

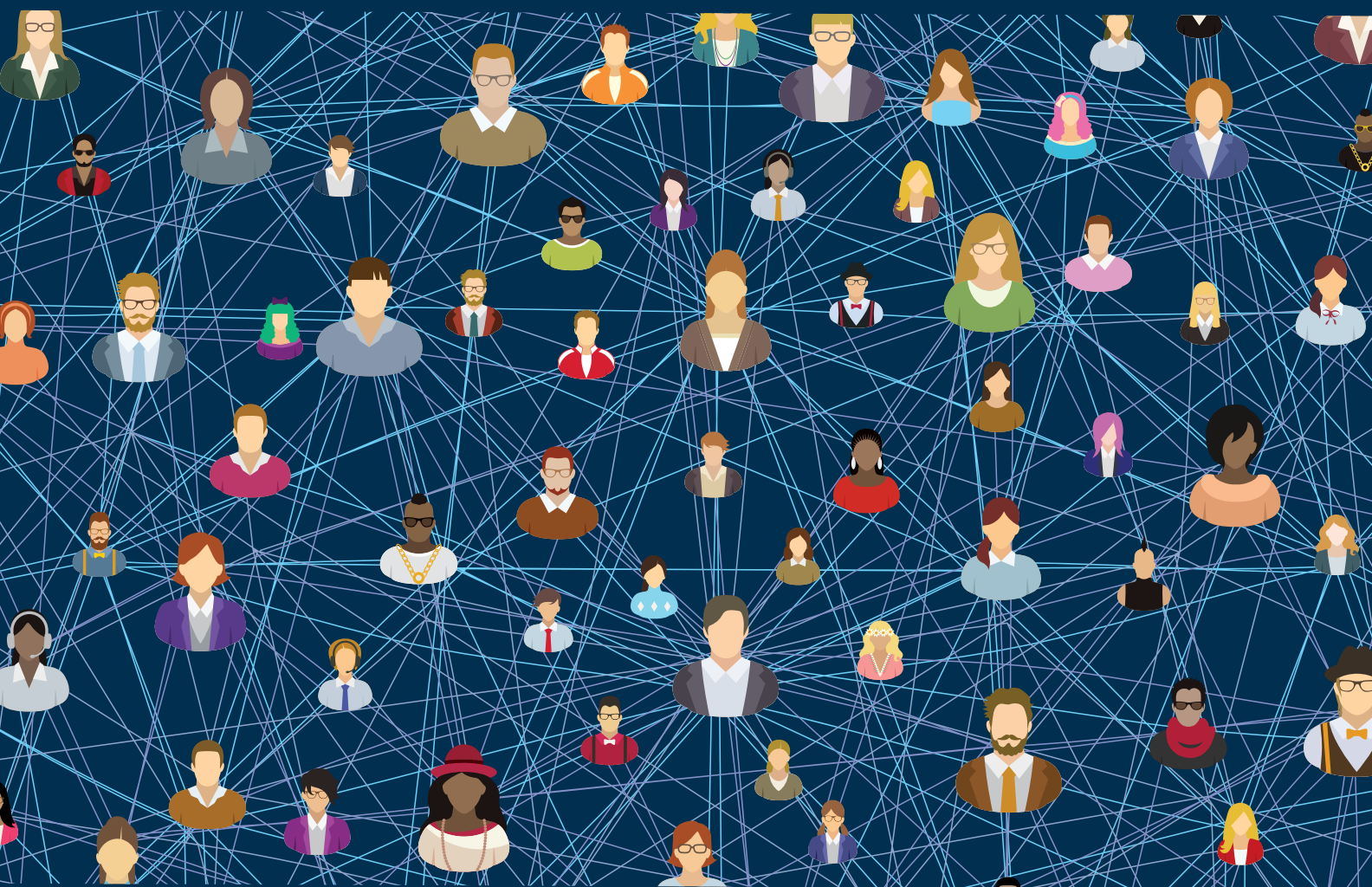
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ASBMB TODAY

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



**Pivoting from
carnivorous plants
to COVID-19**



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PRESIDENT'S MESSAGE

ASBMB journals are going open access

By Gerald Hart

The American Society for Biochemistry and Molecular Biology on Monday announced that it would make its three peer-reviewed journals fully open access beginning in January 2021. As president, I convened a task force responsible for exploring how the society could achieve this longstanding goal, and I oversaw the task force's work. Here, I'd like to explain the reasons for this move, why we decided to partner with a commercial publisher, and what this all means for the society.

I've written before about the intensifying pressure on scholarly publishers to make their journals fully open access. Researchers, funding agencies, patients and other members of the public believe that taxpayer-funded research should be accessible to all. The ASBMB shares this belief, which is why our journals — Journal of Biological Chemistry, Journal of Lipid Research and Molecular & Cellular Proteomics — have for years made accepted manuscripts freely available and have encouraged authors to post their manuscripts in public repositories. Still, those measures aside, the writing is on the wall: In the future, anything short of full open access isn't going to cut it.

Although both subscription and open-access models are funded by research grants, moving from a subscription model, in which institutional libraries pay for journal access (mostly from indirect costs, F&A), to an open-access model, in which authors pay the full cost of publishing

(currently mostly from direct costs) and making their papers public, is complicated, to say the least.

To begin with, it incentivizes high-volume publishing, rather than high-quality publishing. You've probably noticed that some open-access publishers have pretty low standards: The more papers they publish, the more money they make. For the ASBMB, based upon the volume of papers it currently publishes in its three journals, subscriptions provide more income than author fees will.

The society is willing to take that financial hit to do what's right for the community. It is not willing, however, to lower its standards in order to increase volume. Let me be very clear about this: ASBMB journals are committed to publishing papers that our reviewers, all of whom are active scientists, deem important, relevant, rigorous and reproducible.

On top of loss of subscription revenue, open-access publishing requires different workflows, platforms and technologies. As authors, we don't often think about these operational requirements for publishing, but it's important to get them right. While the task force explored the possibility of ASBMB cobbling together new and existing systems on its own, it determined that even if the society could line everything up for a January launch, it would immediately lag behind the competition. Frankly, we did the math, and ASBMB simply does not have the finances to go open access on its own. If we want to do this quickly and keep pace thereafter,

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I have written before about why we should review for and publish in society-owned journals, and my position remains unchanged. JBC, JLR and MCP are still society-owned journals, and they need your contributions now more than ever.

the task force determined, we need help.

The task force then produced a request for proposals, making it clear that the society needed a publishing partner with experience transitioning subscription journals to open access and with the ability to do it by January. The task force evaluated seven proposals and shortlisted four potential partners to present to the ASBMB Council in February. While each proposal had its own strengths, Elsevier's was the strongest. The task force recommended that the society partner with Elsevier, and Council voted unanimously in April to do so.

Now, it's fair to say that Elsevier has a number of critics in our community, in some cases because of historical practices and in some cases because of more recent ones. I'm not here to defend Elsevier; I am here to explain to you why it was our best choice.

For starters, Elsevier has extensive experience working with societies. Many of you likely publish in the Biophysical Journal, which is owned by the Biophysical Society but published in partnership with Cell Press, an imprint of Elsevier. In just the past year, Elsevier has worked to make at least 100 journals open access, almost half of them with societies. In addition, Elsevier has submission, production, online publishing, analytics and marketing systems that we can immediately adopt and then tailor as needed.

ASBMB journals, as you likely know, have significant archives that must be migrated to any new system.

JBC alone has been publishing for more than a century. It's important to us that we continue to be good stewards of that archive of knowledge, and Elsevier has committed to preserving it.

A key point in our negotiations was pricing, and the good news is that it will be cheaper for everyone, but ASBMB members especially, to publish open-access papers in our journals. The standard article processing charge will be \$2,500, and ASBMB members will pay only \$2,000. This is a very good price in the current marketplace and is much cheaper than most open-access journals.

Finally, given the subscription revenue we'll be losing, Elsevier promised us a short-term income guarantee that will hold us over while the journals, after becoming open access, gradually reach new readers and authors.

What does all this mean for the ASBMB?

The most important thing I want to emphasize is that the ASBMB retains ownership and complete editorial control of its journals. We will continue to select our editors-in-chief, associate editors and editorial board members. We will continue to manage the peer-review process. We will make editorial decisions based upon merit, not flashiness or volume. We will always be scientists working to support other scientists. There will be no non-scientist gatekeepers.

I have written before about why

we should review for and publish in society-owned journals, and my position remains unchanged. JBC, JLR and MCP are still society-owned journals, and they need your contributions now more than ever.

Below are some key points to remember:

- All ASBMB journals will be gold open access beginning in January.
- The ASBMB will continue to own 100% of its three journals.
- All editorial decisions will remain with the society.
- All peer review will continue to be done by working scientists — YOU (no nonscientist gatekeepers).
- All appointments of editors-in-chief, associate editors and editorial board members will continue to be the society's to make.
- There will be a new and improved manuscript tracking and submission system.
- There will be improvements to the author experience.
- Fast turnaround will remain a top priority.
- There will be improvements in operations.
- All ASBMB journals will be in full compliance with Plan S and other open-access initiatives, resulting in greater global reach and visibility.
- There will be improved search functionality within the board to find the best reviewers for manuscripts.

Making our journals fully open access is the right thing to do to

PRESIDENT'S MESSAGE

advance science, but — as explained above — it will result in a substantial loss of revenue (subscription income). The society will continue its many programs that support our members, including education, public affairs, outreach and many other activities that support our field. We have determined that, with careful stewardship of the ASBMB's resources, we will be able to keep the society in great shape in perpetuity. Unfortunately, as I have stated in earlier columns, many small society journals and societies themselves won't likely survive the

coming mandates for open access due to loss of revenue. We are indeed fortunate that both the current and past ASBMB managers have been great stewards of our financial resources. In short, open access is not only great for science, but also the ASBMB will survive this transition in great shape!

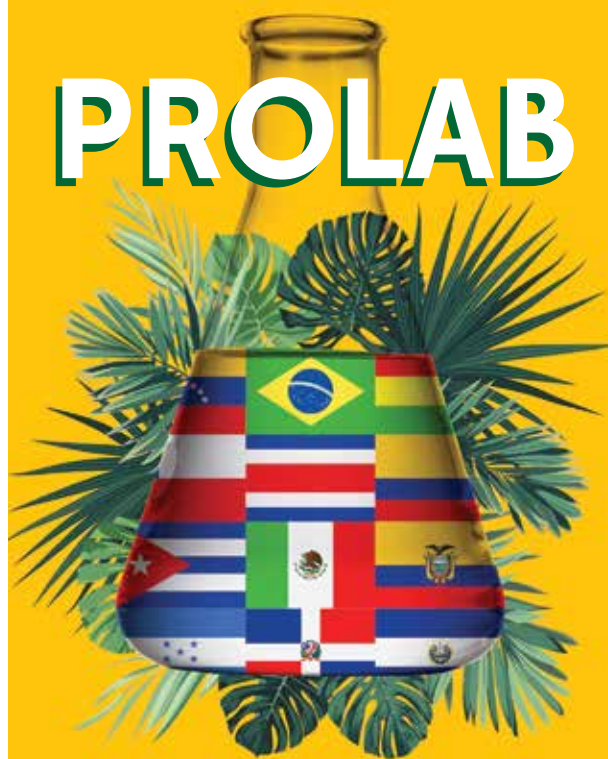
The decision to go open access was not made lightly and involved the hard work of many people who considered all of the options. As president, I would like to thank the many people who put in long hours to develop our plans for this transition.

