RESEARCHERS ON THE RISE
Journal talks by early-career investigators
ASBMB professional-development resources

Job board
asbmb.org/jobboard
The ASBMB job board has listings from academia, government and industry. Looking for your next hire? Members can post jobs for free.

Grant-writing training
asbmb.org/grantwriting
This Washington, D.C.-based summer workshop yields impressive results; 75% of participants end up with successful grants within two years.

Communications training
asbmb.org/commcourse
Can’t travel for training? Take the ASBMB’s “The Art of Science Communication” online course to gain the skills, knowledge and mindset necessary to become a great presenter.

Small meetings
asbmb.org/specialsymposia
Small meetings are offered throughout the year on a wide range of scientific topics. Interested in organizing a meeting? Members can work with the ASBMB to plan and organize a special symposium.

Careers blog
asbmb.org/careersblog
Every week, our careers blog presents insights into the current job market.

Webinars
asbmb.org/webinars
We offer live webinars and recordings of past webinars on topics including getting funding, salary negotiation, research careers in industry and more.

Video tutorials
asbmb.org/careers/tutorials
Our video series has tips on networking, dressing professionally, building a personal brand and more.

Advocacy Training Program
asbmb.org/advocacy/atp
The ASBMB ATP is a six-month externship that provides hands-on science policy and advocacy training and experience.
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ASBMB TODAY
EDITOR’S NOTE

Be a writer

By Comfort Dorn

Now still looms in the Maryland weather forecast as I type this, but thoughts here in the American Society for Biochemistry and Molecular Biology office are turned to the sunny flip-flop weather of Orlando. Preparations are well underway for the annual meeting and likely to consume us for the next month or so.

Here at the magazine, we’re focused on providing you with lots of meeting-related articles and useful information (check out our speakers’ profiles starting on page 22) in this issue and the next, but, as always, I’m looking beyond the horizon, toward late spring and summer. These pages won’t fill themselves.

Here at ASBMB Today, we have a wonderful crew of volunteer writers who cover news of cutting-edge research and the scientists who make it happen (all the annual meeting profiles in this issue were written by volunteers). And we have staff writers who provide our deep-dive feature stories. Their contributions might be considered the brains of this publication.

But you, our members, provide much of its heart and soul. (Don’t poke this analogy too hard, please.) I like to think that this is a members’ magazine in the best sense of the term. It rightly belongs to the members, and it’s a place where you can share your stories and opinions. It’s also a great venue for civil discourse and debate. Consider this your invitation.

We have two essay series running this year: “Night shift” and “What I wish people understood about ____.” In this issue, I’ve taken on the second of these topics (even though my bumper sticker reads, “I’d rather be editing”) in the hopes that you’ll feel encouraged to pick up a pen or flip open your laptop and pour out a story from your experience. Deadline (rolling): first Monday of the month, through October.

We have an education and careers issue scheduled for August. If you’ve faced and surmounted professional challenges, we want you to share what you’ve learned. If you’ve had failures and setbacks, we want, perhaps even more, to read about those too. Deadline: June 3.

Did you read our wellness issue in January? It was absolutely chock-full of inspiring stories and good advice from (you guessed it) members. This is such a huge topic for the science community that we’re tentatively planning another such issue for January 2020. Do you have a story to tell about how you take care of yourself or about obstacles to staying well? You know what I want you to do. Deadline: TBD.

So many great topics swirl around this community. You have opinions. You have stories. You have ideas for making things better. Deadline: the sooner the better.

And you have an editor (me). Send me your words, and I’ll work with you to make them say what you want to say in the clearest, most elegant, most honest way possible.

I look forward to reading you.
Five members honored by academy of inventors

Five American Society for Biochemistry and Molecular Biology members are among 148 individuals elected as 2018 fellows of the National Academy of Inventors.

The highest professional distinction bestowed upon academic inventors, election to NAI fellow status is based on creating or facilitating inventions that have had a profound impact on society.

There are over 1,000 NAI fellows, who have generated more than 11,000 licensed technologies and companies and over $190 billion in revenue.

The 2018 NAI fellows will be inducted as part of the eighth NAI annual meeting in April in Houston.

They are:

- Susan J. Baserga, professor of molecular biophysics and biochemistry, of genetics, and of therapeutic radiology at Yale University.
- Elaine V. Fuchs, Rebecca C. Lancefield professor of mammalian cell biology and development at The Rockefeller University and Howard Hughes Medical Institute investigator.
- Bert W. O’Malley, professor of molecular biology and chancellor of Baylor College of Medicine.
- Susan S. Taylor, professor of chemistry and biochemistry, professor of pharmacology, and Howard Hughes Medical Institute investigator at the University of California, San Diego.
- Ruiwen Zhang, professor of pharmacology and toxicology and director of the UH Center for Drug Discovery at the University of Houston.

Sonenberg receives biomedical research prize

Nahum Sonenberg, a McGill University professor, has received the Wilder–Penfield prize for biomedical research.

Awarded since 1993, the Wilder–Penfield prize is the highest honor bestowed by the government of Quebec to an individual for significant research in the biomedical field. Sonenberg holds the Gilman Cheney Chair in biochemistry and is a senior researcher at the Rosalind and Morris Goodman Cancer Research Centre at McGill.

His research focuses on the molecular basis for controlling protein synthesis in eukaryotic cells.

While completing postdoctoral studies at the Roche Institute of Molecular Biology, Sonenberg discovered and established the role that the eIF4E molecule plays in translating genetic information into proteins.

The Wilder–Penfield prize is one of several awards that make up the Prix du Quebec, which recognizes outstanding cultural and scientific accomplishments.

Arroyo chosen for Rhodes scholarship

The Rhodes Trust at the University of Oxford, U.K., has selected Chapman University senior Vidal M. Arroyo to receive a 2019 Rhodes scholarship.

Arroyo is pursuing an undergraduate degree in biochemistry and molecular biology with a minor in computational science.

Chapman University’s first Rhodes scholar, Arroyo studies the link between cancer and obesity as well as outcome disparities among survivors of childhood cancer.

Arroyo is the founder and president of the Chapman STEMtors, a student organization dedicated to peer support and mentorship in the scientific community. He was a 2018 winner of the ASBMB’s Marion B. Sewer undergraduate scholarship.

He will pursue studies in statistical science during his time at Oxford.

Barr–Gillespie named chief research officer

Peter Barr–Gillespie has been appointed as the chief research officer at Oregon Health & Science University.
Barr–Gillespie will serve as the chief adviser on research strategy to the university’s president, overseeing the institution’s research divisions with a budget of over $460 million. During his research career, his work has focused on understanding the molecular mechanisms that enable our sense of hearing.

A member of the faculty at OHSU since 1999, Barr–Gillespie has served as professor in the departments of otolaryngology, cell biology and development, and biochemistry and molecular biology.

He has been the interim senior vice president for research since 2017 and is also a senior scientist with the Vollum Institute at OHSU.

In memoriam: Julián Gómez–Cambronero

Wright State University professor of biochemistry and molecular biology Julián Gómez–Cambronero died Nov. 12. He was 59 years old.

Born in Manzanares, Ciudad Real, Spain, Gómez–Cambronero received his Ph.D. in biochemistry and immunology at the Complutense University of Madrid. He then traveled to the United States, first working as a postdoctoral fellow at the University of Connecticut Health Center and later serving on the university faculty as a research assistant. In 1995, he joined the faculty at Wright State as an assistant professor in the department of physiology and biophysics. He was promoted to associate professor in 2000 and full professor in 2004.

Among his many research accomplishments, Cambronero discovered a key protein, phospholipase D, that plays a critical role in the development of breast cancer tumors and the spread of the disease to the lungs.

He is survived by his wife, Teresa Madrid, and his two children, Julia and David.

In memoriam: Henry Metzger

Henry Metzger died Nov. 20, 1938. He did his undergraduate studies at the University of Rochester before attending the College of Physicians and Surgeons at Columbia University.

He completed a residency at the New York–Presbyterian/Columbia University Medical Center and then, in 1959, went to the National Institutes of Health, where he spent most of his career.

Metzger pursued basic research in molecular aspects of the immune system. He served as the first director of intramural research with the National Institute of Arthritis, Musculoskeletal and Skin Diseases.

He authored more than 250 scientific articles, was elected to the National Academy of Sciences and was a fellow of the American Association for the Advancement of Science.

He is survived by his wife of over 60 years, Deborah, and their children, Eran Daniel, Renee Butler Metzger, and Carl Elias.

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!
SACNAS honors young scientists

By Stephanie Paxson

The Society for Advancing Chicanos/Hispanics and Native Americans in Science, known as SACNAS, hosts the annual National Diversity in STEM Conference to support scientists in every stage of their educations and careers. At the conference, attendees present research, listen to keynote speakers, participate in workshops and network.

Student research presentations are a part of the conference’s mentoring program. Undergraduates present posters, while graduate students make oral presentations about their work. They receive constructive feedback and guidance from SACNAS mentors who help aspiring scientists from all backgrounds succeed in their education and careers.

The American Society for Biochemistry and Molecular Biology is among the sponsors of the student presentation awards, which honor the graduate students’ presentations in a number of disciplines. Here are the awardees from the 2018 conference in San Antonio who presented research in the ASBMB-sponsored categories of biochemistry and molecular biology.

Jonathan Hurtado
Arizona State University

Hurtado is a fifth-year Ph.D. candidate in molecular and cellular biology at Arizona State University working in Qiang “Shawn” Chen’s lab in the Biodesign Center for Immunotherapy, Vaccines and Virotherapy. Hurtado presented his research on plant-produced, anti-dengue virus monoclonal antibodies’ ability to reduce antibody-dependent enhancement and to protect mice from dengue virus.

Hurtado wants to work as an academic faculty member.

Patrick Cervantes
University of Wisconsin–Madison

Cervantes is a fourth-year Ph.D. candidate in cellular and molecular biology at the University of Wisconsin–Madison campus working in Laura Knoll’s lab in the department of medical microbiology and immunology. His research showed that Z-DNA binding protein 1 (ZBP1) is independent of necroptosis during Toxoplasma gondii infection.

Cervantes wants to work in private or government research.

Jose (Joey) Luis Olmos Jr.
Rice University

Olmos is a fifth-year Ph.D. candidate in biochemistry and cellular biology at Rice University working in George N. Phillips Jr.’s lab. Olmos presented his collaborative work on time-resolved protein crystallography by mix-and-inject serial crystallography in the BioXFEL community, a National Science Foundation Science and Technology Center that, in part, aims to address the dynamic nature of proteins using X-ray free electron lasers.

Olmos wants to become a tenure-track professor because he is passionate about outreach and mentoring. “I believe science is a human endeavor that stands on the shoulders of giants,” he said, “and I find it very enjoyable and natural to give back by mentoring others on things that I’ve had to previously navigate or experience.”

Every summer, he helps recruit and mentor students for a summer research experience at Rice University that he co-directs with Phillips. Outside of the lab, Olmos enjoys reading and discovering new music.
Frank Talamantes (1943 – 2018)

By Takita Felder Sumter

Frank Talamantes was a renowned scientist who spent much of his career advancing the research community’s understanding of endocrinology. Specifically, Frank was known for his work elucidating the mechanisms of placental lactogens, prolactins and growth factors in reproduction. He also was known for his mentoring of younger scientists and colleagues.

With his peaceful death on Oct. 8, we all lost a trusted friend.

Frank joined the University of California, Santa Cruz, faculty in 1974 as a member of the molecular, cell and developmental biology department. There, he and his research group conducted seminal studies of the roles of placental lactogens in pregnancy. He later was appointed to administrative roles, including vice provost and dean of graduate studies from 2000 to 2004.

In 2004, Frank retired from UC Santa Cruz and subsequently joined the faculty of the Paul L. Foster Medical School at the Texas Tech University Health Sciences Center in El Paso in 2005 as a professor and assistant dean for research. He was recognized widely for his pioneering research on reproductive hormones and hormone receptors.

Frank was deeply committed to supporting the careers of students and early-career scientists, particularly those who have not been historically well-represented in molecular biology and biochemistry. He was a charter member of the Society for the Advancement of Chicanos and Native Americans in Science, or SACNAS, and later served as the society’s president at a pivotal time in its history, 1987–1990. His outstanding work in that arena was recognized in 1989 with a national award from the American Association for Higher Education. After his death, SACNAS established a scholarship in Frank’s name to help students travel to the annual SACNAS conference, honoring his commitment and advocacy.

Frank was recruited to the American Society for Biochemistry and Molecular Biology Minority Affairs Committee in 2006 and served two terms. During that time, the MAC established the Ruth Kirschstein Diversity in Science Award and nominated a number of renowned scientists for other national awards. The MAC will remember his ability to mentor and inspire other members of the committee effortlessly and often without even knowing it.

Frank was a native of El Paso, Texas. He earned a bachelor’s degree in biology from the University of St. Thomas in Houston and a master’s in biology from Sam Houston State University in Huntsville, Texas. He earned his Ph.D. in endocrinology from the University of California, Berkeley, in 1974.

Throughout his life, Frank was a bold trailblazer who took risks in many aspects of the scientific enterprise. After his retirement, he continued to promote diversity from his home in El Paso for as long his health allowed. His legacy continues through his former students and mentees.

Frank is survived by two daughters, Margaret and Laura Talamantes, and three grandchildren.
Remembrances

While I was a member of the Minority Affairs Committee, Frank was one person that I counted on for support. He never pulled me aside to pump me up, but instead he had this ability to speak about the issues we addressed during meetings that made one feel supported. As I pushed for the ASBMB to have a bigger presence in K–12 education, Frank would cite the many reasons why this mattered and should matter to us all. His words help me continue to work on tough issues.

— Regina Stevens-Truss
professor of chemistry, Kalamazoo College

Frank and I were both endocrinologists, and he was a member of the inaugural Endocrine Society Minority Affairs Committee, which I organized and established over 20 years ago. I recommended him for membership on the American Society for Biochemistry and Molecular Biology MAC and the Federation of American Societies for Experimental Biology’s Maximizing Access to Research Careers program. His work with these groups was based on his tremendous commitment to and advocacy for underrepresented minorities in science.

As the consummate academic/scientific mentor, Frank mentored everyone, from students to peers, minorities to non-minorities, and he mentored constantly, at conferences, meetings, in Starbucks, even at weddings (he was my best man). I considered myself a mentor in many of the same areas as Frank, but I always held him up as the mentor I most wanted to emulate.

Frank was also just a fun and nice guy to be around. I remember when he and I were at an International Congress of Endocrinology meeting in Osaka, Japan, we were walking around, not sure where we were or where we were going and obviously not able to speak or understand the native language. As I started to worry a bit, Frank calmly said, “Don’t worry, we will be fine. They will think that I am a famous sumo wrestler and you are my manager.”

Frank often said, “A mentor is like a tattoo. Once you have it, you have it forever.” Anyone who was touched by Frank will never forget him.

— Thomas Landefeld, professor of biology, California State University, Dominguez Hills

Frank was a wonderful person and an important mentor, and he lived what he loved. As I look back on my many interactions with him I realize now that he was always my “guide on the side.” He never shone the spotlight on himself or what he was doing for others, but whenever needed he was always willing to share his insights and experience. It is clear to me now that Frank knew that his accomplishments would only be as deep as his legacy — and that legacy is in the many people he mentored, guided, supported, and promoted. I owe a great deal of my personal success to him, as he was a role model for me and I’m a far better person because I had him in my life. I hope to keep his spirit alive by paying forward what he did for me. He will be dearly missed, but not soon forgotten, and his legacy and spirit will live on for many years.

