education, I am never surprised at the institutional bias that rears its ugly head in the treatment of underrepresented students, staff and colleagues. When we experience the isolation, dismissive tones, microaggressions, and implicit and explicit biases, it is akin to a thousand cuts that slowly lead to our demise.

Women of color are often undervalued, subjected to negative evaluations, overlooked for promotions, overmentored in the most ineffective way, undersponsored and rarely given opportunities to have a seat at the table, because our voices do not count.

These are only a few of the ways that the higher education system has failed us.

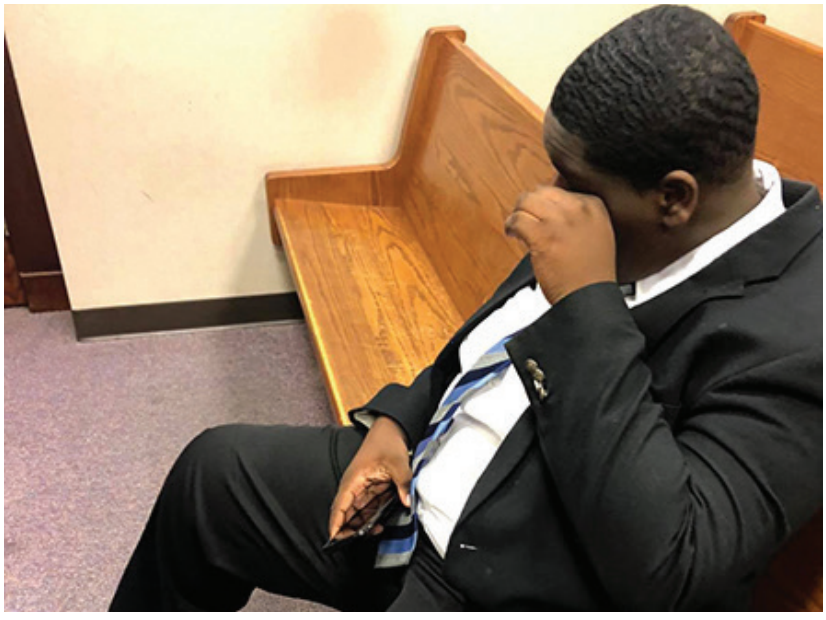
I have seen countless examples of women of color who have left academia due to the inequalities that disproportionally affect us. Everyone suffers when a person of color leaves academia due to racism, inequalities or marginalization, because a lifetime of productivity, scholarly contributions, discoveries and student mentoring is lost when that individual exits.

Our country is at a crossroad. We must reckon with inequalities that exist in the justice system, health care and education. We need to have a conversation about the fact that not all of us are afforded the same privilege.

Although I give back and raise my son to be a good and productive citizen, I constantly fear for his safety because of how other people may perceive him. I have to tell him that if he is making someone feel uncomfortable, he needs to go the other way or fall back. It isn't fair that he has to apologize through his body language or his mere presence because of someone else's bias.

We all need to reflect on what is happening in our country and determine our individual roles, and then we need to act to combat injustices and inequality. We must have a conversation about being white and white privilege. We must understand the toxic world that Blacks, especially Black men, live in every day. White people must use their privilege to expose the gross disparities that exist in the education system, health care and criminal justice.

We need a major paradigm shift to heal the racial divide in this country. We must all vow to be change agents, even when we recognize that doing so involves risk. Silence is not an option. We need your voice.



COURTESY OF KAYUNTA JOHNSON–WINTERS

The author's son, Kailand, at the time just 14 years old, attends a court hearing. The pair traveled frequently, and at great expense, between their home state of Texas and Wisconsin for hearings over many months.

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CLASSIFIEDS

Molecular Biologist
Biotech.WS
Peoria, Illinois, United States

BioTech.WS

WS BioTech is accelerating commercial production of nonpolluting, environmentally sustainable practices. We are seeking highly talented and motivated staff to join our cause and solve environmental crises.

As a Molecular Biologist, you'll support a developing interdisciplinary team to understand plant nutrition and metabolism by adding your own expertise. You'll design and carry out studies to characterize plant interactions and leveraging those findings in practice using our bench-to-industry platform.

https://careers.asbmb.org/job/molecular-biologist/54358982/

Postdoctoral Fellow
Brigham and Women's Hospital
Boston, Massachusetts, United States

BWH

A postdoctoral position is available for a highly motivated individual to study the molecular genetics of skeletal physiology at Harvard Medical School and Brigham and Women's Hospital. Research in the laboratory is focused on understanding the cellular and molecular mechanisms underlying muscle physiological growth and functionality, and how dysregulation of these processes may lead to a diseased state. Current research projects within the lab investigate 1) the mechanistic role of lncRNAs on skeletal muscle transcriptional regulation, and 2) the role of alternative splicing in modulating skeletal muscle metabolism, regeneration, and paracrine signaling.

Highly motivated PhD and/or MD applicants are encouraged to apply.

https://careers.asbmb.org/job/postdoctoral-fellow/54364955/

Postdoctoral Associate
Boston University
Boston, Massachusetts, United States

BOSTON UNIVERSITY

We are recruiting a post-doctoral associate to work on NIH supported projects in the Zaia group at Boston University.

The project will involve quantitative glycoproteomics of influenza and coronavirus proteins for studies on viral evolution. We have recently received funding for a Waters Cyclic IMS instrument that will be dedicated for this work. The postdoctoral scientist will conduct viral protein sample preparation and glycoproteomics LC-MS experiments. S/He will work within a collaborative team including biochemists, analytical chemists and bioinformaticians to develop and validate a statistically rigorous method for determining the changes to viral protein glycosylation that occur during viral evolution and that inform understanding of viral antigenicity and immunogenicity. The candidate should have Ph.D degree in biochemistry or a related field and a strong background in proteomics and/or glycoproteomics.

https://careers.asbmb.org/jobs/view/postdoctoral-associate/54168278/

Lecturer
University of Washington
Seattle, Washington, United States

The Department of Biochemistry at the University of Washington School of Medicine in Seattle invites applications for a faculty position at the rank of lecturer, to serve as course director and instructor for Honors Biochemistry 451, a small (~25 students) undergraduate biochemistry course presented in winter quarter. The course emphasizes conceptual concepts in biochemistry, active learning, and is open to Honors students and others who meet eligibility criteria.

This recruitment is for two positions. The anticipated start date is December 16, 2020. This position has an annual service period of (3) months and is non-tenure eligible.

https://careers.asbmb.org/job/lecturer/54393964/

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