You may still have questions about this decision and its impact. We are doing our best to provide information and be as transparent as possible. You can find a list of frequently asked questions here, and I also invite you to contact me or any of the journal editors with your thoughts, questions and concerns.

Gerald Hart (gerald.hart@uga.edu) is a professor and Georgia Research Alliance eminent scholar at the University of Georgia and president of the ASBMB.



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Baserga named Fleming professor



Baserga

Susan J. Baserga, chair of the American Society for Biochemistry and Molecular Biology's Women in Biochemistry and Molecular Biology

Committee, was recently appointed as the William H. Fleming, M.D. '57 professor of molecular biophysics and biochemistry at Yale University.

Baserga is also the director of medical studies in the department of molecular biophysics and biochemistry and program director of the predoctoral program in cellular and molecular biology at Yale. She performed postdoctoral work with Joan Steitz, and began her academic career as an assistant professor of therapeutic radiology and of genetics at the Yale School of Medicine. She became a full professor in 2007. Her laboratory examines the fundamental aspects of ribosome biogenesis and its impacts on cell growth, cell division and cancer.

In 2018, Baserga was elected as a fellow of the National Academy of Inventors. She has received the Connecticut Technology Council Women of Innovation in Research and Leadership Award, the Charles W. Bohmfalk Prize for basic science teaching at the Yale School of Medicine and the ASBMB's William C. Rose Award for outstanding research and commitment to training young scientists.

The William H. Fleming, M.D. '57 professorship was established in 2009 to help Yale maintain the highest standard of excellence in the biological sciences.

Bryant receives recognition among plant biologists



Bryant

Donald Bryant, professor of biochemistry and molecular biology at The Pennsylvania State University and a member of the Journal of Biological Chemistry editorial board, has received the Charles Kettering Award from the American Society of Plant Biologists in recognition for his work on bacterial photosynthesis.

Bryant, who also holds the Ernest C. Pollard professorship in biotechnology, joined the Penn State faculty in 1981. His lab studies cyanobacteria and other

chlorophotoautotrophs.

Bryant has studied the physiology, metabolism and ecology of cyanobacteria for nearly 50 years. Recently, his group discovered the process of far-red light photoacclimation, or FaRLiP, in which the expression of a 20-gene operon allows cyanobacteria to modify their photosynthetic apparatus to enable growth in far-red light, something previously thought to be impossible. The acclimation process involves the synthesis of two new types of chlorophyll, d and f, and substantial modifications of phycobilisomes and photosystems I and II. Biotechnologists hope that this discovery may someday be used to improve productivity in crop plant

The biannual Kettering Award, supported by the Kettering Foundation, was established in 1962 to recognize excellence in photosynthesis research with a monetary prize.

Butler named UCSB faculty research lecturer

Alison Butler has been awarded the Faculty Research Lecture Award for 2020 by the University of California, Santa Barbara, Academic Senate.



Butler

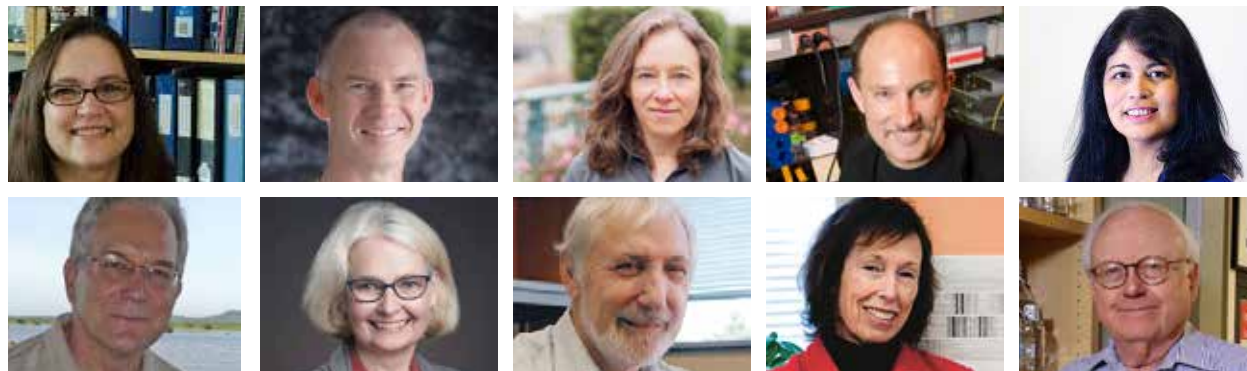
Butler, who studies metallobiochemistry in marine microbes and algae, is a distinguished professor in UCSB's department of chemistry and biochemistry. Her research focuses on microbial iron acquisition through secreted chelators called siderophores.

Among her many honors, Butler has received the American Chemical Society's 2019 Cope Scholar Award and 2018 Alfred Bader Award and the Royal Society of Chemistry's 2019 Inorganic Reaction Mechanisms Award. She previously served as president of the Society for Biological Inorganic Chemistry and was elected as a fellow of both the American Academy of Arts and Sciences and the Royal Society of Chemistry in 2019.

"I congratulate Alison on receiving the highest honor bestowed by UC Santa Barbara's faculty senate," Pierre Wiltzius, executive dean of the college of letters and science, said to the UCSB Current. "As a pioneer in the field of metallobiochemistry, and a leading scholar on this campus, she is most deserving of this recognition."

Have you recently been promoted or honored? Do you have good news to share? Email it to us at asbmbtoday@asbmb.org — and don't forget to include a photo!

AAAS announces new members



The ASBMB members recently named to the American Academy of Arts and Sciences are, top, from left, Catherine Drennan, Christopher Hill, Kathleen Collins, Joseph Heitman and Blossom Damania; bottom, from left, Thomas Welles, Trisha Davis, George Stark, Susan Wallace and Thoru Pederson.

The American Academy of Arts and Sciences announced recently that 276 artists, scholars, scientists, and leaders in the public, nonprofit and private sectors have been elected to the academy in the areas of mathematical and physical sciences, biological sciences, social and behavioral sciences, humanities and art, and public affairs, business and administration. They include 10 members of the American Society for Biochemistry and Molecular Biology.

Among this year's new members in the interclass section is one ASBMB member.

Catherine Drennan is a professor of chemistry and biology at the Massachusetts Institute of Technology and a Howard Hughes Medical Institute investigator. Her lab studies the structural biology of metalloenzymes, using X-ray crystallography to investigate how conformational changes enable catalysis and how these enzymes might be targeted. As a postdoctoral fellow, Drennan started the undergraduate poster competition at the ASBMB's annual meeting, and she has maintained an interest in pedagogy, developing active lectures and research-based undergraduate courses. In March, she

won the Protein Society's Dorothy Crowfoot Hodgkin Award. She was nominated in the mathematical and physical sciences class, chemistry section, and in the biological sciences class, biochemistry, biophysics, and molecular biology section.

Among this year's new members in the biological sciences class are nine members of the ASBMB.

Microbiology and immunology section

Blossom Damania is a professor of immunology and microbiology, molecular bases of disease and signal transduction at the University of North Carolina at Chapel Hill. Her work focuses on understanding the molecular pathogenesis of oncogenic viruses, including Kaposi's sarcoma-associated herpesvirus.

Joseph Heitman is the James B. Duke professor and chair of the department of molecular genetics and microbiology at Duke University School of Medicine. His research focuses on sexual reproduction and evolution of pathogenic eukaryotic microorganisms, antimicrobial drug resistance via RNAi-dependent epimutation, and targets and mechanisms of action of natural products

including the discovery of FKBP12 and TOR as targets of rapamycin.

Biochemistry, biophysics and molecular biology section

Kathleen Collins is a professor of molecular and cell biology at the University of California, Berkeley, historically focused on the structure and regulation of the telomerase enzyme and now focused on the reverse transcriptases and biology of retroelement mobility. She is also the founder of a company developing enzymatic tools for RNA sequencing. She was a member and chair of the ASBMB Publications Committee from 2012 to 2016.

Christopher Hill is a distinguished professor of biochemistry and vice dean of research at the University of Utah School of Medicine. Hill's structural biology lab studies protein-protein interactions and catalysis in a variety of contexts, including proteasome activity, gene expression and protein quality control.

George Stark is a distinguished scientist in the Cleveland Clinic Lerner Research Institute. His interests include interferons and cytokines, signal transduction, p53 and mammalian cell mutants.

Susan Wallace is a distinguished professor emerita of microbiology and molecular genetics at the University of Vermont. Her research interests include oxidative DNA damage and repair and the interaction between DNA damages and DNA polymerases.

Cellular and developmental biology section

Trisha Davis is the Earl W. Davie/Zymogenetics professor and chair of biochemistry at the University of Washington. Her lab investigates mechanisms of chromosome dynamics, including chromosome capture and movement and microtubule nucleation and organization during mitosis.

Intersection

Thomas Wellemis is chief of the Laboratory of Malaria and Vector Research at the National Institute of Allergy and Infectious Diseases at the National Institutes of Health. He was nominated in the medical sciences section and the section of cellular and developmental biology. His research focuses include antimalarial drug response and protection conferred by human hemoglobinopathies and red cell polymorphisms.

Thoru Pederson is the Vitold Arnett professor of cell biology and a professor of biochemistry and molecular pharmacology at the University of Massachusetts Medical School. He was nominated in the biochemistry, biophysics and molecular biology section and the cellular and developmental biology section. His lab's research focuses on the functional significance of specific protein-RNA interactions in eukaryotic gene expression, with emphasis on RNA traffic and processing.

Seven ASBMB members elected to NAS



The ASBMB members elected to the National Academy of Sciences are, top, from left, Janet Smith, Christopher Lima, Joan Conaway and Ivet Bahar; bottom, from left, Peter Tontonoz, Michael Rosen and Kim Orth.

The National Academy of Sciences announced the election of 120 members and 26 international members. Seven of them are members of the American Society for Biochemistry and Molecular Biology. Here's a little about each:

Ivet Bahar is a distinguished professor and the founding John K. Vries chair at the University of Pittsburgh School of Medicine's computational and systems biology department. Bahar developed widely used elastic network models for protein dynamics. She co-founded the computational biology Ph.D. program offered jointly by the University of Pittsburgh and Carnegie Mellon University. Just last year, Bahar won the Kadir Has Outstanding Achievement Award, which recognizes outstanding accomplishments Turkish scientists have made at the national and international level. Bahar is an elected member of the European Molecular Biology Organization.