— Phillip A. Ortiz, assistant provost, undergraduate and STEM education, The State University of New York
Welcome, New ASBMB Members

Hossameldin Abouhish, Augusta University
Toyosi Adewunmi, Baylor College of Medicine
Fatema Alatawi, University of Tabuk
Sati Alexander, San Diego State University
Asma Alodaini, North Central College
Carmen Alvarez, Manhattan College
Jose Alvarez, National University
Carina Amaya, San Jose State University
Brooke Andrews, Emory University
Borhane Annabi, Université du Québec à Montréal
Rachel Antuna, Augustana College
David Ashline, University of New Hampshire
Jeovanna Badson, Manhattan College
Joshua Ballard, Loxo Oncology
Katherine Banftch, Monmouth University
Wade Bell, Virginia Military Institute
Dobrusia Bialonska, University of North Georgia
Sheila Bonitatibus, Boston University
Hunter Bourdon, Georgia Southern University–Armstrong Campus
Marcus Bowser, Ohio Northern University
Keetra Branch, Abraham Baldwin College
Melyssa Bratton, Xavier University of Louisiana
Hannah Brown, Duke University
Martin Buckley, Slippery Rock University
Christian Bühl, Copenhagen Center for Glycomics
Michael Burns, Loyola University Chicago
Sabrina Castano, Chestnut Hill College
Esra Celik, Monmouth University
Amit Chandra, Council of Scientific and Industrial Research–Institute of Genomics and Integrative Biology
Shereen Chaudhry, Manhattan College
Kathy Chen, Monmouth University
Yue Chen, University of Minnesota
Alexandra Chirakos, University of Notre Dame
Kiersten Chong, Chapman University
Morgan Christenberry, National University
Janelle Chuah, West Virginia University
Charmaine Bing Bing Chung, Hobart and William Smith Colleges
Ella Clifford, Providence College
Sabrina Cline, Auburn University
Meghan Collins, University of Texas
William Conrad, Lake Forest College
Miranda Crouse, Missouri State University
Lauren Dalton, Oregon State University
Emily D’Amico, Westminster College
Tiziana Dao, École Polytechnique Fédérale de Lausanne
Marino De Leon, Loma Linda University School of Medicine
Evelien De Meulenaere, University of California, San Diego
Kristine Deibler, University of Washington
Alex Demrick, University of Texas at Austin
Patrick DePaolo, Stevens Institute of Technology
Jessica Desamero, City University of New York Brooklyn College
Adi Dubash, Furman University
Mark Eckert, University of Chicago
Jessica Encinas, Facultad de Medicina de ABC
Kristen Engevik, University of Cincinnati
Harrison Esterly, Appalachian State University
Frances Evesson, Children’s Hospital at Westmead, The University of Sydney
Linglan Fang, University of Washington
Charli Fant, University of Colorado Boulder
Audrey Farthing, Ohio Northern University
Brianna Ferrell, Chestnut Hill College
Shannon Forty, Manhattan College
Melissa Franco, Northeastern University
Jaime Garcia, National University
Loraa Gendy, California State University, Los Angeles
Sunil George, Wake Forest University
Daniel Gewirth, Hauptman–Woodward Medical Research Institute
Margo Goldfarb, Kenyon College
Alicia R. Gomez, Chestnut Hill College
Yisett González, El Instituto de Investigaciones Científicas y Servicios de Alta Tecnología de Panamá
Paris Grey, University of Florida
Claire Griffith, Ohio Northern University
Haiwei Gu, Arizona State University
Svilen Guenov, Nova Southeastern University
Danielle Guillen, Monmouth University
Vandana Gupta, Vertex Pharmaceuticals
Kevin Hackshaw, The Ohio State University
Mohammad Heidarian, California State University, East Bay
Julia Hoeng, Philip Morris International
Nick Hofmaier, University of Nebraska–Lincoln
Michael Hoy, Duke University
Bo Huang, Wayne State University
Tameryn Huffman, Manhattan College
Elizabeth Hunsaker, Duke University
Angelina Huyhn, San Jose State University
Seung-Soon Im, Keimyung University
Shabrina Jarrell, Georgia Southern University–Armstrong Campus
Basava Jitta, Washington Adventist University
Kayla Johnson, Michigan State University
Elshad Kadeer, California State University, East Bay
Michal Kaisz, Monmouth University
Srimathi Kasturirangan, University of Toledo
Dorsilla Katimbwa, Kyungpook National University
Kumari Kavita, National Institutes of Health
Jacob Kazenelson, University of North Carolina Wilmington
Alisha Kellner, University of Central Florida
Shannon Kelty, Ohio Northern University
Konstantin Khrapko, Northeastern University
Eun-Young Kim, University of Ulsan College of Medicine
Olivia Kouses, University of Michigan
Anjali Krishnan, Kent State University
Stephanie Kristo, Manhattan College
John Lamar, Albany Medical College
Kirsten Lawson, Monmouth University
Richard Lee, Bronx High School of Science
Xinwei Li, Jilin University
Bo Lin, Nexcelom Bioscience
Mara Livezey, University of Detroit Mercy
Christopher Lore, Manhattan College
Sonja Lorenz, University of Wuerzburg
Anin Luo, Yale University
Adam Luthman, University of North Carolina at Chapel Hill
Sibongile Mafu, University of Massachusetts Amherst
Emmanuel Mahounou, National University
Sudipta Maiti, Tata Institute of Fundamental Research
Tamara Mans, North Hennepin Community College
Kristen Marzano, Monmouth University
Yuji Masuda, Nagoya University
Fatimah Matalkah, West Virginia University Health Sciences School of Medicine
Marissa McFadden, Hobart and William Smith Colleges
Ashley Melendez, University of Puerto Rico, Mayagüez
Maria Isabel Mendonça, Faculdade de Medicina do ABC
Jayshree Mishra, Texas A&M Health Science Center
Nadeen Moawiah, Manhattan College
William Molina, University of Puerto Rico, Mayagüez
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Laine Morris, Monmouth University
Shakeel Mowlaboccus, The University of Western Australia
Sara Naessig, Manhattan College
Kristos Negron Teron, Purdue University
Khue Nguyen, University of North Carolina at Chapel Hill
Scott Nguyen, University of California, Santa Cruz
Nhu Nguyen, University of Missouri
Kyara Nichols, Xavier University of Louisiana
Elena Nikitkina, Russian Research Institute of Farm Animal Genetics and Breeding
Jisun Oh, Kyungpook National University
Rachel Okoje, University of Benin
Ayekunle Olarewaju, University of Washington
Gabrielle Padley, Georgia Southern University–Armstrong Campus
Matthew Parramore, Gulf Coast State College
Devon Pawley, University of Miami
Marisín Peiró, El Instituto de Investigaciones Científicas y Servicios de Alta Tecnología de Panamá
Carlos Henrique Peiró, Faculdade de Medicina do ABC
Esther Peterson, University of Puerto Rico
Cassidy Pfister, Ohio Northern University
Benjamin Pinsky, University of Michigan
Lenore Pitstick, Midwestern University
Elena Polovnikova, Kilpatrick Townsend and Stockton LLP
Peter Reinhart, Kenyon College
Brianna Remache, Manhattan College
Carlos Restrepo, El Instituto de Investigaciones Científicas y Servicios de Alta Tecnología de Panamá
Meagan Rhoades, National University
Rebecca Riggs, Auburn University
Keisha Rodriguez Mártil, University of Puerto Rico, Río Piedras
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Noor Sarsar, Monmouth University
Linda Sasset, Weill Cornell Medicine
Allison Schier, University of Colorado Boulder
Mika Schieveldbeen, Monmouth University
Camille Schneider, The Ohio State University
Sabrina Segura, Manhattan College
Arun Seth, Sunnybrook Research Institute
Savanna Sharum, University of Illinois at Urbana–Champaign
Jeremy Shaw, University of Virginia
Jose Silva, Universidade Nove de Julho
Kristin Slade, Hobart and William Smith Colleges
Aaron Smith, University of Maryland, Baltimore County
Miranda Smith, Georgia Southern University–Armstrong Campus
Edward Snell, Hauptman-Woodward Medical Research Institute
Teis Sondergaard, Aalborg University
Subah Soni, Monmouth University
Nathan Southwell, Ohio Northern University
Kathryn Spilios, Boston University
Savannah Spitalne, Ohio Northern University
Wolfdieter Springer, Mayo Clinic
Benjamin Stenson, National University
Hanna Stewart, Nova Southeastern University
Hayden Stoebner, Texas State University
Arohan Subramanya, University of Pittsburgh School of Medicine
Odunayo Taiwo, Federal University of Agriculture, Abeokuta, Ogun-State, Nigeria
Kelly Tatchell, Louisiana State University Health Science Center
Calla Telzrow, Duke University
Balaji Thas Moorthy, University of Miami
Yee Mon Thu, Allegheny College
Kaleb Todd, Fort Lewis College
Kathleen Tran, Ohio Northern University
Magali Trayssac, Stony Brook University
Aiko Turmo, Michigan State University
Lilian Turner, Christopher Newport University
Zachary Unracht, University of Central Florida
Fabiola Velazquez, Stony Brook University
Thiagarajan Venkatesan, Nova Southeastern University
Schuyler Vickers, West Virginia University
Brian Villalba, University of Texas at Austin
Kristen Walker, Morgan State University
Xingya Wang, Zhejiang Chinese Medical University
Yael Wang, Texas A&M University
Max Warner, Kennesaw State University
Ingrid Wernstedt Asterholm, University of Gothenburg
Abigail Wiggins, Saint Leo University
Morgan Will, Nova Southeastern University
Jiwon Woo, Yonsei University College of Medicine
Shusong Wu, Hunan Agricultural University
Sila Yanardag, West Virginia University
Sophia Yang, Appalachian State University
Kwan Yoon, University of Massachusetts Amherst
Mallory Zabieliski, Ohio Northern University
Haihan Zeng, Otterbein University
Yanqiong Zhang, University of North Carolina
Xia Zhou, Southern Illinois University Carbondale
Junhui Zhou, University of Delaware
For March, it’s a renal three-fer: sodium, potassium and chlorine

By Quira Zeidan

Every month in 2019 we are looking at one or more chemical elements essential for life in commemoration of the 150th anniversary of Mendeleev’s periodic table. For January and February, we selected hydrogen and iron, respectively, and described their function in biochemical reactions involving electron transport.

March is National Kidney Month, so we are highlighting three elements central to renal function: sodium, or Na; potassium, or K; and chlorine, or Cl.

Sodium and potassium, atomic numbers 11 and 19, respectively, are highly reactive metals with similar chemical properties, both listed in group 1, the alkali metals, of the periodic table. Both have a single valence electron in their outer shell, which they readily donate, creating positive ions, or Na⁺ and K⁺ cations. Chlorine, a gas at room temperature with atomic number 17, is a highly reactive element with an affinity for electrons. As a strong oxidizing agent, chlorine is abundant as chloride anions, or Cl⁻, that combine with Na⁺, K⁺ and other cations to form chloride salts.

Sodium is the seventh most abundant element on Earth, and potassium is the 17th. They exist in rock-forming minerals such as salt and granite. Chlorine is the 21st most abundant element in the Earth’s crust, occurring exclusively as ionic chloride compounds. Sodium and chlorine, constantly leached by water from mineral salts, are the most abundant elements dissolved in the oceans.

Sodium and potassium ions are crucial for most cells. Microorganisms use transmembrane ion pumps, such as the Na⁺/H⁺ antiporter or Na⁺ translocation systems coupled to metabolic reactions, to move Na⁺ ions against their concentration gradient, generating electrochemical energy to drive solute transport or to move flagellar motors (in bacteria) and to produce reducing power for biochemical reactions. K⁺ is the main monovalent cation in prokaryotes; it is essential to maintain intracellular pH, to generate energy via electrochemical gradients and to sustain turgor pressure.

In animals, the Na⁺/K⁺ ion pump pushes sodium and potassium across the cell membrane in opposite directions, maintaining a low Na⁺ concentration and a high K⁺ concentration inside the cell. This ionic imbalance between the cytosol and the extracellular medium creates a transmembrane potential — or voltage difference — essential to conducting electrical signals in excitable neurons and myocytes. A similar ion transporter moves H⁺ and K⁺ ions across the membrane of parietal cells, helping mammals acidify stomach contents and digest food.

Chloride ions are also necessary for all known life. Some prokaryotes use chloride compounds as a carbon and energy source and chlorine ions as terminal electron acceptors during anaerobic growth. In most cells at rest, the concentration of Cl⁻ is lower in the cytosol than in the extracellular fluid via activity of gated ion channels that contribute to the polarization of cellular membranes. In animals, parietal cells in the stomach secrete Cl⁻ ions to produce hydrochloric acid required for food breakdown. In humans, the defective protein in the disease cystic fibrosis is an ion channel specific for Cl⁻ whose impaired activity results in less bactericidal activity — and more infections — in the lungs.

Quira Zeidan (qzeidan@asbmb) is the ASBMB’s education and public outreach coordinator. Follow her on Twitter @quirazeidan.
Norovirus is the most common cause of gastroenteritis worldwide; it causes hundreds of thousands of deaths each year and is particularly risky for children under 3 years old. If someone gets norovirus in a setting like a hospital, it’s critically important to protect others from getting infected. Research from universities in Germany, published in the Journal of Biological Chemistry, suggests that it may be easier than anticipated to find a compound that could be used as a food supplement to stop the spread of norovirus in children’s hospitals.

Norovirus causes disease after entering cells in the gut by binding to fucose, a sugar molecule found on cell surfaces. Fucose also is found in breast milk and other foods. Norovirus can’t tell the difference between fucoses that are part of cells in the gut and those that are simply passing through; for this reason, adding a fucose-based supplement to the diet as a decoy could be a way to capture the virus and keep it from infecting cells.

To develop this strategy, however, researchers needed to understand which features of fucose and virus molecules affected how well they attach to each other. In cells, foods and milk, fucose rarely is found as a single molecule; rather, it’s part of chains or networks of sugars and proteins. Franz-Georg Hanisch, a researcher at the University of Cologne, led a project to disentangle these molecular elements and understand what kind of fucose-based product best would distract noroviruses. He started by screening the many types of fucose-containing human milk oligosaccharides, or HMOs.

To Hanisch’s surprise, the strength of the binding between the norovirus protein and HMOs did not depend much on the structure of the HMO or the types of fucose molecules it contained. Rather, what mattered was how many fucoses the HMO contained. Each individual fucose stuck weakly to the virus protein, but the more fucoses there were in the compound, the better the compound and the viral protein stuck together.

“The binding of the virus is not dependent in any way on further structural elements (of HMOs),” Hanisch said. “It’s only the terminal fucose which is recognized, and the more fucose at higher densities is presented, the better is the binding.”

Hanisch turned to the industry standard of where to get a lot of fucoses fast. Brown algae — the family of seaweed that includes kelp — produce a compound called fucoidan, which is a complex network of many fucoses. (Fucoidan has been explored independently as a treatment for HIV and other viruses for unrelated biochemical reasons.)

“There are procedures for isolating the stuff in quite high yields and in high purity,” Hanisch said. The organization of the fucoses in fucoidans looks nothing like any fucose-containing molecules found in the human body, but fucoidan nevertheless tightly bound to the virus protein in the team’s experiments. This means fucoidan could be a safe and cheap food additive to block viruses from infecting cells. It also suggests researchers will be able to design an even better fucose-containing compound.

Hanisch and his collaborators are moving on to experiments with live viruses and live organisms, with the goal of developing a fucose-based food supplement that could be given to a group of people, such as hospitalized children, at the first sign of a norovirus outbreak, to prevent the circulating viruses from entering their cells and causing disease.