Joan W. Conaway holds the Helen Nelson distinguished chair at the Stowers Institute for Medical Research in Kansas City, Mo. She studies the mechanisms of gene transcription, and her work helped define

mechanisms that regulate initiation and elongation of mRNA transcripts by the enzyme RNA polymerase II. She shared ASBMB's Amgen award with her husband, Ron, in 1997 and that same year was named an associate investigator of the Howard Hughes Medical Institute, a position she held until 2001. She was elected in 2002 to the American Academy of Arts and Sciences. She has served as an associate editor for the ASBMB's *Journal of Biological Chemistry* and as a member of the ASBMB Council, finance committee and meetings committee. Today she is the society's treasurer.

Christopher D. Lima is a Howard Hughes Medical Institute investigator and holds the Alfred P. Sloan chair as member and chair of the structural biology program in the Sloan Kettering Institute of Memorial Sloan Kettering Cancer Center. He is also a professor at the Weill Cornell Graduate School of Medical Sciences. Lima's laboratory studies the mechanisms underlying RNA processing and post-translational modification by ubiquitin and ubiquitinlike proteins, such as SUMO. Lima was elected to the American Academy of

MEMBER UPDATE

Arts and Sciences in 2017.

Kim Orth is a Howard Hughes Medical Institute investigator and the Earl A. Forsythe chair in biomedical science at the University of Texas Southwestern Medical Center's molecular biology department. Orth works to elucidate the activity of bacterial virulence factors on the molecular level, providing insights into how bacteria cause disease and how eukaryotic host cells signal in response to infection. She has served on the ASBMB awards committee and is currently on the nominating committee. She won the ASBMB–Merck Award in 2018 and the ASBMB Young Investigator Award in 2012. Read an essay in the *Journal of Biological Chemistry* by Orth about her career.

Michael K. Rosen is a Howard Hughes Medical Institute investigator and chair of the University of

Texas Southwestern Medical Center's biophysics department. Rosen's lab studies how the interior of the cell is organized and, in particular, membrane-independent compartmentalization. His group uses a range of techniques to investigate the assembly, composition, and function of biomolecular condensates. In February, he was recognized with the Wiley Prize in Biomedical Sciences. Read our 2015 feature on Rosen's career path.

Janet L. Smith is the Margaret J. Hunter collegiate professor at the University of Michigan Life Sciences Institute and professor of Biological Chemistry. Her lab uses X-ray crystallography to solve protein structures of natural product biosynthetic enzymes as well as viral and antiviral proteins. She is regarded as a key developer of the multi-wavelength anomalous diffraction (MAD)

method and its single-wavelength counterpart (SAD) and is the scientific director of the GM/CA@APS beamlines for crystallography at the Argonne synchrotron. She was elected as a fellow of the American Association for the Advancement of Science in 2007 and won her university's Distinguished Faculty Lectureship Award in Biomedical Research in 2016.

Peter Tontonoz is the Frances and Albert Piansky chair at the University of California, Los Angeles, pathology and laboratory medicine department. Tontonoz studies lipid metabolism and metabolic disease. He is a member of the editorial board for the ASBMB's *Journal of Lipid Research*. In 2017, he gave the Havel Lecture at the society's Deuel Conference on Lipids, and in 2019 he was a program co-chair for the conference.

Bumpus named department chair



Bumpus

Namandjé Bumpus has been appointed chair of the department of pharmacology and molecular sciences at the Johns Hopkins University School of Medicine after a nationwide search. As director, Bumpus will hold the E.K. Marshall and Thomas H. Maren professorship in pharmacology. She is the first Black woman to chair a department at the school of medicine.

Bumpus joined the Hopkins faculty in 2010 after earning her Ph.D. from the University of Michigan and completing postdoctoral work at the The Scripps Research Institute (now called Scripps Research). Since then, she has advanced into leadership roles, becoming the first associate dean of institutional and student equity at Hopkins and then the school of medicine's associate dean for basic research.

Bumpus' research focuses on drug metabolism, specifically of antiretroviral drugs used to treat and prevent HIV. The work includes investigating genetic variation in kinases that activate certain anti-HIV drugs and liver cytochromes that facilitate drug clearance, as well as developing assays to measure drug metabolites and model their distribution into various tissues.

Accolades for Bumpus' work include the PECASE (Presidential Early Career Award for Scientists and Engineers) from the NSF, a Presidential Early Career Award, invited lectureships at the National Institute of General Medical Sciences and the Congressional Biomedical Research Caucus, and awards from the American Society for Pharmacology and Experimental Therapeutics.

Regev takes leadership position at Genentech



Regev

Aviv Regev is leaving the Broad Institute of the Massachusetts Institute of Technology and Harvard University to become Genentech's research and early development chief in August. She also will be a member of the executive committee for Roche, Genentech's parent company. In a statement, Severin Schwan, chief executive officer of Roche, said of Regev's appointment: "She brings a rare combination of expertise that will help us unlock even more possibilities in data-based drug discovery and development."

Regev's lab uses experimental and computational approaches to study molecular circuits governing the function of mammalian cells and tissues in health and disease.

Regev won the American Society for Biochemistry and Molecular Biology's Earl and Thressa Stadtman Scholar Award in 2014, the same year she became a Howard Hughes Medical Institute investigator. She is also a founding co-chair of the Human Cell Atlas initiative, which aims to map the location and gene expression of all human cell types, and founding director of the Klarman Cell Observatory at the Broad. She was elected to the National Academy of Sciences and won FASEB's Excellence in Science Mid-Career Investigator Award last year.

She earned her master's degree and Ph.D. in computational biology at Tel Aviv University. She joined MIT's biology department as a faculty member and a core member of the Broad in 2006. She has served on advisory boards of several biotechnology and pharmaceutical companies, as well as research centers, institutes and hospitals.

Regev will be based at Genentech's South San Francisco headquarters.

Lemire, McGaunn named rising researchers



Lemire

Among the eight undergraduates at the University of Massachusetts Amherst to receive Spring 2020 Rising Researcher awards are **Colin Lemire** and **Joseph McGaunn**, both members of the UMass American Society for Biochemistry and Molecular Biology Student Chapter.

Colin Lemire, a graduating biochemistry and molecular biology major in the Commonwealth Honors College, is involved in independent research in Sibongile Mafu's lab focusing on the biosynthesis of natural products in plants and fungi. His work involves gene discovery and pathway reconstruction of terpene molecules in fungi that have demonstrated activity as antimicrobials, with a goal of better understanding the metabolic pathways of natural products for future research into their function and potential pharmaceutical applications.

In addition to this award, Lemire has received a grant from the UMass Amherst Center for Agriculture, Food and the Environment; an ASBMB Student Chapter Travel Award to present his research at the 2020 ASBMB Annual Meeting (since canceled); and a UMass Life Sciences



McGaunn

Junior Fellow award.

Joseph McGaunn, a graduating senior with a double major in biochemistry and molecular biology and psychology in the Commonwealth Honors College, has worked on five research projects in Alexander Suvorov's lab. He has investigated the role of molecular mechanisms in mediating interactions between an individual's

genetics and their environment and in transferring nongenetic information from one generation to the next, as well as the potential clinical applications for such mechanisms. This includes investigating the effect of paternal exposure to chemicals such as phthalates on offspring behavior and metabolism using a mouse model.

McGaunn has presented his work at the Northeast Society of Toxicology Regional Chapter annual meeting and the annual meeting of the Society of Toxicology and is a coauthor on four manuscripts that will be published by Suvorov's lab.

The 2020 Rising Researcher awards celebrate these students for their unconventional and inspiring approaches to research, scholarship and creative activity.

Jan Miernyk

Jan A. Miernyk, a supervisory research molecular biologist whose career spanned 33 years at the U.S. Department of Agriculture, died April 2. He was 72.

Born Oct. 4, 1947, in Boulder, Colorado, Miernyk attended Fort Lewis College in Durango

and the University of Colorado, Boulder before earning a B.A. in biology and an M.S. in plant physiology at West Virginia University. He earned his Ph.D. in plant cell biology at Arizona State University, Tempe in 1980, then completed a postdoc in biology research at Queen's University in Kingston, Ontario.

Miernyk began his career with the USDA at the Northern Regional Research Center, in Peoria, Illinois. He transferred to the Plant Genetics Research Unit at the University of Missouri in 1999, where he was also an adjunct professor in the department of biochemistry. He loved his work and was known for his expertise, with 156 scientific publications and 3,351 citations. He was elected an American Association for the Advancement of Science fellow in 2007.

A major focus in Miernyk's lab was systems biology. He used a descriptive platform to define periods of cell division and specialization, lipid and protein accumulation and preparation for quiescence in soybeans, then isolated and compared total proteins from each stage. After analyzing patterns of change in protein abundance, the lab used systems cartography to describe relationships among protein function, expression, localization, and biological interaction for an evolving cartograph.

In his younger years, Miernyk was a wrestler and football player. He later earned a black belt in Okinawan karate, and he taught free martial arts classes at Mizzou for students and faculty. A longtime fan of muscle cars, in retirement he restored and modified a '62 Ford Falcon. He was a craft beer enthusiast and enjoyed cataloguing new breweries he encountered on his travels.

Miernyk is survived by his wife, Elizabeth Hoyos-Miernyk, and his daughter, Briana Saucier, and her family.



Peter Lengyel

Peter Lengyel, a professor of molecular biophysics and chemistry at Yale University for more than four decades, died April 21. He was 90.

Lengyel was born May 24, 1921 in Budapest, Hungary. He and his parents sur-

vived the Holocaust, but many of their relatives perished. He graduated from the Technical University of Budapest in 1951, then served two years in the Hungarian army before returning to his studies. He and his wife, Suzanna, moved to the U.S. in 1956 after the collapse of the Hungarian uprising against the USSR, settling in New York City where he pursued his Ph.D. under Severo Ochoa. He did a postdoc with Jacques Monod in Paris and worked briefly on the faculty of New York University before being recruited to Yale in 1965.

According to an article by Robert Forman on the Yale website, Lengyel "was famous at Yale for his tremendous recall, vast knowledge of science and all things cultural, and his meticulous, precise, and fluent lectures delivered without notes, using only chalk and a blackboard to convey the most complex subjects."

Lengyel's graduate work on deciphering the genetic code resulted in the correct determination of the nucleotide composition of codons for 18 amino acids. At Yale, his lab was the first to demonstrate that formylMet-tRNA was required for the translation of bacteriophage f2 RNA in a cell-free system. He spent many years studying protein synthesis, the interferon system and the regulation and modulation of cell proliferation and differentiation. Research from his laboratory led to the discovery, of an RNase activated by interferons as a defense against infecting viruses. He also studied the proteins p202, a regulator of transcription, and p204, a modulator of cell proliferation and differentiation.