“I hope that in about three years we will have a product which can be used in norovirus defense and to go into clinical studies,” Hanisch said. DOI: 10.1074/jbc.RA117.001369
In a collection of articles highlighting recent discoveries in sperm and egg biology, a special issue of the journal *Molecular & Cellular Proteomics* celebrates the contribution of the field of proteomics to a deeper understanding of reproductive biology.

Edited by MCP Associate Editor Tim Karr of the Bio-design Institute at Arizona State University, the issue showcases the versatility and multiplicity of proteomic technologies for analysis of protein abundance, post-translational modifications, protein–protein interactions and subcellular localization in reproduction.

According to Karr, proteomic approaches are particularly well-suited to studying reproductive biology. “Sexual reproduction in many cases can be thought of as cellular action at a distance, that is, sperm travels outside the body in which it was produced,” Karr said. “Therefore, we can expect that a majority of interactions and interesting biology takes place predominantly at the protein–protein interaction level.”

Sperm are known to transmit packaged RNAs, but compared with somatic cells, sperm are transcriptionally inactive, further highlighting the importance of protein interactions.

Proteomics is also important in the study of interactions between the male ejaculate and the female reproductive tract. There is little experimental evidence that gene expression or other gene–gene interactions play a major role once the ejaculate is delivered to the reproductive tract.

“For these cases, proteomics is a fruitful approach if one wishes to understand the molecular mechanisms involved,” Karr said.

The special issue dives into a few major themes in reproductive biology. A series of papers investigates how proteomes of reproductive cells change throughout the reproductive processes, such as spermatogenesis, sperm maturation and capacitation, and oocyte activation.

Human fertility also is explored in depth in this special issue. A few studies delineate the proteomes of infertile sperm and sperm that undergo different abstinence periods. Another study provides the first draft map of the human ovarian proteome and its extracellular matrix, which can inform the development of artificial ovaries and provide greater understanding of fertility in women.

Two papers seek to understand polyandry, a pattern of mating in which a female animal has more than one male mate. One study investigates how polyandry drives sexual selection, and another looks to understand the protein–protein interactions that mediate sperm competition dynamics and preservation.

The special issue includes studies in various organisms, from humans to insects and even crocodiles. The diversity of organisms highlights the importance of studying reproduction. One study discovered that crocodile sperm undergo capacitation, a functional maturation that was thought to be restricted to mammals. The fact that an analogous process was observed in a distant reptilian species could challenge what we know about the evolution of species.

“Sperm and egg are the only cell types for which their function is universal throughout the animal kingdom,” Karr said. “From an evolutionary viewpoint, sperm and egg are the glue that binds life, and therefore their constituent proteomes may represent our deepest links to the evolution of eukaryotic life on the planet.”

Saddiq Zahari (szahari@asbmb.org) is the editor of manuscript integrity at MCP. Follow him on Twitter @saddiqzahari.
Technique boosts omega-3 fatty acid levels in brain 100-fold

Getting enough docosahexaenoic and eicosapentaenoic acid, or DHA and EPA, into the brain to study their effects on conditions such as Alzheimer’s and depression — which they have been shown to help — is no easy task. While supplements containing these omega-3 fatty acids exist, there is scant evidence showing that the supplements actually increase DHA or EPA in the brain. To increase levels of EPA in the brain measurably, a person would have to consume a small glass of it each day, quite possibly with the side effect of smelling like fish.

Now researchers from the University of Illinois at Chicago report that adding a lysophospholipid form of EPA, called LPC-EPA, to the diet can increase levels of EPA in the brain 100-fold in mice. The amount of LPC-EPA in the diet required for this increase is rather small for mice — less than a milligram per day. The human equivalent would amount to less than a quarter of a gram per day.

DHA and EPA are known to have anti-inflammatory effects and protect against various neurological and metabolic diseases. DHA has been shown to be good for memory and cognitive deficits associated with Alzheimer’s disease, and, in studies, EPA has been shown to be effective in treating and preventing depression.

DHA is already prevalent in the brain, and there is little evidence to support the idea that eating lots of fish oil, either through whole fish or supplements, increases levels of DHA in the brain. EPA is found in very low concentrations in the brain, and boosting those levels through consuming EPA has proved difficult, because the amount that would need to be ingested to show increases in brain EPA levels is quite large — 40 to 50 milliliters daily. And researchers still don’t really have a great understanding of how EPA works to reduce depression and how much is needed in the brain to have these anti-depressant effects.

Papasani Subbaiah is a professor of medicine and biochemistry and molecular genetics in the UIC College of Medicine and corresponding author of a paper about the new work published in the Journal of Lipid Research.

“In order to do the trials to determine the proper dosage and how EPA works in regards to depression, we need to have a better way of getting it into the brain because you need to consume so much of it that it’s just not practical, at least for human trials,” Subbaiah said.

EPA provided in the form of lysophospholipid escapes the degradation by pancreatic enzymes that prevents the type of EPA in fish oil supplements from passing into the brain, he said.

“It seems that there is a transporter at the blood–brain barrier that EPA must pass through in order to get into the brain, but EPA in fish oil can’t get through, whereas LPC-EPA can,” Subbaiah said. “You don’t have to consume all that much LPC-EPA to have significant increases of EPA show up in the brain, so this could be a way to do rigorous studies on the effects of EPA in humans.”

Producing LPC-EPA is not difficult, and it can be incorporated into feed pellets that Subbaiah fed to laboratory mice. After eating 1 mg per day of the LPC-EPA in their feed for 15 days, these mice had up to 100 times more EPA in their brains than mice eating plain EPA. Interestingly, the mice eating LPC-EPA also had two times more DHA in their brains.

“This study is proof of the concept that we can increase levels of both EPA and DHA in the brain via supplements or by incorporating LPC-EPA in the diet,” Subbaiah. “Using this technique, we can now perform critical studies to see if increasing concentrations of these fatty acids in the brain can help prevent and treat Alzheimer’s and depression in mouse models, and then move into human trials if results are promising.”

DOI:10.1194/jlr.M090464

This article is adapted from a press release produced by the University of Illinois at Chicago News Bureau.
We offer a selection of recent papers on a variety of topics from the Journal of Biological Chemistry, the Journal of Lipid Research, and Molecular & Cellular Proteomics.

How to tackle stress

The tumor suppressor protein p73 is known to induce apoptosis in response to stress, but the details of this pathway are poorly understood. In a paper in the Journal of Biological Chemistry, Mi-Kyung Yoon and colleagues from the Korea Research Institute of Bioscience and Biotechnology and the Korea Research Institute of Chemical Technology show that p73-mediated apoptosis occurs via a mitochondrial pathway. Moreover, the process requires an interaction between a p73 domains and a noncanonical site on the anti-apoptotic protein Bcl-XL. This study unexpectedly expands the known modes of Bcl-XL recognition and reports a new apoptotic pathway that may be relevant for cancer treatment. DOI: 10.1074/jbc.RA118.003061

Identifying dysregulated signaling in ovarian cancer

High-grade serous carcinoma, or HGSOC, is the most aggressive and common form of ovarian cancer, accounting for about 70 percent of all cases. Studies have shown that post-translational modifications, or PTMs, play a role in reprogramming signaling networks that contribute to the cancerous phenotype. However, PTMs are more challenging to identify than genetic or proteomic changes. A study in Molecular & Cellular Proteomics uses a new

Understanding the lipid situation in bone cancer

Osteosarcoma is the most common form of primary bone cancer in humans. Most people diagnosed with the disease are under the age of 25. Treatment is aggressive, consisting of tumor excision and multiple forms of chemotherapy. Even then, the average five-year survival rate is 65 percent at the non-metastatic stage and 20 percent after metastasis. Development of new therapeutic approaches requires a better understanding of the metabolic pathways involved in the development and progression of osteosarcoma.

Significant research has been done to explore the transcriptomics and proteomics of various cancer types, but the lipidomic profile of osteosarcoma is poorly understood. Lipids are an important component of the cell machinery both structurally and functionally. In fact, dysregulation of lipid metabolism has been associated with breast and prostate cancer.

Aditi Das and her group at the University of Illinois Urbana-Champaign have compared the lipid profiles of metastatic and non-metastatic osteosarcoma cells to that of normal fetal osteoblast cells to better understand the mechanism of bone tumor formation and metastasis. Their findings were published in the Journal of Lipid Research.

Using high-throughput assays, the group has identified 15 distinct classes of lipids that are differentially expressed in cancerous cells compared to normal bone cells; these include phospholipids, glycolipids and cholesterol. Diacylglycerol was overexpressed in metastatic osteoblasts such that blocking diacylglycerol synthesis reduced cell viability and migration in metastatic osteosarcoma.

These findings help the researchers understand how the lipid profile is altered when cells are metabolically reprogrammed to support uncontrolled growth and proliferation and, in the future, might pave the way for alternative therapeutic approaches for treating pre-metastatic osteosarcoma. DOI: 10.1194/jlr.M088559

— Isha Dey
human proteome microarray-based approach to identify dysregulated PTMs associated with ovarian tumors, providing insight into PTM alterations in tumor samples. Guang Song and colleagues at Johns Hopkins University established tumor lysate-based reactions to identify multiple PTMs in cancer samples. They performed kinase phosphorylation reactions with total tissue lysates on an array of human proteins and then identified phosphorylated substrates. They looked for activated kinases upstream of these substrates to identify the enzymes capable of producing the PTM and thus possibly involved in cell signaling dysregulation. They specifically focused on tyrosine phosphorylation for their analysis and identified 19 tyrosine kinases that may play a role in signaling pathway dysregulation observed in HGSOC. Their method provides a novel means to identify PTMs in tumor samples, providing insight into dysregulated signaling networks that may contribute to cancer.

DOI: 10.1074/mcp.RA118.000851

A new player of cholesterol biosynthesis in the liver

Long noncoding RNAs, or IncRNAs, are at least 200 nucleotide-long RNA sequences that do not translate into proteins. However, they have been associated with regulation of gene expression and developmental processes as well as with various disease states.

A study by Wei Li and his group at Wenzhou Medical University in China published in the Journal of Lipid Research has identified one such IncRNA as an important player in cholesterol biosynthesis. Hepatic transcriptomic analysis revealed more than three dozen IncRNAs were differently expressed in mice fed with a high-fat diet (a model system for cholesterol synthesis and fatty liver disease) compared with mice fed a standard chow diet. A correlation analysis of IncRNA and protein-coding RNA interpreted the functions of the identified IncRNAs. Connecting the IncRNAs to metabolic pathways using cell-based assays, the authors identified an IncRNA called NONMMUG027912 that was regulated by PPAR-alpha, a key regulator of lipid metabolism in the liver, such

DOI: 10.1074/jlr.RA118.005015

— John Arnst

Scorpion venoms vanquish viruses

The four dengue viruses, which cause fevers on their own and hemorrhages in concert, emerged over eight centuries in Southeast Asia and Africa, where they became endemic with the aid of mosquitoes and occasional nonhuman mammalian reservoirs. As shipping containers and trade agreements seemed to shrink the globe after World War II, they also opened up dozens of other tropical and subtropical countries to the dengue-carrying mosquitoes Aedes aegypti and Aedes albopictus, which arrived hidden away in cargo ships.

Today, nearly 2.5 billion people live in areas where dengue transmission is a risk. Despite preclinical successes, the leading antiviral and vaccine candidates for treating and preventing dengue, balapiravir and dengvaxia, were both found to have dangerous side effects.

Zhijian Cao and his colleagues at Wuhan University in China may have a new antiviral candidate. They recently found that venom peptides from the scorpion Euscorpiops validus, native to southern China, are effective at blocking dengue virus type 2 from entering bacterial cells. They published their results in the Journal of Biological Chemistry.

The researchers tested a purified version of the venom peptide Ev32, called rEv32, against dengue virus type 2 in both Escherichia coli and Staphylococcus aureus. There, it was able to raise the pH of acidic organelles within the bacteria, preventing the viruses’ pH-dependent membranes from fusing with the inner bacterial membranes. This effectively trapped the viruses in cells after they already had entered and replicated, shutting down the viral infections.

Subsequent experiments found that a purified form of the venom, rEV32, acted against hepatitis C virus, Zika virus and herpes simplex virus 1, which all have cellular entry processes similar to dengue. The researchers hope to begin testing rEV32 as an antiviral drug candidate in the near future.

DOI: 10.1074/jbc.RA118.005015

— John Arnst
Phosphoproteomics correlate cellular effects of chemotherapy

Synthetic sphingolipids can be used as chemotherapy agents to starve cancer cells. These lipid therapeutics trigger downregulation of nutrient transporters and block lysosomal fusion events to kill the cell. It is known that sphingolipids activate protein phosphatase 2A, or PP2A, and negatively regulate signaling pathways that promote expression of nutrient transporters.

Pierre Thibault and colleagues from the Université de Montréal in Canada used quantitative phosphoproteomics to determine how PP2A alters cell fusion events in a mouse cell line. They treated the cells with a synthetic sphingolipid called SH-BC-893 that has been investigated pre-clinically as a means to target and kill cancer cells. They also separately treated the cells with a related lipid, ceramide, one that is known to stimulate PP2A but isn’t used as a chemotherapy agent, and also with a specific PP2A inhibitor. Using metabolic labeling, they identified phosphorylation sites that were regulated by the treatments and therefore could be putative PP2A substrates.

The researchers’ analysis confirmed that SH-BC-893 does affect PP2A activity, and they identified several putative PP2A substrates. A significant proportion of these targets were found to be involved in actin cytoskeleton organization and cell migration pathways. Analyses of these substrates suggest that they may contribute to the intracellular trafficking defects observed in cells treated with sphingolipids. They further identified that treatment with ceramide, but not SH-BC-893, dysregulates two proteins called Akt and Gsk3b, explaining why only SH-BC-893 produces a lysosomal fusion defect.

Their work, recently published in *Molecular & Cellular Proteomics*, demonstrates the utility of using dynamic phosphoproteomics to correlate signaling events with cellular phenotype.

DOI: 10.1074/mcp.RA118.001053  
— Courtney Chandler

An insect toxin grabs with two hands

When farmers want to avoid using pesticides, they often turn to transgenic crops containing the crystalline Cry toxins produced by Bacillus thuringiensis, or Bt. These plants are used worldwide because the concentrations of toxins in plants only harm the insects that are feeding directly on them. In 2017, Bt crops were cultivated on more than 240 million acres. However, pests including the pink bollworm and Indian-meal moth have evolved rapidly to resist the toxins.

To improve the efficacy of the Cry toxins, which kill by binding to insect midgut receptors, Arlen Peña-Cardeña and colleagues at the Universidad Nacional Autónoma de México investigated the binding activity of Cry1Ab’s C-terminal region. This region previously was believed to be an inactive part of the Cry1Ab toxin that just needed to be cleaved by proteases before the toxin could begin binding.

In a study published in the *Journal of Biological Chemistry*, the researchers found that Cry1Ab’s C-terminal region provides additional binding sites for alkaline phosphatase and aminopeptidase insect receptors but not for cadherin, a target of the main toxin. By discovering that the components of Cry1ab target insect guts with a variety of receptors, the researchers may be able to alter the specificity and increase the toxicity of the proteins.

DOI: 10.1074/jbc.RA118.005101

Describing the secretome of a Gram-positive bacteria

Protein secretion is an essential biological process. Studying the array of proteins secreted by a bacterial or eukaryotic cell, called the secretome, can give insight into its response to surrounding stimuli. A paper published in *Molecular & Cellular Proteomics* describes the secretome dynamics of the Gram-positive bacterium Streptomyces lividans. A team led by Tassos Economou at the Rega Institute in the Katholieke Univer-
siteit Leuven, Belgium, used mass spectrometry and transcriptomics to analyze protein secretion across a variety of growth conditions. They identified several so-called housekeeping proteins that were secreted in stable amounts irrespective of growth conditions or genetic background, suggesting they are essential for cell proteostasis. They also observed that bacteria growing more slowly, which therefore had lower cell mass, secreted higher amounts of protein. They hypothesize that this is due to shutting of metabolic intermediates toward secretion instead of cellular growth, thereby linking metabolism and secretion. Additionally, not all changes in the quantity of individual secreted proteins were explained by changes in transcription. This suggests another level of downstream regulation that has not been identified. Their findings have implications for how secretome, proteome and metabolome studies can be integrated to better understand regulation of vital cell processes.

**A dead domain creates dimers**

Mutations in a group of magnesium transporters called the cyclin N family are associated with several diseases, including familial primary hypomagnesemia, a blood disorder, and Jalili syndrome, which affects the eyes. A better understanding of how these transporters function could potentially aid in treating these diseases. Yu Seby Chen and colleagues at McGill University in Canada and Osaka University in Japan now have characterized one particularly mysterious part of the proteins: the cyclic nucleotide binding homology domain. The authors, publishing in the *Journal of Biological Chemistry*, found that the domain is required for transporter function but that mutations may be responsible for it losing the ability to bind nucleotides. Instead, these domains cause protein dimerization in vitro, with dimer strength inversely correlating with transporter activity. The authors postulate that these domains therefore may inhibit protein function, providing a new framework to evaluate disease-linked sequences.

**DOI**: 10.1074/mcp.RA118.000899

**Neuronal GIRK currents and blood cholesterol level**

G protein-mediated inwardly rectifying potassium channels, or GIRKs, translate chemical transmissions in the brain into electrical signals at the post-synaptic regions of hippocampal neurons to mediate the effects of inhibitory neurotransmitters. Another component essential for normal neuronal activity is cholesterol, which forms up to 50 percent of the membrane lipids. About 20 percent of the total cholesterol in the human body is in the brain. Abnormal cholesterol levels in the brain have been associated with such neurodegenerative conditions as Alzheimer’s disease.

A recent collaborative study by the University of Illinois at Chicago, the University of Tennessee Health Science Center and the National Institutes of Health established the role of statin therapy (used to treat high cholesterol levels in the blood) on hippocampal GIRK currents. The findings were published in the *Journal of Lipid Research*. A research team led by Anna N. Bukiya in Avia Rosenhouse-Dantsker’s lab used a rat model to show that a high-cholesterol diet increased hippocampal cholesterol levels and neuronal GIRK currents. However, a high-cholesterol diet combined with statin therapy counteracted the effect. This finding is interesting, as researchers expected the cholesterol pool in the brain to be shielded from blood cholesterol fluctuations.

The study sheds new light on the regulation of ion channel function by lipids. It also provides a better understanding of the multifaceted effects of statin therapy in the brain.

**DOI**: 10.1074/jbc.RA118.005672

**A selection simulation**

Newborn babies often are tested for a condition called phenylketonuria, in which deleterious mutations to phenylalanine hydroxylase, or PAH, lead to elevated levels of phenylalanine, which can result in intellectual disabilities, seizures and other problems. Phenylalanine acts as an allosteric regulator of PAH, but the mechanism is not fully understood. Yunhui Ge and colleagues from Temple and Drexel Universities used computational modeling approaches to simulate interactions between Phe and its binding site in PAH. The simulations implicated a conformational selection mechanism in which a gate in the protein must open to allow Phe binding. These mechanistic details, published in the *Journal of Biological Chemistry*, could offer new directions for therapeutic development.

**DOI**: 10.1074/jbc.RA118.004909

John Arnst (jarnst@asbmb.org) is ASBMB Today’s science writer. Follow him on Twitter @ArnstJohn.

Courtney Chandler (cochand@umaryland.edu) is a graduate student at the University of Maryland, Baltimore. Follow her on Twitter @CourtneyEChan.

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

Catherine Goodman (cgoodman@asbmb.org) is the Journal of Biological Chemistry’s scientific editor.
RESEARCHERS ON THE RISE
Journal talks by early-career investigators
The 2019 American Society for Biochemistry and Molecular Biology Annual Meeting in Orlando will include talks on Tuesday, April 9, by five winners of the 2019 Journal of Biological Chemistry/Herbert Tabor Young Investigator Awards.

“These are young scientists who have already made outstanding achievements that they will share during the JBC symposium,” said George DeMartino, professor of physiology at the University of Texas Southwestern Medical Center and a JBC associate editor. “This is an opportunity to see the plenary lecturers of tomorrow at an early stage of their careers.”

The awards, named for Herb Tabor, who served as JBC’s editor-in-chief from 1971 to 2012, recognize early-career first authors of standout JBC papers published the previous year for their creativity and scientific excellence.

For this year’s awards, a committee of JBC associate editors reviewed nominated articles, all Editors’ Picks, from 2018. After consulting experts in the field and evaluating the quantitative impact of the papers, the committee selected six award-winning first authors.

“We are very pleased to celebrate these early-career investigators who have authored top-notch papers in JBC that report exciting and significant research,” said Lila Gierasch, distinguished professor at the University of Massachusetts Amherst and editor-in-chief of JBC.

At the ASBMB annual meeting in Orlando, five of the six award winners will give talks about their research findings, which span a diverse array of topics within biological chemistry.

The 2019 JBC/Tabor Award winners

Eugene Serebryany, a postdoctoral fellow in Eugene Shakhnovich’s lab at Harvard University, has developed a new model for how crystalline proteins aggregate and cause cataract disease. (see page 20)

Margaret Wangeline, a postdoctoral fellow at the University of California, San Diego, found that binding to a downstream product drives allosteric misfolding of a sterol biosynthesis enzyme and targets it for degradation. (see page 21)

Fernando Damasceno, an adjunct professor at the Federal University of Vale do São Francisco, uncovered a new role for the labile iron pool as an antioxidant that competes with the oxidant peroxynitrite. (see page 22)

Caroline Soliman, a graduate researcher in Paul Ramsland’s group at the Royal Melbourne Institute of Technology, determined the structural basis for how an antibody recognizes polysaccharides on microbial surfaces and in biofilms, making it protective during infections. (see page 23)

Sandeep Eswarappa, an assistant professor at the Indian Institute of Science in Bangalore, developed a model that suggested that increased cellular demand for proline and depletion of glutamine around 1 billion years ago drove the fusion of two enzymes to form the bifunctional glutamyl-prolyl-tRNA synthetase. (see page 24)

Kirstine Lavrsen, a postdoctoral researcher with the Danish Cancer Society in Copenhagen, identified an enzyme that converts normal colon into cancerous tissue by attaching a sugar to certain cellular proteins. (Lavrsen is unable to attend this year’s ASBMB annual meeting but is scheduled to speak at the 2020 meeting. We will profile her next year.)
Growing up in Russia, Evgeny “Eugene” Serebryany mostly enjoyed humanities-related courses. He developed new interests after he moved to the U.S. as a teenager and faced a language barrier.

At his Massachusetts high school, Serebryany began to translate Russian poetry, which he still does, and he started to embrace science.

“Experimental science offered a way to contribute to advancement of knowledge in a very concrete way,” he said.

His path wasn't always easy. “Immigration status has been the biggest roadblock,” he said.

As an international student, he wasn't eligible for federal grants or loans for college, and his family couldn’t afford the tuition. Yale University offered him full financial aid from endowment funds, and he earned a bachelor's degree in molecular biophysics and biochemistry while doing research in the laboratory of Elsa C. Y. Yan.

Federal training grants also cannot fund graduate students who lack permanent U.S. residency. The Massachusetts Institute of Technology granted Serebryany a private fellowship, and he completed his Ph.D. in biochemistry with Jonathan A. King. He is now a postdoctoral fellow in Eugene I. Shakhnovich's research group at Harvard.

Serebryany said he is grateful to both Yale and MIT for the education he received “on their own dime.”

As a postdoc, he petitioned the U.S. government for a green card based on exceptional scientific ability in the national interest. His request was approved in February 2018, and he gained permanent resident status in time to receive the National Institutes of Health National Research Service Award, which now funds most of his research.

“I couldn't travel abroad. Now I can,” he said. “But beyond the funding and travel restrictions, just the fear of someday not being able to extend my string of temporary statuses … and then having to leave or get deported, made it that much harder to focus on the research.

“The sense of freedom and security that a green card gives, though not complete, is priceless.”

Pingdewinde Sam (psam1@jhu.edu) is a Ph.D. candidate in the department of cellular and molecular physiology at Johns Hopkins University School of Medicine and the founder of Teebo.org.

Disulfide bonds offer new insights into cataracts

Cataracts impair vision by clouding the eye’s lens, mostly in older people. Most proteins in the lens belong to the crystallin family; as we age, the crystallin proteins can start to clump together, causing the lens to scatter light and become less transparent.

Serebryany and his colleagues used biochemical approaches including mass spectrometry and mutational analysis to develop new mechanistic insights into disulfide bond formation and exchange in crystallins, which led them to propose a “redox hot potato” competition model: under physiological conditions, stable gamma-crystallin molecules in the lens continually exchange disulfides. However, if a stable molecule passes the disulfide to a structurally unstable one, the latter becomes trapped in a structure prone to aggregation, which results in light scattering, the hallmark of cataracts.

Cataracts can be addressed in two ways. When prescription eyeglasses become ineffective, patients are left with the option of surgery, which is effective but expensive and not available to everyone. Cataracts remain the world’s leading cause of blindness. The work of Serebryany and his colleagues may pave the way to lower-cost therapeutic treatment.
JBC TABOR AWARD
Researcher honored for work on protein quality control

By Isha Dey

Chemistry and its application in biology have always fascinated Margaret Wangeline. This interest drove her to explore how cells “manage, fix, and destroy misfolded proteins,” she said.

Wangeline grew up in northern California and then moved east for an undergraduate program in the department of chemical engineering at the Massachusetts Institute of Technology. There she studied how cells sense and repair damaged DNA, as well as metabolic responses to stress such as trauma.

Intrigued by the general idea of DNA and hence protein quality control and its implications in the human body, Wangeline headed back to the West Coast to pursue a Ph.D. in Randolph Y. Hampton’s lab in the department of biological sciences at the University of California, San Diego. There, she deduced that the misfolding and degradation of HMG-CoA reductase, or HMGR, the rate-limiting enzyme for cholesterol biosynthesis, is controlled selectively by a compound called geranylgeranyl pyrophosphate, or GGPP, in an allosteric manner (meaning the compound binds to HMGR at a site other than its catalytically active site). She and Hampton termed this allosteric misfolding “mallostery.” Their findings were published in the Journal of Biological Chemistry.

Besides troubleshooting experiments and writing manuscripts, Wangeline enjoys teaching, and in 2013 she won a UCSD excellence in teaching award. Her other interests include writing fiction stories, cooking and hiking. She also participates in science outreach activities through the university and elsewhere.

Wangeline plans to continue her research as a postdoc to understand better how protein quality control affects metabolism and how this applies to neurodegenerative diseases in general.

Looking back, she said her biggest lesson as a graduate student was to “not get discouraged from trying new things, and to step out of my comfort zone.”

In Hampton’s lab, Wangeline and colleagues looked at the selectivity of the ERAD pathway to design strategies for controlling protein levels in the system. They discovered that a compound called GGPP selectively interacted with Hmg2, a yeast isozyme for HMGR, and directed Hmg2 for degradation. However, two different structural analogs of GGPP failed to do so.

Using a combination of biochemical methods, the lab deduced that GGPP bound to an allosteric site and caused changes in the folding state of Hmg2 to mark it for ERAD. The effects of GGPP could be reversed by chemical chaperones (analogous to proteins that assist in the correct folding of other proteins).

Margaret Wangeline and her PI Randolph Hampton coined the term “mallostery” for an allosteric misfolding of the rate-limiting enzyme for cholesterol biosynthesis.

Margaret Wangeline

The misfolding that makes “mallostery”

Protein quality control, including the selective degradation of misfolded proteins and getting rid of toxic products, is essential to maintain normal functioning of a cell. In mammalian systems, the most prominent pathway for protein quality control is endoplasmic reticulum-associated degradation, or ERAD.

Physiologically important enzymes often undergo controlled degradation as a feedback mechanism for their function. One such enzyme is the HMG-CoA reductase, or HMGR, the rate-limiting enzyme of the sterol synthesis pathway. On receiving signals to stop sterol production, HMGR is degraded by the ERAD pathway.

In Hampton’s lab, Wangeline and colleagues looked at the selectivity of the ERAD pathway to design strategies for controlling protein levels in the system. They discovered that a compound called GGPP selectively interacted with Hmg2, a yeast isozyme for HMGR, and directed Hmg2 for degradation. However, two different structural analogs of GGPP failed to do so.

Using a combination of biochemical methods, the lab deduced that GGPP bound to an allosteric site and caused changes in the folding state of Hmg2 to mark it for ERAD. The effects of GGPP could be reversed by chemical chaperones (analogous to proteins that assist in the correct folding of other proteins).
Driven by a desire to tackle unanswered questions and learn about “something that has no explanation,” Fernando Damasceno became fascinated by iron signaling and metabolism in the human body. As a graduate student at the Universidade de Sao Paulo, he has taken on a challenging topic: the labile iron pool.

Growing up in southeastern Brazil, Damasceno watched the 1990s science TV show “Beakman’s World” and later learned about atoms and molecules in high school. This was all part of a “process comprised of many small successive events” that motivated him to study chemistry at the Universidade Federal de Goias and then pursue doctoral studies in bioinorganic chemistry, Damasceno said. His college professors, parents and friends all supported his academic journey.

Damasceno enjoys doing research and teaching in Brazil. Although he doesn’t always have access to all the resources he needs for his work, he still likes to tackle important biological questions and collaborate with others in the field.

Experimenting on the labile iron pool, or LIP, is no easy task, Damasceno said, because its composition is not known. His team “could not synthesize (the LIP) to test reaction directly,” he said.

The results were initially confusing because they showed that chelated LIP increased oxidation in their fluorescent assay (details below). Damasceno and his advisor José Carlos Toledo Jr. were both very surprised, he said, and they “spent hours and hours talking and discussing how we could possibly explain that.” The process was “very difficult, but very exciting.”

For his work on the labile iron pool, published in the Journal of Biological Chemistry, Damasceno received a JBC Herb Tabor Young Investigator Award. He said he was surprised but very happy to receive the Tabor award. He will give a talk on his paper at the ASBMB annual meeting in April.

He next hopes to pursue nitric oxide signaling, a related aspect of his work.

Can iron be used to prevent dangerous oxidative species?

Iron in the human body is typically bound to other groups such as heme and iron-sulfur clusters to carry out important reactions. However, a small amount can be bound instead to chelators that neutralize its effect, and this is called the labile iron pool, or LIP.

Researchers initially believed the LIP was harmful because of its lability. Damasceno said his team’s work changes the paradigm; while the LIP is reactive with an important oxidant called peroxynitrite, it could act as an antioxidant against this type of damage. Peroxynitrite has been implicated in many pathologies, but its connection to the LIP was uncertain.

Damasceno and colleagues used a fluorescence spectroscopy assay where oxidation and nitrosylation, downstream effects of reacting with peroxynitrite and harmful additions to proteins, were monitored by fluorescent indicators. They found an increase in oxidation and nitrosylation when the LIP was chelated and a decrease when cells were treated with iron.