In 2014, Lengyel retired from the Yale faculty and was named professor emeritus. "His erudition, refined manner, polite friendliness, abundant curiosity, and sincere concern for others were considered to be among his defining features," Forman wrote.



Tomoko Ohnishi

Tomoko Ohnishi, a professor of biochemistry and biophysics at the University of Pennsylvania for more than 52 years, died March 17. She was 88.

A native of Kobe, Japan, Ohnishi was a competitive figure skater and downhill slalom skier



in her youth. She earned a bachelor's degree in chemistry in 1956 and a master's in biochemistry in 1958, both from Kyoto University. She earned a Ph.D. in biochemistry in 1962 from Nagoya University and did a postdoc in Osaka with Bunji Hagihara.

Ohnishi arrived at the Johnson Research Foundation in the Penn School of Medicine in 1967 to work as a postdoctoral fellow with its director, Britton Chance, who called her "the queen of iron sulfur." She remained at Penn, where she built a world-class research laboratory that produced more than 200 publications, the last one when she was 87.

According to Kristen Lynch, chair of Penn's department of biochemistry and biophysics, Ohnishi was "a true pioneer" in understanding the inner workings of the respiratory electron transport chain that couples oxidation to the production of ATP. Her work provided a map with which to locate dysfunction of that ETC's complex I in neurodegenerative diseases, neuromuscular diseases and aging.

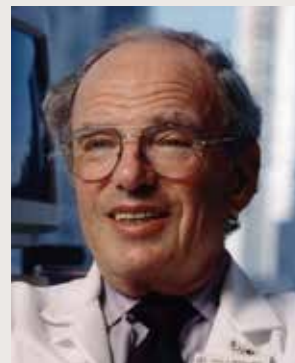
"She appreciated, before most, that understanding the inner workings of Complex I is crucial for the future of medicine and devoted her life's work and passion to deciphering the mysteries of how this key component of the respiratory chain supports life," Lynch said.

In addition to science, Ohnishi loved music. She took singing lessons for many years and enjoyed singing for colleagues at scientific conferences around the world. She spoke some French, German and Russian as well as fluent Japanese and English.

Ohnishi was married for 60 years to S. Tsuyoshi Ohnishi, who died in 2018. She is survived by her children, Hiroshi (and wife Bonnie) and Noriko Lovasz (and husband John); and grandchildren Megumi, Lorelei, Akira and Gavin.

Paul Marks

Paul Marks, a cancer researcher who helped turn Memorial Sloan Kettering Cancer Center into a world-class research institution, died April 28 from pulmonary fibrosis and lung cancer. He was 93.



Marks was born in Mahanoy City, Pennsylvania, on Aug. 16, 1926. After Marks' mother died when he was 4 years old, his father disappeared, leaving his son to a transient life staying with aunts, uncles and grandparents. His father reappeared with a new wife and son five years later and took Marks back.

Marks attended high school in Brooklyn and, with a teacher's encouragement, applied to Columbia University. He was accepted and awarded a full scholarship. At Columbia, he became interested in genetics and clinical research. He graduated with his bachelor's degree in 1945 and his medical degree from the university's College of Physicians and Surgeons in 1949. He then performed postdoctoral work at the National Institutes of Health before returning to Columbia in 1955 to work on glucose metabolism. He served as university's medical school as dean from 1970 to 1973 and as vice president for medical sciences from 1973 to 1980.

When Marks joined MSKCC in 1980 as the center's president—a position he would hold for the next two decades—he sought to apply the strengths and techniques of molecular biology research to cancer research. He helped oversee a top-to-bottom renovation of the center that included revising its tenure system, recruiting emerging talent and, most crucially, refocusing its research priorities from surgical innovations to the molecular basis of cancer.

He retired in 1999, having published more than 350 scientific articles and received numerous accolades that included the National Medal of Science in 1991.

Marks is survived by his wife, Joan Rosen, whom he married in 1953; his daughter, Elizabeth; his sons, Andrew and Matthew; six grandchildren; and two great-grandchildren.

Undergrad chapter members honored

By *Stephanie Paxson*

The American Society for Biochemistry and Molecular Biology Honor Society, Chi Omega Lambda, recognizes exceptional undergraduate juniors and seniors pursuing degrees in the molecular life sciences at colleges or universities with ASBMB Student Chapters. Students are recognized for their scholarly achievement, research accomplishments and outreach activities. ASBMB usually holds an induction ceremony during the annual meeting, but the 2020 meeting was canceled due to COVID-19 so inductees instead will be recognized on the society's website.

ASBMB's Student Chapters program also presents an Outstanding Chapter award each year to recognize a Student Chapter that demonstrates leadership in education activities, exceptional commitment to increasing public scientific awareness, interaction with other campus events, and participation in regional and national meetings. This year's winner is the Northeastern University Student Chapter, advised by Kirsten Fertuck.

2020 HONOR SOCIETY INDUCTEES

Nana Aikins Rochester Institute of Technology	Kevin DiMagno, Rochester Institute of Technology	Marjan Khan Marymount Manhattan College	Wei-Shin Lu Otterbein University
Emily Aleksandrovic Hartwick College	Daniel Do Stockton University	Charya Khun Wesleyan University	Ryan Maki University of Wisconsin— Lacrosse
Ivy Antunes St. Mary's College of Maryland	Madison Donovan University of Tampa	Rochelle Knier, University of Wisconsin— Stout	Megan McClain Otterbein University
Jacob Boyer Purdue University	Danielle Duryea Otterbein University	Sunnie Kong Boston University	Erin McNell St. Bonaventure University
Alon Brown Marymount Manhattan College	Ryan Fink Monmouth University	Austin Lai Emory College	Victoria Miller-Browne Northeastern University
Nina Bui University of Nebraska— Lincoln	Zachary Fralish Florida Southern College	Noah Langenfeld University of Wisconsin— Stevens Point	Daniela Molina Palacios, University of Massachusetts
Nhu Chau St. Mary's College of Maryland	Wihib Hankore University of Nebraska— Lincoln	Renee Lawrence University of San Diego	Victoria Momyer Boston University
Lillian Cool Otterbein University	Cassidy Illum Marymount Manhattan College	Colin Lemire University of Massachusetts Amherst	Rachel Muti Otterbein University
Alexis Craft Lane College	Bailey Jameson Stephen F. Austin State University	Rebecca Leuschen, University of Nebraska— Lincoln	Kathleen Ngo Stockton University
Allison Cruikshank University of Nebraska— Lincoln	Rachel Jansen University of Massachusetts	Sean Lewis Rochester Institute of Technology	Tenzin Ngodup Wesleyan University
	Meera Joshi Wesleyan University	Christopher Lore Manhattan College	Brett Palmero Lake Forest College
			Surya Pulukuri Boston University
			Gwendolyn Pyeatt Boston University



Dr. Sloan Devlin, an assistant professor of biological chemistry and molecular pharmacology at Harvard Medical School, was the keynote speaker at a Student Chapter regional meeting at Northeastern University titled “The Active Site: Promoting Favorable Interactions Among Undergraduates” and also attended by students from Roxbury Community College. Pictured, from left, are Faith Boyd-Mutinga of Roxbury CC; Julian Amirault, Kathleen Merritt and Evan Mun of Northeastern; Sloan Devlin; Anders Lindberg, Ariella Bourdeau, and Jared Subiono of Northeastern; and Lleyan Hashim, Roxbury CC.

Paige Richards
Stockton University

Ashley Robinson
Hamline University

Catherine Rojas
Stockton University

Jordyn Ross
Stevenson University

Braeden Sagehorn
University of
Massachusetts Amherst

Sashrika Saini
University of
Massachusetts Amherst

Diana Sanchez-Zevallos
Stockton University

Sharon Shania
University of San Diego

Raheed Sunesra
Trinity College

Huong Trinh
University of Nebraska–
Lincoln

Chiemeka Uwakwe
St. Johns University

Gina Wade
University of Wisconsin–
Lacrosse

Stephanie Paxson ([@spaxson](https://twitter.com/spaxson)) is the ASBMB’s diversity and undergraduate coordinator. Follow her on Twitter [@stephaniepaxson](https://twitter.com/stephaniepaxson).



Jerry B. Lingrel (1935 – 2020)

By Anil G. Menon & Gary E. Shull

Jeffrey Robbins, Eric A. Schon, Tim M. Townes and John Orlowski contributed to this retrospective.



Jerry Lingrel earned his Ph.D. in biochemistry from the Ohio State University in 1962 and then moved on to postdoctoral studies at the California Institute of Technology, where he developed a deep interest in molecular biology. He subsequently spent a year as a visiting fellow at the University of Cambridge in the famed LMB, or Laboratory of Molecular Biology.

COURTESY OF LYNNE LINGREL-PARTIN

Jerry B. Lingrel, a pioneer in the field of molecular biology, died Feb. 22 at the age of 84. He served with distinction as a member of the faculty of the University of Cincinnati College of Medicine from 1962 to 2019, rising to become chair of the department of molecular genetics, biochemistry, and microbiology, serving in this position for over 30 years and, subsequently, as interim chair of the department of cancer and cell biology for three years.

Jerry was an associate editor of the *Journal of Biological Chemistry* for 28 years; served on and chaired numerous study sections at the National Institutes of Health; chaired national and international scientific conferences; published groundbreaking work; and was an exemplary mentor to dozens of junior colleagues, postdoctoral fellows and graduate students. All who knew him remember him fondly not only for his outstanding scientific contributions but also for his exceptional work ethic, humility, integrity and decency.

“The important thing in science is not so much to obtain new facts as to discover new ways of

thinking about them.”
— William Lawrence Bragg

Jerry poured himself into science with fearless intellectual curiosity. In a career spanning 60 years, he was a pioneer in the invention and use of molecular biological techniques and recombinant DNA technology. Beginning in the mid-1960s, he and his trainees were among the first to identify and characterize mRNA. He identified hemoglobin mRNAs, demonstrated their translation into protein using a reticulocyte cell-free system and determined that hemoglobin mRNA had a poly-A sequence at its 3' terminus. His work contributed to new ways of understanding RNA splicing and stabilization. He later demonstrated that hemoglobin genes occurred in clusters, and his contributions led to the hemoglobin genes becoming a paradigm for our understanding of

gene duplication and evolution in mammals.

To provide historical context, the use of recombinant DNA technology was viewed with considerable public suspicion in the 1970s, and Jerry, with characteristic integrity, was a pioneer in making sure that procedures, institutional review boards and safeguards were in place. In the 1980s, he and his collaborators were the first to demonstrate that a human gene (beta-globin) can function with correct developmental and tissue specificity in a transgenic mouse. This work established a foundation for the production of mouse models of human hereditary disorders and provided an experimental system in which the molecular mechanism of the switch from fetal to adult hemoglobin could be defined.