This work shows that the LIP, when not complexed with chelators, prevents oxidative damage by competing with peroxynitrite, a finding that could prove beneficial for the treatment of peroxynitrite-associated pathologies, including stroke, chronic heart failure, diabetes, cancer and neurodegenerative disorders.
Caroline Soliman discovered her love for lab work as an undergraduate studying biomedical science at Monash University in Melbourne, Australia. She thrived on doing hands-on work to answer the question “What’s my goal, and how am I going to get there?”

Now a graduate student at the Royal Melbourne Institute of Technology, or RMIT, Soliman won a 2019 Journal of Biological Chemistry/Herbert Tabor Young Investigator Award for her work on the structural characterization of antibody candidates that recognize carbohydrates for immunotherapy for infection.

Soliman earned an honors degree at Monash University through the Burnet Institute. For her thesis, she worked with Paul Ramsland, now her dissertation mentor, to develop a peptide-based inhibitor to mimic the binding of a microbial protein to immunoglobulin A. The project sparked an interest in crystallography.

“I gained an appreciation for the importance of structure in terms of function,” she said.

After a short break from research, Soliman returned to Ramsland’s lab for her doctoral training at RMIT. Together, they crafted a project with translational benefits and an international collaboration with Gerald Pier of Harvard Medical School that would give Soliman the chance to develop her crystallography skills.

“My supervisor has been very supportive and encouraging,” she said, adding that Ramsland helped her navigate the roadblocks of learning crystallography, teaching her how to collect data from the Australian Synchrotron and walking her through the process of solving a crystal structure.

When not solving crystal structures, Soliman can be found in the kitchen baking cakes, tarts and other sweet treats. She also enjoys reading, swimming at the beach and spending time with her family in Melbourne.

After completing her Ph.D., Soliman hopes to pursue a career in research and to teach immunology.

“It’s really important to do something you enjoy,” she said.

The findings of Caroline Soliman’s team are crucial for understanding the function of carbohydrate-binding human antibodies as potential microbial therapeutics.

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The findings of Caroline Soliman’s team are crucial for understanding the function of carbohydrate-binding human antibodies as potential microbial therapeutics.
Genetic rearrangements, duplications and fusions have occurred throughout the evolution of life on Earth. In an ancient single-celled ancestor to modern animals, a fusion occurred between two enzymes responsible for adding amino acids to growing protein chains.

Sandeep Eswarappa has devised mathematical models to explain what drove this fusion event.

Growing up in Kadur, a small town in India, Eswarappa became interested in research while observing experiments in his father’s high school science laboratory. After earning an M.B.B.S. degree (equivalent to an American M.D.), he pursued a Ph.D. at the Indian Institute of Science, or IISc, studying host-pathogen interactions in Salmonella.

“During this time I was exposed to the vibrant intellectual environment of IISc and developed interests in theoretical biology, evolutionary biology and genomics,” he said.

After earning his Ph.D., Eswarappa moved to the Cleveland Clinic Lerner Research Institute for postdoctoral work in the laboratory of Paul Fox. While his research focused on the formation and repair of blood vessels in the heart, Eswarappa also was fascinated by the connection between changes in protein production and animal evolution.

Because the earliest unicellular ancestors of modern animals lived about 1 billion years ago, Eswarappa and colleagues needed to develop equations to study them. “The main challenge was to express a purely biological concept in mathematical terms,” he said.

Eswarappa’s models suggest that changes in metabolism provided an evolutionary advantage for the fusion of the two enzymes studied in the Fox lab.

Outside of the lab, Eswarappa keeps his focus on science. He enjoys watching Carl Sagan or David Attenborough documentaries and reading books by Richard Dawkins or Simon Singh.

In 2015, Eswarappa moved back to the IISc to start his own laboratory as an assistant professor; there, he continues to study the regulation of protein production and blood vessel formation.

Protein fusion drives animal evolution

Single-celled ancestors of modern animals lived about 1 billion years ago, when atmospheric oxygen was at less than 1 percent of modern levels. The lack of oxygen slowed the reactions that produce the amino acid proline and its precursor, glutamic acid, from intermediates in the breakdown of carbon-rich molecules to produce energy.

These organisms began incorporating more proline into their proteins, which later would support multicellularity. This further depleted cellular stores of proline, impairing the ability of ancient organisms to produce proteins.

Sandeep Eswarappa and his colleagues suspected that these changes drove the fusion of two genes responsible for incorporating proline and glutamic acid into proteins. To test this hypothesis, they used a series of equations to model the response of organisms with and without the fusion to changes in the supply and demand of proline. Organisms with fused genes responded much better, likely because the fusion connected proline usage to the supplies of molecules needed to produce it.

For the paper reporting this research, Eswarappa received a 2019 Journal of Biological Chemistry/Herbert Tabor Young Investigator Award.

“Our work provides compelling evidence for the close evolutionary relationship between two fundamental processes of life — protein synthesis and the central carbon metabolism,” Eswarappa said.

In the future, the group plans to look for other genetic fusion events that facilitated the evolution of animals.
Early-career researchers to present work from labs of JLR editorial board

The Journal of Lipid Research will showcase work being done in the laboratories of its editorial board members during a symposium on Monday, April 8, at the American Society for Biochemistry and Molecular Biology annual meeting.

George M. Carman, a JLR associate editor based at the Rutgers Center for Lipid Research, explained how the program was designed. “The journal depends on its editorial board members to provide timely, fair and helpful reviews,” he said. “Our board members are also outstanding scientists, and we are using this venue to showcase the current work being conducted by their students and post-doctoral associates.”

The JLR has more editorial board members than can be featured in a single session, so Carman, who organized and will lead the session, and JLR colleagues selected five editorial board members whose laboratories’ work is likely to appeal to the diverse audience that the Experimental Biology meeting attracts.

The JLR early-career investigators

Jacqueline S. Dron of Robert Hegele’s laboratory at the Robarts Research Institute at the University of Western Ontario will give a talk titled “Complex genetic determinants of plasma lipoproteins.” (see page 26)

John Melchior of Sean Davidson’s laboratory at the University of Cincinnati will give a talk titled “The structure of apoA-II on HDL reveals novel insights into its regulation of lipoprotein composition and function.” (see page 27)

Igor Shmarakov of William S. Blaner’s laboratory at Columbia University will give a talk titled “Retinol-binding protein 4 (RBP4) in adipocytes and obesity.” (see page 29)

Daniel Pike of David Ford’s laboratory at the Saint Louis University Health Science Center will give a talk titled “Chlorolipids: mediators and outcome predictors of sepsis.” (see page 30)

Vishal Kothari of Karin Bornfeldt’s laboratory at the University of Washington will give a talk titled “Small HDL, diabetes and proinflammatory effects in macrophages.” (see page 28)
Jacqueline Dron takes her research to heart — literally. When she’s not at the bench, you might find her playing flag football with friends, a hobby of hers for over eight years now.

“Physical sports are part of a healthy lifestyle,” she said. “In a lipids lab, healthy living is always encouraged.”

Dron, a graduate student at Western University in Ontario, Canada, was selected by the Journal of Lipid Research to speak in a special session featuring up-and-coming researchers at the American Society for Biochemistry and Molecular Biology annual meeting. She will highlight her research on human genetic variants that influence plasma lipid and lipoprotein levels.

Dron has wanted to be a researcher for as long as she can remember. She thinks it’s the desire to make discoveries that made research so appealing. “From there, it evolved into wanting to make discoveries that could one day be used to help others,” she said. “That is probably why I was drawn towards human genetics.”

Since starting graduate school in Robert Hegele’s lab in 2015, Dron has analyzed over 1,000 DNA samples from patients that have abnormal levels of cholesterol or triglycerides. Her goal was to identify what genetic factors were involved in influencing these lipid phenotypes.

Unsurprisingly, the answer was not simple. Many phenotypes are influenced by multiple genetic factors, making the analysis complex. Nonetheless, Dron has been able to identify several key genetic variants that influence cholesterol and triglyceride levels in humans.

Dron is still actively analyzing new genetic variants and isn’t daunted by the complexity. “I like being challenged and having a change of pace,” she says. “Almost everything (in research) is a challenge, and the pace is always changing.”

Courtney Chandler (cochandl@umaryland.edu) is a graduate student at the University of Maryland, Baltimore. Follow her on Twitter @CourtneyEChan.

Genetic influences on lipid levels

Elevated levels of cholesterol and triglyceride lipids are risk factors for diseases such as stroke and heart attack, and Jacqueline Dron has a simple research question — what genetic variants cause these abnormal lipid levels?

To find the answer, Dron has studied over 1,000 DNA samples from patients with abnormal lipid levels to identify correlated genetic variants.

It turns out her straightforward question has a complicated answer. Her research shows that most patients have polygenic susceptibility, meaning they are simultaneously influenced by multiple genetic variations. This means that there generally isn’t any one gene that causes the abnormality. Instead, it’s the sum total of many genetic variants.

Despite this additional layer of complication, Dron has been able to identify genetic variants that influence extremely high plasma levels of the “good” HDL cholesterol as well as extremely high levels of triglycerides. She also has described how structural changes in several key genes are correlated with extremely low HDL cholesterol levels in some patients.

Her work has improved our understanding of the underlying genetic causes of variable plasma lipid levels. She has published two papers in the JLR, one in 2017 and one in 2018, related to this work.
JLR EARLY-CAREER RESEARCHER

Lipoprotein researcher to talk about structure studies

By Courtney Chandler

For John Melchior, the thrill of research comes from standing on the precipice of the unknown.

“There is nothing quite like the feeling of striking gold and getting a new piece of critical data,” he said. “At that very moment, you’re likely the only person in the entire world that knows that biology.”

Melchior researches the structural complexity of high density lipoproteins, or HDL, as a postdoctoral fellow in Sean Davidson’s lab at the University of Cincinnati. Based on his work, he was selected by the Journal of Lipid Research to speak in a special session highlighting up-and-coming researchers at the American Society for Biochemistry and Molecular Biology annual meeting.

Melchior said he “fell in love with lipoproteins” during his graduate studies at Wake Forest University, where he was trained in lipid biochemistry. He has continued to study lipoproteins, this time from the protein side. He refined a technique to separate HDL particles based on whether they contain a protein called apoA-II and determined that apoA-II is critical for the positive effects of HDL.

“I found this extremely exciting,” he said. “The logical next steps were to understand the role of apoA-II’s structure in modulating this function.”

His initial attempts to understand the structure of apoA-II were halted when Nature News reported that a previously published crystal structure of the protein was falsified. But Melchior sees what he called an “unfortunate setback” as an opportunity for his structural studies to help fill the gaps of what remains unknown about apoA-II.

Melchior hopes his work will benefit the HDL research community as a whole; for him, this community is almost as important as the research itself.

“I’ve been fortunate to establish relationships with some amazing people who also happen to be excellent scientists,” he said. “I’m really grateful for the community and the friendships that have enriched my life.”

John Melchior refined a technique to separate high-density lipoprotein particles based on the presence of certain proteins.

Dissecting the structure of HDL

High density lipoproteins, or HDL, are known as the “good” cholesterol and are thought to decrease risk of heart disease as well as chronic inflammatory diseases. Though commonly thought of as a single number on a patient’s medical chart, HDL is incredibly complex.

The focus of John Melchior’s research is this complexity. He is developing new ways of physically separating subspecies of HDL. Despite their physical similarity, Melchior has been able to isolate very specific subspecies and has found that particles that contain a protein called apoA-II are better at removing cholesterol from cells compared to particles that lack apoA-II. This ability to remove “bad” cholesterol, called the cholesterol efflux property, has been linked to protection against heart disease in several clinical studies.

Melchior’s work could have a direct impact on medical care in addition to contributing to the field of lipid research. The information he gains from understanding the structures of different HDL particles could be used to develop clinical assays that may better identify patients that are at higher risk for heart disease.
JLR EARLY-CAREER RESEARCHER

Type 1 diabetes work gets special recognition

By Isha Dey

For the love of science and a drive to understand disease, Vishal Kothari crossed continents and switched his career path from industry to academia.

Kothari grew up in India, where he completed a bachelor’s degree in pharmacy and a master’s degree in pharmacology. He then worked as a research scientist at Advinus Therapeutics Limited (now Eurofins Advinus), playing an important role in identifying drugs with improved efficacy for treating diabetes and cardiovascular diseases. This work provided him with much-needed experience, but given the global reach of diabetes and diabetes-associated cardiovascular diseases, Kothari wanted to investigate cardiovascular diseases at the molecular level as a way to pursue better prevention strategies.

“Research in the industry is market-driven, but I wanted to do independent research,” he said.

This passion for scientific research spurred his move from his industry position in India to a Ph.D. program in nutritional sciences at Auburn University in Alabama, where his studies centered on mouse models of diet-induced insulin resistance and insulin signaling.

Since earning his Ph.D., Kothari has worked as a senior research fellow in Karin Bornfeldt’s lab at the University of Washington School of Medicine. His work focuses on the effects of changes in the function and composition of high-density lipoproteins in diabetes-associated risk of cardiovascular diseases such as heart attacks.

In addition to research, Kothari also mentors medical and undergraduate students, which he believes will help him to become an independent researcher. When not in the lab, he likes to travel and hang out with friends.

According to Bornfeldt, Kothari is notable for his “enthusiasm for research, his vision and dedication, his excellence in the lab and his team spirit.”

Addressing small HDLs in heart disease

Cardiovascular disease, or CVD, is the most common cause of death around the world. Factors such as hypertension, diabetes or hyperlipidemia increase the risk of heart disorders. According to the American Heart Association, at least 68 percent of people aged 65 or older with diabetes die from some form of heart disease, and 16 percent die of stroke.

High-density lipoprotein, or HDL, is associated with protection against CVD, perhaps in part by reducing inflammatory activation of macrophages, a key cell type in CVD. However, small populations of HDL also can cause cholesterol depletion and produce an inflammatory response by macrophages under certain conditions.

Vishal Kothari’s research is focused on understanding how small HDLs induce such effects and how Type 1 diabetes mellitus, or T1DM, contributes to this effect, since T1DM increases the risk of CVD including heart attacks. His study has shown that depleting cholesterol by HDL increases proinflammatory responses in macrophages both in vitro and in a transgenic mouse model. His findings further demonstrate that higher levels of small HDL populations, as observed in a mouse model of Type 1 diabetes, can exacerbate inflammatory activation of macrophages and that this process is dependent on a protease called ADAM17.

These findings help provide a better understanding of increased CVD risk in Type 1 diabetes and the possible factors mediating such effects.
JLR EARLY-CAREER RESEARCHER
Biochemist chases the role of retinoids in fat burning
By Gelareh Abulwerdi

When Igor Shmarakov first learned about retinoids, he had no idea his research interest would send him on a journey back and forth across the globe.

Shmarakov was born and raised in Ukraine. While working on his Ph.D. in biochemistry at Chernivtsi National University, he studied the role of retinoids, natural and synthetic derivatives of retinol, or vitamin A, in inhibiting tumor growth in rat models. After earning his degree, he was appointed an associate professor in the university’s department of biochemistry and biotechnology.

In 2008, Shmarakov received a one-year Fulbright scholarship to do a collaborative research study and was matched with William S. Blaner, a professor of nutritional medicine at the Columbia University College of Physicians and Surgeons, thus beginning a fruitful academic relationship.

Shmarakov returned to Ukraine when his fellowship ended, but he was determined to come back to the U.S. to pursue his dream of becoming an independent researcher. He had a lab at Chernivtsi and supervised graduate students, Shmarakov said, “but at the same time, I continued doing collaborative research studies with Dr. Blaner.”

The long-distance partnership was a challenge, but the two published four papers together between 2009 and 2016. In 2016, Shmarakov applied for an associate research scientist position at Columbia, where he now works under Blaner’s mentorship.

“(The) transition from the Ukrainian academic system into the American academic system was the biggest challenge for me,” Shmarakov said. “Dr. Blaner was very supportive. I owe him. … He kept me scientifically active, and that’s how I was able to come back to the U.S.”

The Journal of Lipid Research has invited Shmarakov to talk about his work in the field of metabolic disease at the 2019 American Society for Biochemistry and Molecular Biology annual meeting.

ANNUAL MEETING
Nonalcoholic fatty liver disease is a metabolic disorder caused by accumulation of fat in the liver. Scientists originally thought the sole function of retinol binding protein 4, or RBP4, was to transport retinol to extrahepatic tissues in times of dietary insufficiency. It is now proposed that adipose-derived RBP4 contributes to the pathogenesis of type 2 diabetes, linking type 2 diabetes with obesity and other obesity-related metabolic diseases.

RBP4 is expressed in both white and brown adipose tissue. The latter, called BAT, contains a large number of mitochondrial uncoupling proteins, allowing them to dissipate thermal energy rather than synthesize ATP. Therefore, metabolically active BAT has therapeutic potential in metabolic disorders.

To study the role of adipocyte-derived RBP4 in metabolic disease, Igor Shmarakov uses several transgenic mouse models, including one that overexpresses human RBP4 in both white and brown adipocytes. When fed a high-fat diet, these adi-hRBP4 mice develop nonalcoholic fatty liver disease, obesity and insulin resistance more readily than matched wild-type mice.

Shmarakov’s recent work explores the biochemical cause of this higher weight gain in the adi-hRBP4 mice. The further increase in RBP4 expression in the adi-hRBP4 mice involves a decrease in mitochondrial numbers. Shmarakov proposes that this accounts partially for the excessive weight gain in the adi-hRBP4 mice.

Role of RBP4 in metabolic disorders

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Study of chlorinated lipids could lead to better sepsis treatment

By Adriana Bankston

After a young friend died of cancer, Daniel Pike’s interest in science developed into a path focused on both treating disease and studying it. “Before he died, he talked about how he wanted his doctors to do whatever they wanted to, because what they learned would help the kids that came after him,” Pike said. “That really resonated with me and ultimately inspired me to pursue a career in biomedical research.”

As an undergraduate at Saint Louis University, Pike enjoyed biology and chemistry, he said, “with an emphasis on applications in medicine.” After earning a bachelor’s degree in biochemistry, he applied to M.D./Ph.D. programs and began his studies at the SLU School of Medicine. He spent two years in medical school and then started working in David Ford’s lab in the department of biochemistry and molecular biology.

Pike was attracted by Ford’s “good track record as a mentor, the focus on lipids and the translational aspect of the research that could be applied to a health problem.” His goal is to work in an academic hospital integrating medicine and research. “Daniel is a bright, hard-working student,” Ford said, “and his basic science research efforts in the field of sepsis and lipid biochemistry may lead to better treatments for this ever-growing public health problem.”

One initial sticking point for Pike was working with animals, in particular with rats. “I was never particularly nervous around handling them or anything,” he said. “It was more the practical aspects … I had never worked with animals before, so I had to learn a bunch of new techniques and figure out how to get them to work in our model.”

Outside of the lab, Pike enjoys cycling and playing trumpet in the pep band for the SLU basketball team. “This is actually my ninth year doing it,” he said, “so I’ve sort of become an old vet of the trumpet section.”

A major goal of the Ford lab is to understand the dynamics between bioactive lipids and sepsis. Chlorinated lipids, a species of bioactive lipids discovered by the lab, are produced through white blood cell activation. The lab published a study in the Journal of Clinical Investigation Insight demonstrating the involvement of chlorinated lipids in sepsis. Chlorinated lipids measured in plasma samples taken from sepsis patients on the day of admission to the ICU predicted mortality 30 days out. They found that mortality was largely due to lung failure in these patients.

Additionally, chlorinated lipids can cause a pro-inflammatory change in endothelial cells. The endothelial cells display an increase in permeability, an increase in the surface expression of adherence molecules, such as P-selectin, and an increase in the release of von Willebrand factor and angiopoietin-2, both of which are involved in the endothelial inflammatory response.

Expanding upon these results, Pike is using a rat model of sepsis in the lab to better understand the role of chlorinated lipids in predicting and mediating the severity of sepsis.
The editorial leadership team of the journal Molecular & Cellular Proteomics has chosen four early-career investigators to present their current research during a symposium on Monday, April 8, at the American Society for Biochemistry and Molecular Biology annual meeting.

Al Burlingame, MCP editor and chair of the session, said of the four, “They represent the breadth of biomedical and basic biological research challenges that are being tackled currently by mass spectrometry-based proteomics. They also represent research programs at the forefront of proteomics that develop new methodologies to address and solve particular unmet needs in discovery of protein-level molecular assembly and function in both Europe and the United States. Two were trained in the US and two in Europe.”

Jennifer Abelin, a group leader at the biotech company Neon Therapeutics, is supporting research of how genetic mutations, a hallmark of cancer, can result in specific immune targets called neoantigens, and how neoantigens can be used to develop cancer immunotherapies. (see page 32)

Jana Zecha, a graduate student in Bernhard Küster’s lab at the Technical University of Munich, has developed a methodology for studying turnover of proteins in cells at a proteome-wide scale. (see page 33)

Fan Liu, a new faculty member at the Leibniz-Forschungsinstut für Molekulare Pharmakologie in Berlin, has studied the architecture of protein super-complexes in heart mitochondria using distance constraints obtained from chemical cross-linking and mass spectrometry. (see page 34)

Samuel Myers, a postdoctoral researcher in Steve Carr’s group at the Broad Institute, has developed a powerful alternative to ChIP that employs a new CRISPR-localized proximity labeling method to capture and identify protein complexes at specific genetic loci. (see page 35)
From art to proteomics: a path to science

By Elizabeth Stivison

Jenn Abelin is now a group leader at Neon Therapeutics working toward developing personalized cancer vaccines, but growing up in Connecticut, she didn’t want to do science at all. She wanted to do art.

“In high school,” she said, “most of the classes I took were writing, reading, art and math.”

Looking back on these choices, she sees an emerging interest in recognizing patterns. But she got her initial push toward science from her grandmother, who encouraged her to study something more practical than art. She picked a random class at Guilford College about ancient medicine; that set off a chain of events and introduced her to many role models and mentors in science who encouraged her. She took organic chemistry taught by her undergraduate advisor Anne Glenn and loved the idea that just memorizing facts and spitting them back out wasn’t going to cut it. She saw there was real creative thinking and problem solving in science.

Before she knew it, she was majoring in biology and chemistry and doing proteomics research. She went on to pursue her Ph.D. at the University of Virginia mentored by Donald Hunt and Jeffrey Shabanowitz, studying cancer with mass spectrometry-based proteomics. As a postdoctoral researcher at the Broad Institute, she was mentored by Steven Carr, Nir Hacohen and Catherine Wu.

Now as a leader of a research lab doing groundbreaking work, Abelin says the best part of her job is getting to work on basic science that directly impacts people’s lives for the better.

Outside the lab, she believes it’s important to share her path. She wants young people to know that to be a successful and happy scientist, you don’t have to start as a genius baby doing calculus in your high chair. When she was a kid, she was “likely eating dirt,” she said, and doing other average kid stuff.

“I hope to be able to do mentoring in the future,” she said. “I’ve had the most amazing mentors during my career, and I hope to continue that.”

Abelin is one of four young investigators chosen by the editorial team of the journal Molecular & Cellular Proteomics to present their research at the ASBMB annual meeting.

**Using mass spectrometry to develop personalized cancer immunotherapies**

Jenn Abelin’s work focuses on generating data that helps predict peptide antigens presented by cancer cells, with the goal of creating personalized immunotherapies to help patients’ immune systems fight their cancers.

To do this, researchers must understand how cells’ human leukocyte antigen, or HLA, complexes present antigens from inside the cell. The HLA complex presents to the immune system peptides from many proteins within cells. If those presented are self-peptides, the immune system does not react. However, if the peptides are from something non-self, like a virus, the immune system attacks the cell. Personalized cancer vaccines work by training the immune system to attack the cells presenting peptides that are unique to cancer. For this to work, however, we must know what these peptides are.

Humans have six HLA proteins that function in different combinations in each of us, and each of these combinations favors different peptides. Using high-throughput mass spectroscopy, Abelin’s group has generated data to help decode a set of rules for how HLAs present peptides. With these data, Neon Therapeutics can predict with high accuracy what neoantigens may be presented by tumor cells and can be used as targets for personalized immunotherapy.
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MCP EARLY-CAREER INVESTIGATOR

Seeking new techniques to track protein breakdown

By Alyson Smith

Cells are protein factories, constantly making new proteins and breaking down damaged or unnecessary ones. Cells must regulate these processes tightly for thousands of proteins to support cellular function, and Jana Zecha has developed a new technique to monitor this protein turnover.

During her early biology courses in Burghausen, a small town in Bavaria, Zecha became curious about how single molecules work together to produce a functioning organism. She earned a bachelor’s degree at the Technical University of Munich, completing a thesis project on gene expression in gestational diabetes. She became interested in technologies that scientists could harness to investigate the molecular bases of disease.

Zecha remained in Munich to work in Bernhard Küster’s group, earning a master’s degree and then beginning her Ph.D. research, studying how protein modifications determine their breakdown rates at a cell-wide level. Her project built on earlier work in the Küster lab that suggested established methods had difficulty tracking modified proteins. “Using the classical approaches for the measurement of cellular protein turnover,” Zecha said, “many important aspects of cell biology have so far been overlooked or remained ‘invisible.’”

After developing new techniques and data analysis approaches, she could track breakdown and production of thousands of modified proteins over time. Her work has laid the foundation for future investigations into how protein modifications can affect their stability.

Zecha enjoys teaching young scientists. She has mentored undergraduate researchers in the Küster lab and has taught courses in Munich and Taiwan. “Although teaching is, of course, always lots of work,” she said, “for me it is also great fun and a pleasure to pass on my enthusiasm for science and guide and help students to recognize and develop their potential.”

Zecha is in the final stage of her Ph.D. thesis work in Bernhard Küster’s lab.

Tagging and tracking modified proteins

Multiple versions of the same protein can arise from a single gene, either through alternative splicing of messenger RNA or through chemical modifications of the final protein product. These modifications can change the protein’s life span, affecting how long it can carry out its function.

Jana Zecha and her colleagues developed a strategy to measure the life spans of thousands of proteins simultaneously. They fed cells amino acids made with heavier carbon and nitrogen isotopes. As the cells digested old proteins and produced new ones, more and more proteins incorporated heavy amino acids. They combined this system with a tagging method to track protein replacement over time.

The protein lives they measured spanned several orders of magnitude; some were broken down and replaced in minutes, while others lasted weeks. Because their data set captured thousands of proteins, the researchers could detect relationships between protein life span and protein abundance, chemical composition and cellular location. They also detected new relationships between modifications and life span.

“Our study has broad implications for basic as well as pharmaceutical research, since many neurodegenerative, age-related and cancer diseases are associated with altered protein life spans,” Zecha said.

The researchers plan to leverage their new tools to connect protein life span with cancer drug efficacy and side effects.
MCP EARLY-CAREER INVESTIGATOR

Using cross-linking to analyze protein interactions in mitochondria

By Courtney Chandler

Any introductory biochemistry student learns about mitochondrial proteins. We take it for granted that these protein assemblies must coexist in a super-complex. However, actually studying protein interactions in organelles remains challenging.

Fan Liu, a postdoctoral fellow in Albert Heck’s lab at the Leibniz-Forschungsinstitut für Molekulare Pharmakologie in Berlin, is making this picture clearer by using cross-linking mass spectrometry to describe the interactome of intact mitochondria. Based on her work, she will be featured in a special session highlighting up-and-coming researchers hosted by the journal Molecular & Cellular Proteomics at the American Society for Biochemistry and Molecular Biology annual meeting.

Liu isn’t afraid of challenges. When she began as a postdoc, she learned computer programming and then developed a novel algorithm for analyzing mass spectrometry cross-link data. She then applied the cross-linking approach to mitochondria to understand the organization and arrangement of protein complexes.

“I like the challenges of tackling technical difficulties,” she said. “It’s fascinating to think about how thousands of proteins are organized to large macromolecular assemblies.”

For Liu, this project is just the beginning. She thinks the next logical step is to use quantitative cross-linking mass spectrometry to understand how the mitochondrial interactome changes in different biological conditions. She also said this approach could be applied to other cellular organelles to describe their distinct interactomes.

This novelty and creativity are the reasons she finds research exciting.

“I like the freedom of thinking about interesting scientific questions,” she said. “I also enjoy inspiring discussion with colleagues and friends.”

Though she is dedicated to developing better analysis software and analytical procedures, Liu recognizes the importance of balance. She enjoys outdoor activities in her spare time.

“’I like climbing in summer and skiing in winter,” she says. “It’s a good complement to sitting in front of the computer all day.”

Fan Liu is shown. Liu believes her cross-linking approach to analyzing mitochondria could be applied to describe the interactomes of other cellular organelles.

Probing the proteins in mitochondria

Mitochondria are responsible for an immense number of cellular functions. However, the protein-level structural basis for most of these processes is not well understood.

To address this, Fan Liu and colleagues used cross-linking mass spectrometry on intact mitochondria to probe the protein interactome. Their work was published in MCP in February 2018.

Their approach captures native protein contacts using a small cross-linker molecule. They can then localize the cross-links using mass spectrometry. Using intact mitochondria, Liu used this approach to identify the sub-mitochondrial localizations of protein assemblies.

The team identified four proteins that previously were unknown to be associated with the mitochondria, thus enriching the database about mitochondrial proteins and function.

Their studies also confirmed that the proteins involved in oxidative phosphorylation, which is probably the best-known function of the mitochondria, do interact. Their analyses suggest that all five of the oxidative phosphorylation complexes coexist in close proximity in intact mitochondria. Complexes CI, CII, and CIV also were confirmed to interact in a super-complex.

Liu’s work provides the first detailed analysis of protein interactions in intact heart mitochondria and paves the way for similar studies in other organelles.
Growing up as an aspiring artist, Sam Myers became interested in science later in life. When he took a human biology class at his junior college, it blew him away.

Myers majored in biochemistry with an emphasis in chemistry at California Polytechnic State University and then did graduate work at the University of California, San Francisco, where he studied O-GlcNAc signaling in pluripotent stem cells in Al Burlingame’s lab. He did his postdoctoral research in Steven Carr’s proteomics laboratory at the Broad Institute in Cambridge, Massachusetts, where he is now a research scientist.

Myers knew he wanted to “bridge biology and technology development,” he said, especially as “science moves toward requiring more interdisciplinary approaches to research.”

He has developed a unique skill set to bridge this gap in the field of proteomics, an area of research with great potential for discovery, he said. “Many people work at the genomics level measuring RNA levels, but proteins and proteomes haven’t been studied nearly as much.”

Many sample types do not have enough material for proteomic analyses, so Myers has reduced the sample requirements needed to study the proteome, enabling researchers to answer new biological questions by looking at proteins at a single locus in the genome.

“This has been needed for a long time,” he said, and he just “had the perfect alignment” of scientific expertise in Cambridge. He was able to draw on the skills of Alice Ting (APEX2), Feng Zhang (Cas9) and Carr (quantitative proteomics) to perform this work.

In addition to doing research, Myers enjoys being part of outreach programs that get children interested in science, technology, engineering and math. He is able to connect with youngsters in part, he said, because “I don’t look like a typical scientist.”