“Within the infant rind of this small flower, poison hath residence and medicine power”
— William Shakespeare

Jerry was especially skilled at identifying critical bottlenecks in science. For example, hunters long used ouabain, the active ingredient in arrow poison, to kill prey, but traditional healers also used it to treat heart disease. Similarly, digoxin, the active ingredient from the foxglove (*digitalis*) family of plants, is toxic at doses that are barely above therapeutic doses. Breakthroughs in the 1960s had shown that ouabain and digoxin both acted by binding sodium–potassium adenosine triphosphatase, or Na,K-ATPase, the critical ATP-dependent pump that maintains sodium and potassium gradients across the plasma membrane of every cell in the body. However, further understanding of the physiology of this key ion pump had reached a bottleneck because the genes encoding its subunits were still unidentified, and there was no way to evaluate gene function *in vivo*.

Using cDNA cloning techniques, Jerry determined the sequence of the multiple Na,K-ATPase isoforms and identified the amino acid residues involved in cation transport and the binding of inhibitory drugs such as ouabain and *digitalis*. Then he made an inspired leap of imagination to take advantage of the then-nascent technology to create gene-targeted mice.

Before any such mice had been generated, Jerry quickly assembled a gene-targeting team at the University of Cincinnati and started a highly

productive set of studies of the physiological and developmental functions of these cation pumps in the living animal. The members of this team went on to publish groundbreaking work as independent scientists and earned Cincinnati an international reputation as a center of excellence for transgenic and gene-targeting studies.

Jerry fearlessly explored cutting-edge gene-targeting techniques for making global and conditional gene knockouts and for gene modifications, and he identified unique functions of the Na,K-ATPase isoforms in heart and skeletal muscle and the brain. His gene modification studies provided conclusive evidence

that an endogenous ligand regulates Na,K-ATPase activity and elucidated some of the physiological functions of these important ligands. He generously shared the gene-targeted animals that he developed with researchers around the world, and many of them are still being used today in a wide variety of studies.

“Chance favors the prepared mind” — Louis Pasteur

Jerry exemplified the alert mind that scans a wide scientific landscape, chooses questions carefully and then marshals the best forces to answer them. His team made major contributions to the understanding of atherosclerosis from his serendipitous

COURTESY OF LYNNE LINGREL-PARTIN



Jerry Lingrel with his two children, Doug and Lynne, sit on a tractor during a visit to the family farm in the early 1970s. His background as a farmer contributed to the work habits that served Lingrel and all who worked with him throughout his career.

COURTESY OF LYNNE LINGREL-PARTIN



Jerry Lingrel was an avid gardener, both outside, where he grew many vegetables and flowers, and inside his greenhouses, where he grew an astonishing array of orchids and cacti.

discovery, decades earlier, of the zinc finger transcription factor Kruppel-like factor 2, or KLF2. The key observation was that KLF2 is highly expressed in endothelial cells that are subjected to high hemodynamic shear stress, and this prompted them first to identify the DNA sequence that responded to shear stress in the KLF2 gene and then to identify higher order transcription factors that regulate its expression.

Using gene targeting, the team showed that loss of KLF2 in myeloid cells results in a significant increase in atherosclerosis due to an increase in migration and adhesion of both neutrophils and macrophages to endothelial cells. They further showed that widely used statin drugs induce KLF2 and likely confer some of the protective effects of statins (beyond inhibiting cholesterol biosynthesis) by reducing inflammation, a major risk factor in atherosclerosis.

“The meeting of two personalities is like the contact of two chemical substances: if there is any reaction, both are transformed.” —Carl Gustav Jung

The contribution for which Jerry Lingrel will be remembered most is his transformative impact on the many graduate students, postdoctoral fellows and medical fellows whom he trained. Lab meetings were held every week without fail, and everyone from the newest graduate student to the most experienced postdoc would be in the rotation to present their latest findings and to discuss any difficulties they had encountered. In these meetings, there was remarkably little pressure; one was simply presenting data and ideas to a group of interested friends and colleagues. Regardless of experience, everyone was treated as an equal. Jerry actively sought out opinions,

listened to and acted on good ideas, and pursued new directions, with new grant submissions often resulting from this process.

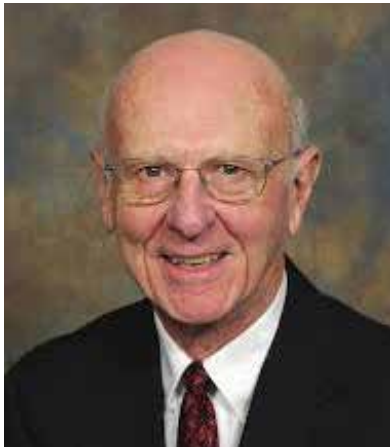
Jerry enjoyed challenging his mentees and being challenged by them in turn. His genuine enthusiasm and wonder at where the scientific path was taking him and what could be learned were both delightful and inspiring. He was eager to embrace new technologies but only in the pursuit of a “good biological question,” and he had a farmer’s good sense for quickly sizing up scientific papers and grants. This kept the lab fresh and productive as Jerry continued to make important contributions to the literature well into his 80s.

Jerry believed and acted on the principle that everyone was capable of coming up with new ideas and approaches. When it was time to prepare a new grant submission or a renewal application, he expected everyone in the laboratory who was working in that area, including graduate students, to participate. He made it clear that this was not merely a training exercise but a result of his belief that everyone in the lab was fully capable of participating in a shared scientific endeavor.

“The poetry of the earth is never dead” — John Keats

Jerry loved the poetry of the earth and the rich soil of Ohio. He was born and raised on a farm in Byhalia, Ohio, which he visited frequently. It remains in the Lingrel family to this day. He had an interest in farming, gardening and landscaping that he pursued throughout his life.

Jerry was deeply devoted to Sally,



Jerry Lingrel was an associate editor of the *Journal of Biological Chemistry* for 28 years.

his wife of 60 years, and to his children, Doug and Lynne. His devotion and loyalty extended to colleagues who worked in his laboratory, department and university, and indeed around the world. Shortly after his death, Sally told us that hundreds of daffodils Jerry had planted were blooming in their yard. This image reminds us of the great good that one individual can do on his journey from a farm boy to a leading scientist and educator — a flowering that transcends death and that lives in all who have had the privilege of knowing him. He will be greatly missed.

“No bubble is so iridescent or floats longer than that blown by the successful teacher” — William Osler

All who contributed to this narrative were Jerry’s trainees and knew him at a deep and personal level over many decades as a teacher, colleague and friend. While our zone of comfort is writing scientific papers guided by data, writing this retrospective was guided by emotions and memories. This is a final act of gratitude to Jerry, our teacher, whose influence on our scientific and personal success cannot be expressed in mere words.

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Upcoming ASBMB events and deadlines

JUNE

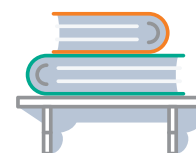
1–30 2020 ASBMB Annual Meeting virtual content: Visit asbmb.org/meetings-events/2020-annual-meeting for a full schedule

JULY

1 Deadline to vote in ASBMB Election

1–7 2020 ASBMB Annual Meeting virtual content: Visit asbmb.org/meetings-events/2020-annual-meeting for a full schedule

10 Virtual meeting: Best practices in online teaching for BMB classrooms



ASBMB

Michael J. O. Wakelam (1955 – 2020)

By Valerie B. O'Donnell & Edward A. Dennis

Robin F. Irvine, Dan Raben, Friedrich Spener and Shankar Subramaniam provided vignettes included in this article.

Michael Wakelam, a noted British biochemist, institute director and associate editor of the *Journal of Lipid Research*, who pioneered studies into elusive signaling lipids in health and disease including developing innovative ways to measure them, died March 31 in the United Kingdom.

Education and career

Michael was born July 15, 1955. Following his secondary education, he attended the University of Birmingham, graduating in 1977 with a B.Sc. in medical biochemistry. He stayed on at Birmingham for his Ph.D., graduating in 1980. During this time, Michael met Jane Fensome, who became his wife in December 1980. After his Ph.D., Michael moved with Jane to Konstanz, Germany, for postdoctoral studies, followed by a return to London in 1983 on a Beit Memorial Fellowship.

Michael worked in the department of biochemistry at Imperial College until 1985, when he moved to the University of Glasgow as a lecturer. He returned to Birmingham as a professor of molecular pharmacology in 1993 and was based there until 2006, when he moved to the



COURTESY OF SIMON RUDGE

Michael Wakelam works in his laboratory at Birmingham University in 2006 with one of his beloved mass spectrometers. This photo was taken for a press release, most likely that announcing his move to the Babraham Institute.

Babraham Institute, Cambridge, as institute director. During this time, Jane and Michael welcomed their sons, Alex and Patrick, into the world.

The Biochemical Society awarded Michael the Morton Award Lectureship in 2018 for outstanding contributions to research in lipid biochemistry. He was elected a member of the Academia Europaea in 2019.

Reflections on ^{32}P , IP_3 and mass spectrometry

During Michael's time in Germany, he became interested in lipids because of his work on the sugar molecule inositol, the headgroup for phosphoinositide phospholipids. Measuring inositol phosphates was not trivial and required ^{32}P -labeled IP_3 , which was generated from red blood cell ghosts (as invented by Peter Downes). But the ^{32}P half-life of

two weeks was an issue, and Michael had to keep generating new batches before using up the previous one. When Michael and Robin Irvine met up in London in the mid-1980s, they discovered both were making the same thing, and from then on they coordinated their efforts; each time one made a batch, they would split it and send half to the other, which cut the number of times they made batches by half. The thought that they were happily sending ^{32}P through the post makes Robin a little wobbly at the knees now.

Michael continued his work on inositols after his move to Glasgow. He made several seminal discoveries, including that diacylglycerol is generated from phosphatidylcholine. Working with Susan Pyne (then Palmer), he developed a mass assay for IP₃, which subsequently was marketed by Amersham. Michael's lab was known for being exciting, vibrant and hardworking. His infectious passion for research abounded, and results were discussed over beers on Byres Road almost in real time.

When Michael returned to Birmingham in 1993, he had moved fully into lipid mass spectrometry, leaving behind thin-layer chromatography for new approaches that produced unprecedented information about how lipids behave in cells, particularly in cancer. He developed state-of-the-art methods that enabled key discoveries concerning the roles of PLD1 and PLD2 in signaling, uncovering the role of the PH domain in PIP2 regulation. He published seminal papers in the *Journal of*

Lipid Research and Nature Methods, describing methods for phosphoinositide analysis that included crucial steps that stabilized the molecules sufficiently for MS analysis.

Importance of scientific conferences

Michael enjoyed scientific meetings with other lipidologists, many of whom were close collaborators and friends. During a 1998 Keystone symposium on lipids in Taos, New Mexico, Michael and Robin Irvine set out to go skiing, but neither could ski so they decided to hire snowshoes and go for a hike high in the mountains instead. Michael no doubt enjoyed the sunshine and snow while talking science with colleagues. We will remember him for his wonderful sense of humor and

friendliness; he always was laughing.