When children see scientists who look like they could be artists or in a motorcycle gang, it makes the profession more accessible to more types of people, he said, and diversity is paramount for scientific progress.

Adriana Bankston (abankston81@gmail.com) is a former bench scientist with a passion for improving training and policies for junior scientists. She is a policy activist with the Future of Research. Follow her on Twitter @AdrianaBankston.
Take advantage of EB Career Central

The career center at the Experimental Biology meeting in Orlando is going to have a lot to offer early- and mid-career attendees. Here’s what you can expect.

One-on-one sessions with experts
The five EB host societies have enlisted dozens of academic and industry professionals to work with meeting attendees on their CVs, cover letters, poster presentations, interviewing and career planning. The ASBMB’s careers blogger, Donna Kridelbaugh, will be one of the experts. If you’re interested in getting one-on-one coaching from one of the experts, you must sign up for an appointment at bit.ly/MentorMeEB2019CC. We expect the slots to fill up quickly, so don’t delay. The organizers report that the number of attendees taking advantage of the counseling sessions has grown by 25 percent in the past two years. More than 200 attendees used the service at EB 2018.

Micro-learning hubs
You’ll learn a lot from the short talks presented in the EB Career Central micro-learning hubs. Each speaker will present for 10 minutes and then answer follow-up questions. The talks will cover a variety of career-development topics, such as networking, outreach and science communication. Stop by if you have a few minutes to kill between sessions.

Graduate program booths
Recruiters from master’s and doctoral programs across the country will be on hand to talk to prospective students. If you’re thinking about pursuing an advanced degree, we recommend chewing the fat with the representatives. And, if one or more piques your interest, we recommend talking to students already enrolled in the programs.

Sessions and workshops
A schedule of selected events related to professional development is below. Note: This is not a full schedule; some workshops are more discipline-specific than others, so we didn’t include them. Also, we’ve listed only the titles, times and locations, but you can read the full schedule and full descriptions at www.experimentalbiology.org.

Saturday, April 6

Volunteering for Professional Associations & Societies: What It’s Like & What It Takes
8:30 to 10 a.m. | Convention Center, W208BC

Buckle Up! It’s a Jungle Out There: Navigating the Career Highs and Lows
10:30 a.m. to noon | Convention Center, W208BC

ASBMB Annual Meeting Orientation for Undergraduate Students
11:30 a.m. to noon | Convention Center, W306AB

A Role for Professional Societies in Addressing and Preventing Sexual Harassment in the Sciences
1 to 3 p.m. | Convention Center, W309AB

Career-Development Workshop for Grads and Postdocs: Networking Skills
1:15 to 2:45 p.m. | Convention Center, W305A

Career-Development Workshop for Grads and Postdocs: Constructing Your Elevator Pitch
1:15 to 2:45 p.m. | Convention Center, W307D

Balancing Content, Critical Thinking and Creativity in Graduate Education
2 to 4 p.m. | Convention Center, W206C

ASBMB Undergraduate Workshop: Exploring Careers Speed Networking
4:45 to 5:45 p.m. | Convention Center, W306AB
Sunday, April 7

Career Planning: No Scientist Left Behind
7 to 8 a.m. | Convention Center, W311C

Marketing Yourself for a Successful Career
7 to 8 a.m. | Convention Center, W311B

Publications 101 Workshop
8:30 to 10 a.m. | Convention Center, W309AB

Using Large Sets of Data with Students
10 a.m. to noon | Convention Center, W306AB

ASBMB Advocacy Town Hall Meeting
12:15 to 1:45 p.m. | Convention Center, W307CD

ASBMB Meet the Speakers
12:30 to 1:30 p.m. | Convention Center, Exhibit Hall floor

3 to 5 p.m. | Convention Center, W206B

Organizing a Successful ASBMB Student Chapter
5:30 to 6:30 p.m. | Convention Center, W306AB

Alternative Funding: Driving Philanthropic Support for Basic Science
5:30 to 7 p.m. | Convention Center, W205A

CREST Conversations, Connecting Researchers, Educators and Students
5:30 to 7 p.m. | Rosen Centre, Grand Ballroom B

Storytelling and the Art of Giving a Great Presentation
5:30 to 7 p.m. | Convention Center, W207B

Difficult Conversations at All Levels
5:30 to 7 p.m. | Convention Center, W306AB

Transforming Science Research into Science Outreach
5:30 to 7 p.m. | Convention Center, W307CD

A Word of Advice: Success in Scientific Publishing
5:30 to 7 p.m. | Convention Center, W303ABC

ASBMB Student Flash Talk Science Communication Competition & Reception
7 to 8:30 p.m. | Rosen Centre, Grand Ballroom C

Monday, April 8

Career Planning: No Scientist Left Behind
7 to 8 a.m. | Convention Center, W311C

Marketing Yourself for a Successful Career II
7 to 8 a.m. | Convention Center, W311B

Transitions at the Mid-Career Point
9:30 to 11:30 a.m. | Convention Center, W306AB

The Need for Scientists in Regulation and Policy: Academia, Government, and Industry
2 to 3:30 p.m. | Convention Center, W206C

Ask a NIH Program Officer Workshop: Tips for New and Early Stage Investigators to Improve Funding Success
2 to 5 p.m. | Convention Center, W105B

Surviving an Existential Threat: Creating a Niche for Basic Science Educators
4 to 5:30 p.m. | Convention Center, W206C

Tuesday, April 9

Career Planning: No Scientist Left Behind
7 to 8 a.m. | Convention Center, W311C

Marketing Yourself for a Successful Career III
7 to 8 a.m. | Convention Center, W311B

Lunch and Learn — Science, Dollars, and Outcomes: The Critical Pieces of Budgeting You Can’t Work Without
11:45 a.m. to 1:45 p.m. | Convention Center, W101B

Teaching Blitz: Inventive Teaching Practices and Laboratory Activities
2 to 3:30 p.m. | Convention Center, W206C
Micro-learning hubs: ASBMB offerings

Sunday, April 7

Finding Funding Beyond Federal Agencies
Benjamin Corb
ASBMB public affairs director
11 to 11:15 a.m. | EB Career Central

Achieve Grant-Writing Success with the ASBMB IMAGE Workshop
Squire Booker
ASBMB Minority Affairs Committee Pennsylvania State University
11:15 to 11:30 a.m. | EB Career Central

A Word of Advice: Success in Scientific Publishing
Catherine Goodman
Journal of Biological Chemistry scientific editor
11:30 to 11:45 a.m. | EB Career Central

Improve Your Science Communication Skills
Susanna Greer
ASBMB Science Outreach and Communication Committee American Cancer Society
11:45 a.m. to noon | EB Career Central

Monday, April 8

Picture Perfect: How to Present an Image for Scientific Publication
Kaoru Sakabe
ASBMB data integrity manager
9 to 9:30 a.m. | EB Career Central

All About the ASBMB
Gerald Hart
ASBMB president associate editor, Molecular & Cellular Proteomics and the Journal of Biological Chemistry University of Georgia
12:30 to 1 p.m. | EB Career Central

How to Get Started with Science Writing and Build a Portfolio
Laurel Oldach
ASBMB science writer
3 to 3:30 p.m. | EB Career Central

How to Develop a Comprehensive Job-Search Strategy: Part 1
Donna Kridelbaugh
ASBMB careers blogger
3:30 to 4 p.m. | EB Career Central

Tuesday, April 9

How to Develop a Comprehensive Job-Search Strategy: Part 2
Donna Kridelbaugh
ASBMB careers blogger
9 to 9:30 a.m. | EB Career Central

Don’t miss these ASBMB talks at EB Career Central
NEW JERSEY MEDICAL SCHOOL

Director, Public Health Research Institute

Rutgers New Jersey Medical School (NJMS) invites applicants for the position of Director of the Public Health Research Institute (PHRI) center. We are seeking an individual with outstanding leadership qualities and a record of accomplishment as a well-funded biomedical researcher to direct a major biomedical research center at NJMS.

Over 120 scientists at PHRI pursue infectious disease research, focusing on HIV and other viruses, mycobacteria and other bacterial pathogens, and opportunistic fungi.

The successful candidate should be a leader committed to maintaining PHRI as a global leader in basic and translational science, supported by federally funded research and strategic initiatives in private partnerships.

The center is located on the Rutgers New Jersey Medical School Newark Campus in the International Center for Public Health (ICPH) building, which is home to the NJMS Department of Microbiology, Biochemistry and Molecular Genetics, a National Regional Bioscience Laboratory, BSL2 laboratories and BSL3 small-animal vivarium space, and the Global Tuberculosis Center. PHRI is one of three major centers within the Rutgers Biomedical Health Sciences Institute for Infections and Inflammatory Diseases. Further information about PHRI can be found at: https://phri.njms.rutgers.edu/

Interested individuals must apply online at http://jobs.rutgers.edu/posting and submit a Curriculum Vitae and letter of inquiry to: Vivian Bellofatto, Ph.D., Professor and Chair (Interim), Department of Microbiology, Biochemistry & Molecular Genetics; Chair, Search Committee for Director, Public Health Research Institute, c/o Michael Pettit, Executive Assistant to the Dean, Rutgers New Jersey Medical School, 185 South Orange Avenue, MSB C-071, Newark, NJ 07103-1749; E-mail: Pettitt@njms.rutgers.edu

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Meet Phyllis Hanson

JBC associate editor assumes chair of biological chemistry at Michigan med school

By John Arnst

When our cells come into contact with pathogens, particulates and phagocytosed material, they tend to come out of it the worse for wear, often gaining nanometer-size holes. Were it not for the mysterious work of filamentous ESCRT proteins, these holes might soon spell rupture and death.

These proteins — which drive various membrane remodeling events such as fission reactions that release intralumenal vesicles into endosomes and viruses from the cell surface — are one of Phyllis Hanson’s many research interests.

Hanson earned a bachelor’s degree in biophysics and biochemistry from Yale University in 1985 followed by both an M.D. and a Ph.D. in cancer biology at Stanford University in 1993. She returned to Yale for a postdoctoral fellowship in membrane trafficking before joining Washington University in St. Louis as an assistant professor in 1997.

After two decades researching protein–protein and protein–membrane interactions involved in membrane trafficking at WUSTL, Hanson recently moved her lab to the University of Michigan Medical School’s department of biochemistry — which she now chairs.

Hanson joined the ranks of associate editors at the Journal of Biological Chemistry in November 2017. She spoke with John Arnst, ASBMB Today’s science writer, about her work. The interview has been edited for clarity and length.

What is your group focused on?

My long-term overall interest is in the cell biology of molecular machines, with a particular interest in understanding how proteins regulate the structure and organization of membranes, both inside and outside the cell.

Much of our current work is focused on a set of proteins known as the ESCRT machinery — in particular, the part of that machinery that’s called ESCRT-3. (Author’s note: ESCRT stands for endosomal sorting complexes required for transport.) We’re looking at their role in an increasingly huge range of cell biological processes, and we’re particularly excited right now about a recent discovery that the ESCRT machinery responds to and facilitates the repair of super-small-scale damage in membranes that can be caused by any number of insults from the environment. A big question that we’re trying to address is how the ESCRTs deal with these nano-size disruptions.

What was your academic background and training?

My focus has always been on understanding biochemical mechanisms, but I’ve consistently been drawn to complex puzzles for which there often isn’t a clear road map, and observations from the realm of cell biology have been key for guiding my work. When I did the research part...
of my M.D./Ph.D., I was working on understanding how the protein CaM kinase II potentiates calcium signaling and, through its autophosphorylation, provides cells and especially neuronal synapses with an important “molecular memory.”

As a postdoc, I wanted to learn more about the nuts and bolts of synapses and moved to study the biochemistry of proteins responsible for synaptic vesicle trafficking. These include SNAREs, which mediate vesicle function, and NSF, a AAA+ ATPase that maintains protein dynamics of the SNAREs, and thus membrane trafficking. Author’s note: SNARE stands for soluble NSF attachment protein receptors, and NSF stands for N-ethylmaleimide sensitive fusion protein.)

When I started my own lab, I continued to work with these but also was drawn to less well-charted problems. I used a set of enzymes, AAA+ ATPases, as my group’s entry point, because I knew how to study them and could see that key members, including the ESCRT-regulatory AAA+ ATPase VPS4 and the dystonia-associated AAA+ ATPase torsinA, were regulating cellular membranes in different and unexpected ways.

From there, we’ve taken big advantage of imaging to help understand what the molecular machinery we study can do, which helps define our problems. One important approach for us is the technique of deep-etch electron microscopy pioneered by my Washington University colleague John Heuser. It involves making platinum replicas of biological material to provide unique three-dimensional information about the spatial relationships between proteins and the membranes they act on; it has really helped piece together the biochemical and cellular
puzzles that we're interested in.

Many years ago, I read a review article about membrane fusion, which I was working on at the time, with a title that raised the ever-present question of mimicry and mechanism in model systems. In other words, how well do the things we study in the test tube mimic the complicated processes in the cell? The significance of this question is that we have to understand biochemical mechanisms but also work to validate and extend what we learn into cells. One of the exciting aspects of today’s biochemistry is that there are new ways to do this and clearly much more on the horizon in what I like to call cellular biochemistry.

Did anything occur in a milestone sort of way that made you choose science as a career?

My father was an experimental physicist, a real tinkerer, and so it was probably both nature and nurture, as it were: I’ve always been fascinated with figuring out how things work.

I also was very much drawn to biomedicine, and I had the good fortune to study separately for a Ph.D. and an M.D. at Stanford. I liked both parts of my training, and the different experiences helped me bring into focus what I really wanted to do. My heart was always in driving the research forward, wanting to answer questions beyond the edge of what was really known. The privilege of having trained alongside truly outstanding clinicians at Stanford makes it easier for me to understand how doctors and other people who are on the front lines of solving health-related problems think about and build on advances in fundamental biomedical science.

What factors were important to your decision to move to Michigan?

It was a combination of things, but I think, really, it was the realization that I want to and can make a difference in helping lead a biochemistry department at a medical school. I cannot emphasize enough how important basic research is to medical schools. Part of why I was drawn to this role is that I think I can both advocate for what we’re doing in a biochemistry department and help find connections between what people in biochemistry can do and medical problems that need solving — as a matchmaker of sorts.

There’s also the caliber of science in my own area at Michigan, with a lot of membrane-trafficking research and an incredible diversity of strong cell biology, biochemistry, biophysics and chemistry spread all across the campus. The number of collaborative interactions that are possible is truly mind-blowing.

And I’m thrilled to be in a department with a storied history. JBC Deputy Editor Fred Guengerich trained here, and several of the JBC AEs have been through this department. I also am joining current Michigan AEs Ruma Banerjee, Eric Fearon and Ursula Jakob.

There’s just a huge energy at Michigan right now, and expanding biological chemistry in this environment is going to be fun.

When did you first become involved with JBC, and how is your new role so far?

When I was a Ph.D. student at Stanford, my adviser, Howard Schuman, was really dedicated to the JBC, as were a bunch of AEs who were there and leaders at that time. I sent one of my most important papers on inhibitory autophosphorylation
Researchers in Hanson’s lab made stereoimages like this by taking two photos with a slight angle offset from each other and turning them into anaglyphs, where the two pictures are overlaid in two different colors. When viewers don red-green glasses, those colors are sent separately to their eyes, giving them a 3D view of the structure. The box measures 500 nm by 500 nm.

**What do you do outside the lab? Any advice for balancing life in the lab with life outside of it?**

I like to spend time with my family. I certainly am a big believer in exercise, for its own sake and for its energy-multiplying effect, and I love to cook.