Michael and Dan Raben shared an interest in signaling lipids and regulation of their enzymes. The two met at American Society for Biochemistry and Molecular Biology annual meetings, the Lipid Gordon Research Conferences, and Federation of American Societies for Experimental Biology conferences, where the excitement of their scientific discussions was complemented by Michael's humor and caring demeanor. Dan always will remember Michael's enthusiasm, intelligence and generosity of scientific spirit.

Michael was also a scholar. His deep-rooted interest in philosophy of science led him to read up on the conceptual foundations of quantum mechanics. One of his last passions was discussing with his colleagues

COURTESY OF ROBIN IRVINE



Michael Wakelam (right) went snowshoeing with fellow conferees at the Keystone Symposium on Signal Transduction and Lipid Second Messengers in Taos, New Mexico, in 1998.

COURTESY OF EDWARD DENNIS



The first meeting of the LIPID MAPS International Lipid Classification and Nomenclature Committee was held in July 2006 in La Jolla, California. Pictured, from left to right, are Christian Raetz, Masahiro Nishijima, Takao Shimizu, Eoin Fahy, Edward Dennis, Manish Sud, Michael Wakelam, Fritz Spener, Robert Murphy, Yousuke Seyama, Gerrit van Meer and Shankar Subramaniam.

the philosophical foundations of the field, having read “Are Quanta Real” by J.M. Jauch during a systems biology conference in Crete in 2019. Discussions (particularly with Shankar Subramaniam, who introduced him to the book) went on late into the evening.

Babraham onward and LIPID MAPS

In 2007, Michael became director of the Babraham. He was motivated to take this role by both the challenge of leading a large institute and proximity to cutting-edge phosphoinositide researchers who could benefit from his analytical capabilities. He successfully juggled multiple roles, including rapidly developing a campus with a significant industrial footprint while overseeing a successful lipidomics facility. Colleagues at Babraham, including Wolf Reik, Simon Rudge, Phillip Hawkins, Len Stephens and Simon Cook, remem-

ber Michael as a terrific role model who lived for his research and the good of the wider institute as well as a consensus seeker who used his emotional intelligence to great effect and hardly ever overruled others.

Michael became heavily involved in the lipidomics movement around the time he moved to Babraham. According to Fritz Spener of Graz, Austria, who shared with us an obituary he wrote with Christian Wolfrum and Wolf Reik for *Nature Metabolism*, “Editorials about lipidomics appeared in Europe in 2003, but when news arrived from the U.S. that under Ed Dennis’ leadership the huge Lipid Metabolites and Pathways Strategy, or LIPID MAPS, project was granted, this started a major undertaking. In response, Michael helped convince the Directorate General 12 of the European Union to solicit applications for a large collaborative project on high-throughput analysis

of lipids and lipid–protein interactions in mammalian cells.” Then Michael’s group and 20 other investigators submitted a successful application for the LipidomicNet project in 2008.

Spener shared that the project’s coordinator dubbed Michael and other LipidomicNet leaders the “Viennese Coffee Club” because their sometimes diverging opinions led to hilarious and, in the end, fruitful discussions. For example, Viennese Coffee Club members got irritated with literature reporting incorrect MS data, as the levels of structural elucidation claimed for lipid species were not in accord with the existing instrumental resolving power. As a result, a shorthand annotation for the correct presentation of lipid MS data was developed and published in the *Journal of Lipid Research* in 2013 with Michael as senior author. This publication subsequently was adopted by the LIPID MAPS



The first meeting of the LIPID MAPS Wellcome Trust principal investigators (front row) and the International Lipid Classification and Nomenclature Committee was held in the Cardiff Castle in Cardiff, U.K., in March 2017. Pictured in front, from right to left, are Michael Wakelam, Edward Dennis, Valerie O'Donnell and Shankar Subramaniam; in back are Takao Shimizu, Fritz Spener, Marcus Wenk, Al Merrill, Robert Murphy and Eoin Fahy.

International Lipid Classification and Nomenclature Committee, or ILCNC.

The LipidomicNet project strengthened E.U.–U.S. relations; European researchers, among them Michael, took on active roles in the ILCNC and were invited to be co-authors of two fundamental classification papers published in the *Journal of Lipid Research* in 2005 and 2009. By 2013, though, the LipidomicNet grant from the EU had ended, and the long-running LIPID MAPS grant in the U.S. was ending as well.

Michael and Valerie O'Donnell from Cardiff University teamed up with Ed Dennis and Shankar Subramaniam from the University of California, San Diego, to secure a follow-up LIPID MAPS grant from the British Wellcome Trust in 2017. This was a big relief for lipidologists, in particular those involved in lipidomics; this grant safeguards and further

develops not only the informative website but also precious databases. Certainly, the competence of managing big databases at Babraham is an asset, as was Michael's relation to the European Bioinformatics Institute in Cambridge.

When the grant was funded, Michael's reaction was to say, "That is absolutely brilliant! Well done, Valerie."

As part of the new funding, the LIPID MAPS databases were moved to Babraham. Michael's input was essential, providing the new informatics home for the project and working closely with Valerie O'Donnell, Edward Dennis, Shankar Subramaniam and the ILCNC advisory committee. Michael was intimately involved in planning the next renewal cycle for the LIPID MAPS grant to the Wellcome Trust.

Michael had planned to step down from the Babraham director-

ship in late 2020, and we were excited that this would allow Michael to get back in the lab and spearhead the LIPID MAPS renewal application. It feels especially tragic for us all that Michael won't be part of our next phase of LIPID MAPS.

*Note: Edward Dennis and Valerie O'Donnell also have published a memorial article about Michael Wakelam in the *Journal of Lipid Research*.*

Valerie B. O'Donnell (O-DonnellVB@cardiff.ac.uk) is co-director of the Systems Immunity Research Institute at Cardiff University, U.K.



Edward A. Dennis (edennis@ucsd.edu) is a distinguished professor of chemistry and biochemistry, and of pharmacology and chancellor and chair in chemistry and biochemistry at the University of California, San Diego.



A mechanism for remdesivir activity and a platform to test other antivirals

Public–private research partnership between Gilead, Canadian scientists reveals a key residue in the SARS-Cov-2 polymerase

By *Laurel Oldach*

Researchers who showed in February that remdesivir blocks coronavirus polymerases are reporting in the **Journal of Biological Chemistry** that the finding also applies to the novel coronavirus — and they think they can explain the molecular mechanism for how the drug gums up the virus’ gears.

In their earlier paper, graduate student Calvin Gordon and professor Matthias Götte of the University of Alberta and co-authors demonstrated that remdesivir can inhibit the viral replicase of the coronavirus that causes Middle East Respiratory Syndrome, or MERS. The study included co-authors from Gilead Sciences, the company that makes the drug.

In the ensuing months, remdesivir, an adenosine-mimicking nucleotide analog developed to treat other viruses, has emerged as the most promising small-molecule treatment for COVID-19. In late April, the National Institute for Allergy and Infectious Diseases reported qualified success of a clinical trial of the drug,

and the FDA rapidly issued emergency use authorization for the drug.

Now, using enzymes from the novel coronavirus SARS-nCoV-2 itself instead of the related virus that causes MERS, the research team has shown that remdesivir blocks the SARS-nCoV-2 replicase in a test tube. They also examined a selection of other nucleotide analogs to understand more about whether and how each might work against infection.

The Götte lab studies viral enzymology, and Götte has developed a system for expressing large quantities of viral polymerases from insect cells to enable rapid enzymology studies, informed by a World Health Organization pandemic-preparedness blueprint, which regularly updates a list of the most concerning pathogens. “Coronaviruses like SARS and MERS were always on the list,” Götte said.

Most graduate students don’t finish a paper in their first year in the lab — let alone two papers. Calvin Gordon, a first-year graduate student at the University of Alber-

ta in Edmonton, joined the lab in September 2019. When he began the MERS study in October, the risk of a pandemic was still theoretical. By the time the authors were ready to write up their finding that the MERS polymerase easily incorporates remdesivir but stumbles to a halt a short time later, the first cases of COVID-19 had been reported in Hubei province, China. And by the time they published the discovery, Italy was in lockdown and cases had been reported in both the U.S. and Canada.

As soon as the first SARS-CoV-2 genome was published in January, Egor Tchesnokov, a research associate in the lab and co-first author on the new paper, got to work cloning it into their expression system and preparing to test remdesivir’s effect on those enzymes. Their new study, published in April, confirms that, as it did in MERS, the drug works against the enzyme complex the novel coronavirus uses to replicate its genome. This time, thanks to a molecular modeling study run by Gilead’s Jason Perry, the authors



A cartoon rendition shows how remdesivir stops forward motion by the polymerase from the novel coronavirus.



GILEAD SCIENCES

Workers in a manufacturing facility at Gilead produce remdesivir.

are able to explain how it happens.

Using the crystal structure of the polymerase enzyme from another coronavirus — as it happened, researchers from China and Australia published a cryo-EM structure of the novel coronavirus’ replicase on the same day as the second Götte study — and a crystal structure showing how a hepatitis virus enzyme interacts with remdesivir, Perry and other researchers at Gilead put together a computational model of how remdesivir fits into the active site of the novel coronavirus’ replicase.

“As the enzyme incorporates one, two, three more nucleotides, the incorporated remdesivir moves back, so to speak,” Götte said. As it reaches the third position away from the enzyme’s active site, the drug encounters — or causes — a blockage. Because of its unusual 1’ modification, it crashes into a specific amino acid, a serine conserved among most coronavirus polymerases, which prevents the enzyme from moving one step forward to incorporate the next RNA base.

“It’s not perfect chain termination; there’s a little read-through,” Götte said. “The specific wish would be to see whether there’s any other

nucleotide (analog) out there that would cause a stronger termination.”

To find out, the researchers assessed the effect of a variety of other known nucleotide analogs — some of which are in clinical trials — on the viral polymerase. This allowed them both to pinpoint the effect of the drug on a chemical modification at the 1’ in its ribose by comparing the features of molecules that did and did not inhibit the polymerase and to make some predictions about other nucleotide analog drug candidates.

For example, they found that, unlike polymerases from other viruses, the enzyme did not recognize drugs with a 2’ ribose modification as RNA building blocks. For a drug to inhibit the viral replicase, the replicase must recognize it as a building block of new RNA, and for realistic dosing, it’s best if the enzyme picks up the drug more easily than the drug’s natural counterpart. The researchers found that the SARS-CoV-2 polymerase does not prefer a Gilead drug for hepatitis, sofosbuvir, to its natural counterpart, UTP. In a competition assay, Götte said, “UTP wins, by far. So it is very unlikely based on our data that we would expect potent antiviral activity from sofosbuvir.”