I believe that there is a close correlation between people who love doing lab work and people who love to cook, especially when you get to being a PI and don’t get to do as much lab work as you used to. That’s a big hobby, and I enjoy cooking especially for entertaining. One of my favorites is paella, both because I remember this as my mom’s go-to crowd dish and because it’s this beautiful thing that you can creatively choose different ingredients to match the occasion at hand.

As far as balancing life, you’ve got to have fun with the science. If you aren’t having fun, then it becomes difficult to manage everything, because you are spending a lot of your time with this stuff. You’ve got to believe in what you’re doing.

**Do you have any advice for young scientists?**

You have to find the kind of question, or level of question, that works for you. For some people, the pace of experiments matters a lot, and that is something to keep in mind as you choose the approaches that will allow you to satisfy your curiosity, gain traction in a field and contribute to solving puzzles in cellular biochemistry.

And most importantly — enjoy the ride.

Read more

Find more profiles of Journal of Biological Chemistry associate editors, including Karen Fleming, Ursula Jakob, Christopher Whitfield, Ronald Wek, Joseph Jez and Wolfgang Petri, at asbmb.org/asbmbtoday.
What I wish people understood about writing and editing

By Comfort Dorn

Writing is hard.
No. Wait. Think about it. Is that true?
Writing well is hard.
Make a statement. Investigate it.
Poke and prod it. Render it perhaps less graceful but more honest. That’s writing and editing. (See what I did there?)

Most of us can put some words on paper or a screen with a minimum of difficulty. If pressed, many of us even can make sentences and paragraphs.
But writing in a way that makes your reader think and feel? That’s more of a challenge.

I believe we all are up to the challenge.

Each year, ASBMB Today suggests an essay topic or two. These topics are prompts. Our goal is to tickle your mind and get you writing. We want you to share something about your life as a person living and working in the life sciences. We want to read your stories.

I’m sure you can think of a story.
If I gave you the topic for this essay, “What I wish people understood about ___,” you could fill in that blank with something. If I prodded a bit, you could tell me a story or two about that thing you put in the blank, the thing you wish people understood.

As for me, I have this lurching process that involves coming up with themes and phrases in the shower or when I’m driving, then forgetting them before I can jot them down. Then I sit down in front of the computer at the last possible minute and type out what I’m sure will be the perfect first sentence, but it usually gets deleted before I’m done.

I never took a writing class or a grammar class or an editing class. Everything I know about writing I learned on the street. Or, more precisely, in books and magazines. I’ve always read a lot, and I’ve had the good fortune to be steered toward good writers. This is especially important in childhood. If you have young and impressionable children, steer them toward Maurice Sendak’s “Where the wild things are” and away from the Berenstain Bears. A difficult task, but worth it. Once you get a good writer’s rhythms in your head, it’s easy to dance to them.

Set a timer. (I suggest 20 minutes if you’re new to this.) Don’t try to think of a perfect first sentence. Just start telling your story. Don’t try to get the order right. Don’t check your spelling. Just keep going. When your time is up, stop, save what you’ve written, and walk away. Clear your head. Come back in about a half-hour and read it.

Ask yourself a few questions: Is this the story I want to tell? Does it sound like me? Does it make sense? What else does this make me think of?

Then get back into the chair for another round. This time, do some adding, fiddling and rearranging. Don’t aim for perfection. Aim for truth. And when you can’t stand looking at it anymore, send it to me. I’ve been an editor for a few years now, and I have a pretty good idea
Some rules

Most of you reading this have written scientific papers. I have never written such a paper, but I’ve tried to read a few, and I think the kind of rules that govern those papers can also guide you in writing a news article or a personal essay for ASBMB Today.

Here are a few:

• **Only write what you know is true.** Don’t make things up unless you are writing fiction. (ASBMB Today does not publish fiction, but other magazines do.) That said, you can arrange and prioritize your facts to make them interesting. You need to know what’s important to get your point across. Leave the rest on the cutting-room floor.

• **Be specific.** You don’t need to include every detail, but details bring writing to life. Think about a photograph; not every inch will be in focus, but the important stuff needs to be clear and precise.

• **Defer to others (at least sometimes).** If you are writing about an event, this means talking to other people involved and putting their perspectives into your story. Even if you’re writing an essay, it might mean going to the well of poets and philosophers, just in case they’ve said beautifully the thing you struggle to convey.

• **Think about structure.** You don’t need abstracts and methods, but you do need some kind of a plan. It doesn’t have to be intricate, but at least let the reader know what you’re going to tell them at the beginning and then provide a conclusion at the end. It’s easiest to do this after you’ve done some initial free writing.

• **Use only words you know.** A thesaurus can be a dangerous tool. If it’s not a word you’ve ever said in conversation, please don’t put it in your writing. Your writing should sound like you.

• **Show your mistakes.** You wouldn’t manipulate your results, would you? Writing an essay is not about making yourself look good. It’s not a cover letter. The best stories are about internal struggles. People will trust your writing if they see your humanity.

Russell Baker once said that writing is work, “but it’s the kind of work you enjoy having done.” I encourage you to give it a try. I’m right here to help you do it well.

P.S. Full disclosure — My boss, Angela Hopp, edited this essay. Everyone needs an editor.

Comfort Dorn (cdorn@asbmb.org) is managing editor of ASBMB Today. Follow her on Twitter @cdorn56.

Upcoming ASBMB events and deadlines

**National Kidney Health Month**

5–8: ASBMB-DEUEL Conference on Lipids
8: Hill Day applications deadline
14: Evolution and Core Processes in Gene Expression early registration deadline
28: Hill Day

**National Minority Health Month**

1: Evolution and Core Processes in Gene Expression registration deadline
6–9: 2019 ASBMB Annual Meeting
19: IMAGE application deadline
16: Communication Course applications open
**A change of plan**

How the IMAGE workshop helped me rethink grant writing

*By Carlos Castañeda*

In 2016, I was a second-year assistant professor at Syracuse University planning to submit a grant application to the National Science Foundation's Faculty Early Career Development Program, known as CAREER. I was working on the structure and function of a little-known protein post-translational modification, or PTM. While the work built on my skills from my postdoc, my lab was struggling with getting the amounts of precursor proteins that we needed, and I was concerned that some of the work would be too incremental.

I had heard of the Interactive Mentoring Activities for Grantsmanship Enhancement, or IMAGE, grant-writing workshop from friends and colleagues, who had told me that participants get 20 minutes to present their NSF or National Institutes of Health grant and then receive feedback from experienced colleagues as well as peers. I thought this was my chance to see if I could sell my science and project.

That spring, two weeks before the CAREER submission deadline, I was on my way to Washington, D.C., for the workshop, leaving my home and family for one of the first times since the birth of our son, Luke, in November 2015. Getting off the Metro and walking into the hotel, I wondered if my application was ready for submission. This was going to be my first big federal grant attempt. I was nervous.

My nervousness started to fade at the IMAGE opening reception. There I was with 30 other new PIs or soon-to-be PIs openly talking about the challenges of the job: getting lab renovations completed, learning the quirks of purchasing supplies and equipment at our respective institutions, teaching our first classes, and writing grants. I was lucky enough to talk to Sonia Flores, one of the mentors of the workshop. I was really touched when she asked about my family, and so I shared photos and videos of Luke's first laughs and masterful crawling adventures. Sonia was happy to hear about my growing support network at Syracuse University and gave me helpful advice on navigating my tenure-track appointment in two departments (biology and chemistry). I soon realized that the mentors are tremendous people who really care about the success of each attendee.

IMAGE was created in 2013 as a comprehensive workshop targeting underrepresented postdoctoral scientists and assistant professors to provide the tools to succeed in today’s challenging and ever-changing grant climate. At IMAGE, I learned about new PI initiatives from the NSF and NIH such as the National Institute of General Medical Sciences’ Maximizing Investigators’ Research Award for early-stage investigators.

The year I was there, Squire Booker and Sonia led sessions on the art of writing an NIH grant and the importance of getting the flow and language correct for the specific aims page. This is the page that everyone will read, and it really does set the tone for the application. Squire and Sonia emphasized clear and logical presentation of the knowledge gap, project goals, hypotheses and aims. My current mentor at Syracuse University, Sandra Hewett, a Beverly Petterson Bishop professor of neuroscience, emphasizes the same advice.

One of the most eye-opening experiences was a mock grant review panel for NSF and NIH study sections. In this exercise, all the IMAGE attendees were given copies of anonymous sample grants. The mentors and other workshop presenters acted out how the review panels work, discussing each submission and providing critiques, followed by a panel ranking of the grant. They then took questions from the audience. We learned that these panels have a limited amount of time to discuss each grant, so the application must be clear, concise and easy to read. The take-home message: It is worthwhile to read, re-read, and have others read your grant.

Most people come to IMAGE with the intention of submitting a grant within a year, and much of the workshop is devoted to each new or potential PI describing ideas and illustrating a project in 20 minutes and then receiving 10 to 15 minutes of feedback from mentors and peers, who offer advice on hypotheses and experiments as well as alternative approaches. I’ll be honest: It was a nerve-wracking experience but tremendously valuable.

The feedback I received hit on the points I already was concerned about. Everyone in that room could sense...
my gut feelings about the project. Some said that it was too much of a fishing expedition, that I still needed to find targets of the PTM in biological systems, and I got some great ideas on how to run these experiments. Most importantly, I learned that my gut was right — I was rushing a proposal that wasn’t ready. The mentors in the room reminded me that I still had three chances before tenure to hand in that NSF CAREER proposal. I decided not to submit my NSF CAREER proposal that year. The feedback I received at the workshop encouraged me to think more deeply about the whys of the project, and it gave me time to reflect on our lab directions. To borrow language from 2018 American Society for Biochemistry and Molecular Biology mentor Karen Fleming, what was my BBQ — my big biological question?

At the 2016 workshop, I also discussed my lab’s other projects with attendees. I got a lot of encouragement, particularly from Irina Bezsonova, a faculty member at the University of Connecticut Health System. Our lab fortuitously had entered the liquid–liquid phase separation, or LLPS, field just as we had completed preliminary experiments that showed that ubiquilin-2 phase separated into protein-containing droplets. Irina told me some of her colleagues also worked on LLPS.

I’m not sure I realized it at the time, but this was networking at its best. I kept in touch with Squire and Sonia as I began looking for mentors in neuroscience, since dysregulation of ubiquilins is implicated in neurodegenerative and neurological disorders. During the next few months, my lab’s LLPS studies with ubiquilin proteins picked up steam, and it became apparent that this would be the project for my NSF CAREER grant. I remembered my Johns Hopkins University graduate adviser, Bertrand García–Moreno, who always encouraged us to “let the data do the talking.”
After making my IMAGE presentation and listening to others, I honed my approach to grant writing. I now always focus on the reader. Am I able to draw the reader into the grant? Am I able to explain the aims of my project succinctly? Do I adequately explain the experiments and my expected outcomes? Have I clearly articulated potential pitfalls and how I plan to address those in the grant?

Taking advice from others at the IMAGE workshop, I made an effort to write every day (even if only for 15 to 30 minutes), and I noticed that I could write a compelling story explaining our preliminary findings and hypotheses. Taking Irina’s advice, I read up on LLPS, and I met some of her colleagues at Biophysical Society, ASBMB and Society for Neuroscience meetings. (Today, our lab collaborates with many of them.) The lab was building momentum. I submitted my first NSF CAREER proposal in July 2017, and three months later I got the call from my NSF program officer that it had been recommended for funding. The panel noted the proposal’s good grantsmanship and readability.

I cannot emphasize enough the importance of the IMAGE workshop, especially the contacts I made with peers and mentors. Squire and Sonia were two of the people I emailed soon after I learned that I was receiving an NSF CAREER award.

I attended the IMAGE workshop in 2018, but this time it was to share my story. I continue to learn from the network of mentors at the workshop, especially the importance of protecting your time while writing.

Alaji Bah, an assistant professor at the State University of New York Upstate Medical University, attended last year’s workshop. He said he really valued listening to advice from mentors who are grant reviewers themselves.

This year’s ASBMB IMAGE workshop is June 13–15 in Washington, D.C. Will you be there? Go to asbmb.org/grantwriting to apply.

Carlos Castañeda (cacastan@syr.edu) is an assistant professor of biology and chemistry in the College of Arts and Sciences at Syracuse University. You can follow him on Twitter @Castaneda_lab.

Carlos Castañeda and members of his lab at Syracuse University pose for a group portrait. At left is Castañeda’s 3-year-old son, Luke. In the back row are Yongna Lei, Yiran Yang, Thuy Dao, Castañeda, Brian Martyniak, Tongyin Zheng and Barrington Bucknor. In front are Christine Habjan and Julia Riley.
Western New England University:  
Assistant Professor or Professional Educator of Forensic Science

The Department of Physical & Biological Sciences at Western New England University seeks applications for a full-time faculty position in Forensic Science beginning in September 2019. Depending on the education and background, the finalist will be hired either as a tenure-track Assistant Professor or as a Professional Educator with a three-year renewable contract.

Responsibilities of the position include teaching lecture and laboratory sections of forensic science courses on Scientific Evidence, Crime Scene Processing, and advanced Forensic Science courses and laboratories, and guiding student research projects and internships in support of the B.S. in Forensic Biology and B.S. in Forensic Chemistry programs that the University offers.

Full consideration will be given to applications received by April 1, 2019; however, applications will continue to be accepted until the position is filled.

asbmb.org/Careers/Jobs/79417

Gilead Sciences, Inc.:  
Research Scientist, Biophysics

Gilead is seeking a motivated researcher to work in the Biophysics group within the Research organization. The successful candidate will support discovery projects with development and execution of biochemical assays to measure protein activity, oligomeric state and protein-ligand interactions using techniques such as UV-Visible and fluorescence spectroscopy, analytical ultracentrifugation and calorimetry. The candidate must be motivated, driven, creative, and able to work independently, and must display scientific rigor. The candidate will be required to select appropriate experimental approaches to address scientific questions. Responsibilities will include development and troubleshooting of protein activity and protein-ligand binding assays, data analysis and management, writing reports and SOPs, and presentation to project teams and senior leadership. The successful candidate will work in a team environment and will need to communicate effectively.

asbmb.org/Careers/Jobs/79394

Burrell College of Osteopathic:  
Biochemistry Faculty

Successful candidates will function as member of a collaborative teaching team to develop and deliver their instructional content within an integrated curriculum. The primary teaching focus of this position will involve teaching medical students through the systems-based courses of the 1st and 2nd academic year. Responsibilities will involve the development of collaboratively designed and highly integrated curricular elements, in collaboration with other faculty. Service to the College and the community will also be an essential function of the position, including committee membership, faculty development, student advising, interviewing prospective students, and community outreach.

asbmb.org/Careers/Jobs/79405

McGill University:  
Assistant Professor or Associate Professor in Nutritional Pathobiology

The School of Human Nutrition of McGill University's Faculty of Agricultural and Environmental Sciences invites applications for a tenure-track Assistant/Associate Professor of Nutritional Pathobiology. High priority research areas include the pathobiology of nutrition-related diseases throughout the lifespan, nutritional biochemistry of health and disease, epigenetic inheritance of disease susceptibility through generations, and damage to commensal microbiota. The ideal research approach will encompass basic discovery and translational research in the identification of targets and development of novel nutrition-based interventions.

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

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Attend the ASBMB annual meeting to learn about the latest developments in biochemistry and molecular biology straight from leading influencers in the field. Find out how to incorporate the latest tools, software and methodology in a variety of expert-led workshops. Plus, receive critical feedback on your work as you build professional connections for future collaboration and reconnect with old friends.

Register today at ASBMB.org/meeting2019.
Advance registration ends March 20.