They also investigated the influenza drug favipiravir, which is being

tested in fifteen clinical trials around the world for efficacy as a COVID-19 treatment. Like sofosbuvir and remdesivir, favipiravir is a nucleotide analog that has been shown to inhibit other RNA viruses. However, as with sofosbuvir, the SARS-CoV-2 polymerase showed strong selectivity for the natural ribonucleotide over favipiravir, raising some concern about whether favipiravir will have antiviral activity against the new coronavirus. Götte said, “I think it’s very important to reconcile the biochemical data with antiviral data.”

Whether or not remdesivir proves to be an effective treatment for COVID-19, the researchers hope their enzyme platform will help speed up assessment of novel drug candidates as they are developed. They also plan to seek therapeutic combinations of nucleotide inhibitors and drugs with other mechanisms, which could reduce the chances that resistance will develop, Götte said.

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More than skin deep

Novel bacterial lipase structure may lead to new acne treatments

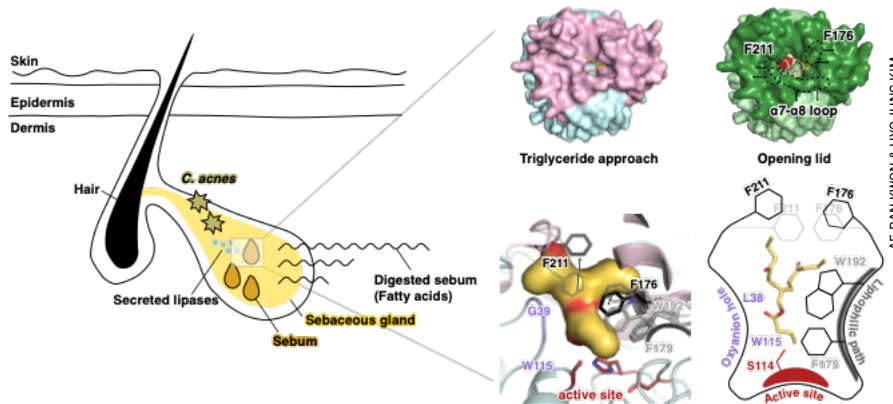
By Nathalie Gerassimov

Acne can have an enormous social and emotional effect on the 85% of adolescents and 40% of adults who have it. Hyo Jung Kim and colleagues in the Republic of Korea recently published a paper in the **Journal of Lipid Research** describing the molecular structure of a key enzyme involved in the skin disorder. This research has the potential to pave a path for new acne treatments.

The top two skin layers are the epidermis, forming the waterproof barrier, and the dermis, consisting of hair follicles and sweat glands surrounded by connective tissue. In the dermis next to hair follicles are sebaceous glands that secrete sebum, a complex mixture of lipids including triglycerides and their derivatives. Acne is chronic inflammation of the sebaceous follicles, resulting in skin elevations such as papules, pustules and cysts that can lead to scarring.

Research into causes of acne focuses on *Cutibacterium acnes*, a Gram-positive bacterium typically found on healthy human skin, where it helps block pathogens. Specifically, *C. acnes* secretes lipases that break down lipids in the sebum and release fatty acids that form a protective layer on the skin surface. However, *C. acnes* colonization of inflamed sebaceous follicles contributes in an as-yet-unknown way to the development of acne.

Recent research supports the idea that acne is caused by imbalances in the *C. acnes* subtypes and their respective lipases. Specifically, *C. acnes* type I subclass, called IA, is associ-



Acne research focuses on strains and types of *Cutibacterium acnes* and their lipase secretion and activity. South Korean researchers solved the structure of a highly conserved *C. acnes* lipase.

ated strongly with acne and displays higher lipase secretion and activity than *C. acnes* type II, which is associated with healthy skin. Excessive production of fatty acids can promote inflammation, so differences in lipase secretion and activity could be a major driver in acne development.

In this study, the investigators solved the structures of *C. acnes* type II lipase by X-ray crystallography in three states: closed, blocked and open. Corresponding author Ae-Ran Kwon explained the research strategy: “The structures solved by X-ray crystallography are often compared to still images. Once you combine several images together you can extract information analogous to a moving animation, so you can see how the protein works.”

Specifically, the researchers found a novel active site gating mechanism, with two key phenylalanine residues forming a lid on top of the active site that controls lipase activity. Since this lipase is highly conserved across *C. acnes* subtypes, this research also applies to the acne-associated IA.

Acne treatments such as benzoyl peroxide, retinoid and antibiotics focus only on symptoms and can have undesirable side effects. Kwon, Kim and colleagues at Daegu Haany University and Woosuk University are working to design compounds that selectively block this lipase.

“Since the lipase is secreted protein, this can be a good target for topical treatment,” Kim said. “We can limit the application area to a local site of infection.”

Kim recalled suffering from mild acne breakouts when she felt stressed as a teen. “I would get so self-conscious, lose confidence in face-to-face conversation and even postpone my dates,” she said.

She is confident about the high market demand for improved acne treatments.

DOI: 10.1194/jlr.RA119000279

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AE-RAN KWON & HYO JUNG KIM

How post-translational modifications affect the DNA sensor cGAS

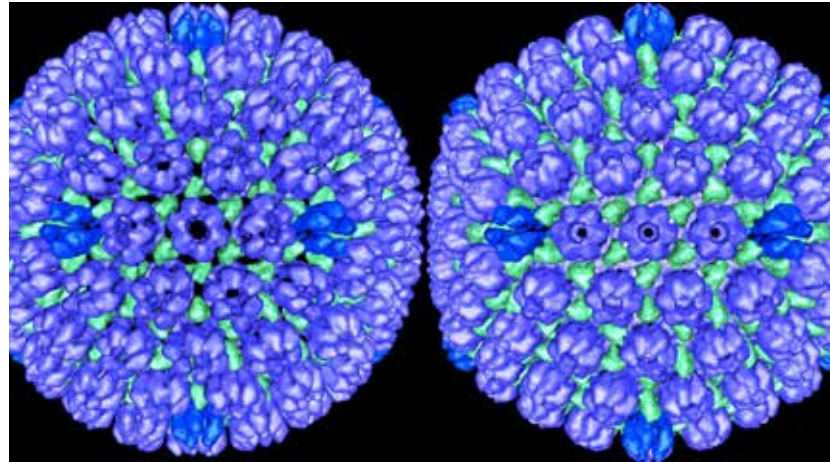
By John Arnst

When a pathogen finds its way inside the human body, the innate immune system springs into action, thanks to pattern-recognition receptors that pick up on molecular patterns associated with the pathogen's genetic material and the damage that they cause. While one of these DNA sensors, cyclic GMP-AMP synthase, or cGAS, has been characterized in recent years as a key part of an immune signaling axis that upregulates the cytokine type I interferon, the role that factors including post-translational modifications play in its recruitment and activation have remained unclear.

To figure out how PTMs regulate cGAS, a laboratory at Princeton University led by Ileana Cristea has identified and functionally analyzed phosphorylations and acetylations of cGAS in various cell types. They published their findings in the journal **Molecular & Cellular Proteomics**.

"I am fascinated by our co-evolution with the diverse array of viral pathogens that are part of our ecosystem," said Cristea, whose research involves the proteomics of host-virus interactions. "A growing body of evidence points to post-translational modifications as modulators of DNA sensor functions, but this area of investigation is still in early stages, so we aimed to expand the understanding of the cGAS PTM landscape and of how these PTMs impact the ability of cGAS to induce immune responses and apoptosis."

The researchers enriched cGAS by applying immunoaffinity purification



The image on the left is the outer protein shell of the herpes simplex virus type 1, the virus that causes cold sores. The image on the right is the mature capsid of the same virus, which Ileana Cristea and her colleagues at Princeton University have used to examine the effect of post-translational modifications on the DNA sensor cGAS.

to THP-1 macrophage-like cells, STING-HEK293T cells that had been immune-stimulated and human primary fibroblasts before and after the cells were infected with herpes simplex-type I virus, finding a total of six phosphorylations and eight acetylations. To assess the functional relevance of each of these PTMs, Cristea's lab then generated a series of single-point cGAS mutations in stable cell lines constructed to express cGAS with amino acid substitutions that would either present phosphorylation and acetylation or that mimicked the modified states.

They found that an acetyl-mimic mutation at Lys198, where lysine was swapped to glutamine, increased cGAS-dependent interferon signaling compared to a control, and they showed that two acetyl-mimic mutations at Lys384 and Lys414 can inhibit the ability of cGAS to induce apoptosis. The researchers also found,

through parallel reaction-monitoring mass spectrometry, that acetylation of Lys198 decreases during infection with both HSV-1 and human cytomegalovirus, which highlights the residue as a regulatory point during virus infection.

"This area of immunity has advanced significantly with the recent identification of different DNA sensors," Cristea said. "Next we need to determine their unique and redundant functions and whether they evolved to recognize diverse pathogens in a biological state- or tissue-specific manner. This information is critical for understanding human immunity, autoimmune disorders and our ability to combat infections."

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BERNARD HEYMANN/NIH

From the journals

By Himanshi Bhatia, Arti Dumbrepatil, & Anand Rao

We summarize a selection of recent papers from the **Journal of Biological Chemistry**, the **Journal of Lipid Research** and **Molecular & Cellular Proteomics**.

Nonspecific nicking by Cas12a

The discovery of the CRISPR-based genome editing system has driven innovation in personalized medicine and incited increased scrutiny of the precision and specificity of the methodologies being employed. Cas12a, an RNA-guided endonuclease in the bacterial type V-A CRISPR-Cas anti-phage immune system, recently has emerged as an alternative gene-editing tool capable of binding and cutting double-stranded DNA targets with high specificity, but this described specificity is paradoxical to the function of Cas12a as an immune responder fighting against rapidly evolving pathogens.

Using high-throughput cleavage assays, Karthik Murugan of Iowa State University and colleagues observed widespread cuts to single strands of double-stranded DNA, known as nicking, and found that these nicks occur nonspecifically when Cas12a binds to a target DNA.

Their results, which appear in a recent paper in the **Journal of Biological Chemistry**, provide important details about the natural role of Cas12a and demonstrate its potential for nonspecific editing.

DOI: 10.1074/jbc.RA120.012933

Cholesterol and the ABCs of ATP signaling

The extracellular signaling of ATP is implicated in a variety of important physiological and pathophysiological roles, but the mechanisms responsible for regulating ATP release are not well understood. Researchers at Yale University are helping to solve this mystery by identifying a link between cholesterol and the release of ATP.

In a paper published in the **Journal of Biological Chemistry**, Patrick Dunn and colleagues used hypotonic conditions to induce ATP release by volume-regulated anion channels in HEK-293 cells and mouse cerebellar granule neurons. They then performed a gain-of-function screen for modulators of ATP release and identified two ATP-binding cassette subfamily G member 1 variants as modulators. These transporters are involved in regulating cellular cholesterol, suggesting that how cells handle cholesterol may affect their extracellular signaling. The authors tested this by using methyl-beta-cyclodextrin to deplete cellular cholesterol levels, resulting in ATP export.

These findings raise interesting questions, such as whether individuals afflicted with cholesterol-linked diseases present with abnormal extracellular ATP release, and the results could be instrumental in developing improved therapeutic regimens for the treatment of cholesterol-related maladies.

DOI: 10.1074/jbc.RA119.010699

The evolutionary emergence of PD-L2

The programmed cell death 1, or PD1, receptor ligands PD-L1 and PD-L2 are transmembrane proteins that play critical roles in modulating immune system activation. However, little is known about the specific function of each ligand and when their roles differentiated.

In a paper recently published in the **Journal of Biological Chemistry**, Elliot Phillips of New York University School of Medicine and collaborators explore what makes PD-L2 unique and describe its moment of evolutionary divergence. Using site-directed mutagenesis, surface plasmon resonance and crystallography, the authors identified an unexpected loss- and gain-of-interaction mutations that resulted in structural differentiation from PD-L2 without affecting function. But why did this protein diverge structurally without an alteration in function? The authors use phylogenetic analysis to answer this question, revealing that the new structural features appeared simultaneously with the emergence of placental mammals. Their results suggest that the emergence of PD-L2 from PD-L1 may be important to immune system adaptations required for placental gestation.

DOI: 10.1074/jbc.AC119.011747

Getting oxidized nucleotides out of the pool

Human MuT homologue 1, or MTH1, reduces genotoxicity by removing oxidized nucleotides from the nucleotide pool to prevent their

Handing over heme for degradation

Heme is a ring-shaped complex formed by four pyrrole molecules that bind iron, and it is an indispensable oxygen-carrying component of hemoglobin in blood and myoglobin in muscle cells. The breakdown of heme into biliverdin, carbon monoxide and iron plays a number of important physiological roles. Biliverdin is a precursor to bilirubin, a natural antioxidant, and endogenous carbon monoxide is a vasodilatory gas that has anti-inflammatory properties. Furthermore, heme itself at high concentrations can be toxic, promoting oxidative stress and lipid peroxidation. Thus, regulating heme levels is critical for human health, but the mechanisms responsible for signaling its degradation are not well known.

Human heme oxygenase-2, or HO2, is an enzyme that converts heme to biliverdin when heme binds to the enzyme's core catalytic active site. HO2 also contains two short amino acid sequences known as heme regulatory motifs, or HRMs, that can bind iron-containing heme and are involved in governing heme function.

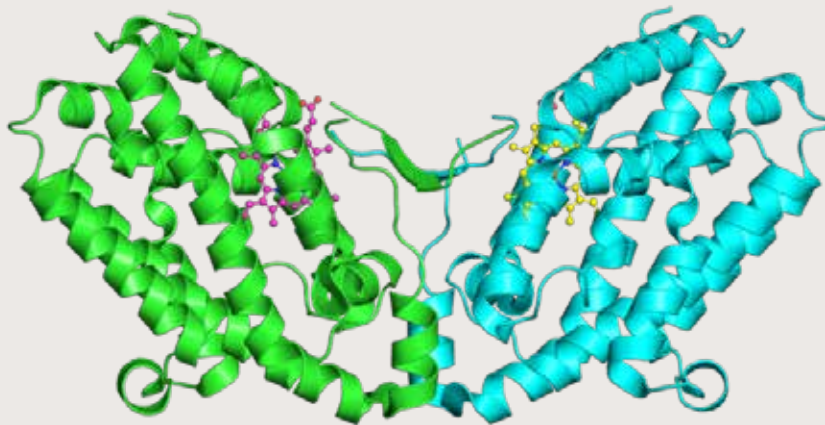
In a recent paper in the *Journal of Biological Chemistry*, Angela Fleischhacker and colleagues at the University of Michigan School of Medicine write that they have detected a protein-mediated transfer of heme between the HRMs and the HO2 core. Using hydrogen–deuterium exchange mass spectrometry, the authors monitored the dynamics of HO2 with and without iron-containing heme bound to the HRMs and to the catalytic core, and they detected conformational changes in the core only when it was in an unbound state. Moreover, the researchers observed heme being transferred to the core from the HRMs and vice versa, achieving equilibration.

Based on these findings, the authors present a new heme transfer model that ascribes functional significance to heme binding of HRMs in addition to the catalytic site on HO2. They suggest that this mechanism may be essential for toggling between the degradation and maintenance of physiological heme levels.

DOI: 10.1074/jbc.RA120.012803

—Anand Rao

MASAKAZU SUGISHIMA, YAMAGATA UNIVERSITY



This image shows the crystal structure of heme oxygenase-2 in complex with heme.

incorporation into the genome. MTH1 also actively removes nucleotides that have undergone methylation, a post-translational modification. This is an important feature because, if allowed to incorporate into the DNA, methylated nucleotides could have detrimental effects on cellular epigenetic programming.

Using mutant zebrafish, crystallography, mass spectrometry and enzyme kinetic assays, Emma Rose Scaletti of Stockholm University and collaborators demonstrate that

MTH1 catalyzes the hydrolysis of N6-methyl-dATP to N6-methyl-dAMP to prevent its incorporation into DNA. The authors also identify the structure of N6-methyl-dAMP-bound human MTH1, revealing why N6-methyl-dATP is a good MTH1 substrate.

Their work, published in the *Journal of Biological Chemistry*, reveals a mechanism that helps to prevent the impaired regulation of epigenetic control and RNA metabolism.

Lipid swaps alter membrane nanodomains

The plasma membrane has a highly asymmetric distribution of lipids and contains dynamic nanodomains surrounded by a different liquid microenvironment. These nanodomains play a role in the vital functions of cells and organisms. However, researchers do not yet understand how these liquid-ordered lipid domains, or rafts, in the plasma membrane are formed, which limits study of their biological functions.

Metabolic labeling of bacterial membranes

Continuous use of antimicrobial drugs in medicine, agriculture and aquaculture to treat or prevent infections has led to the emergence of multidrug resistance, or MDR, in both humans and farmed animals. Pathogenic bacterial species that have acquired MDR cause infections that are effectively untreatable and present a serious threat to public health.

Gram-negative bacteria are intrinsically resistant to many antibiotics because of their unique membrane architecture. Phospholipids, or PLs, constitute the inner layer of the outer membrane, or OM, while the outer layer is composed of lipopolysaccharides. The OM's strict asymmetry functions as a permeability barrier, protecting the cells from the immune system as well as blocking many toxic compounds. This barrier affects drug screening-related research and generally results in a low hit rate when screening compound libraries. Consequently, identifying effective new antibiotics or small-molecule inhibitors against Gram-negative bacteria has been a major challenge. Existing assays to identify a compromised OM by detecting bacterial

PLs are indirect, low-throughput and labor-intensive.

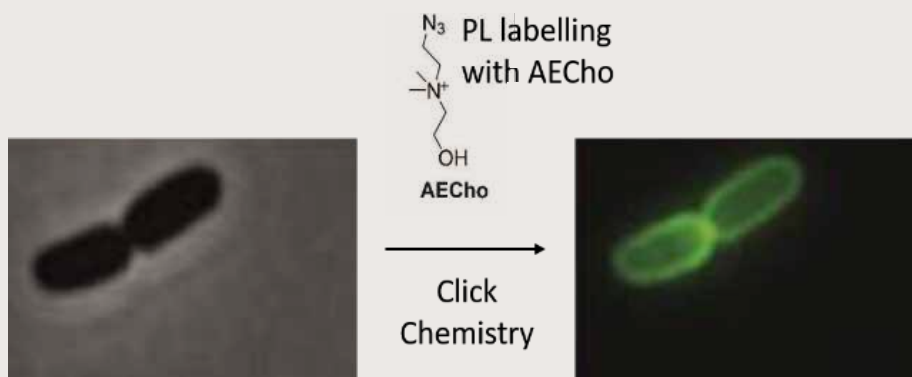
Inga Nilsson and an international team of researchers from the Novartis Institutes for BioMedical Research have used metabolic labeling to detect a compromised OM in intact bacteria. Naturally occurring Escherichia coli lipids are difficult to label, so the researchers explored phosphatidylcholine, or PC, labeling by fluorescent click reagents, because PC is present in most pathogenic bacteria. Their recent study published in the *Journal of Lipid Research* showed successful metabolic labeling of cellular PC with 1-azidoethyl-choline to visualize phospholipids in intact E. coli cells with a biorthogonal fluorescent method.

In the future, this assay could be used to identify compounds that interfere with OM lipid asymmetry, thus facilitating the discovery of new antimicrobial compounds. The authors suggest that it can be scaled up to a medium- to high-throughput whole-cell screening assay for OM asymmetry, phospholipid externalization and OM permeability defects.

DOI: 10.1194/jlr.RA12000654

—Arti Dumbrepatil

ADAPTED FROM NILSSON ET AL./JLR



Escherichia coli cells are grown with 1-azidoethyl-choline and treated with Alexa488-sDIBO to allow fluorescent detection.

A research team led by Guangtao Li at Stony Brook University write in their latest study in the *Journal of Lipid Research* that the propensity of plasma membranes to form ordered domains can be modulated by membrane lipid substitutions. To understand the properties of plasma membrane lipids and proteins, the researchers generated giant plasma membrane vesicles, or GPMVs, in mammalian cells, which represent a natural membrane system. GPMVs are easier to investigate for

domain-forming properties than intact cells. This study improves understanding of the inherent ability of plasma membrane lipids to form ordered nanodomains and implies that lipid substitutions in nanodomains can be used to alter biological processes. With further research, insights from this research could be applied to enhance the utility of lipid exchange as a method to probe the functions of membrane domains in living organisms.

DOI: 10.1194/jlr.RA119000565

Reducing cholesterol in a corneal disease

Schnyder crystalline corneal dystrophy, or SCD, is a rare disease characterized by deposits of cholesterol and phospholipid in the cornea. Most cases of SCD lack an obvious systemic disorder, but high cholesterol levels are common. As SCD progresses, an opaque disc of corneal crystals or other lipids forms, resulting in impaired vision and ultimately in the need for a corneal graft.

SCD is caused by mutations

Algorithm identifies active kinases for AML treatment

Acute myeloid leukemia, or AML, is a cancer of the bone marrow and blood that progresses rapidly if left untreated. An estimated 19,000 new cases will be diagnosed this year with a five-year survival rate of 28.1%. Small-molecule kinase inhibitors are a potential treatment strategy for AML patients. However, due to molecular heterogeneity in AML, no single molecule has been clinically effective.

In their recent study published in the journal **Molecular & Cellular Proteomics**, Carolien van Alphen and colleagues at the Amsterdam University Medical Center relied on an integrative inferred kinase activity, or INKA, algorithm to identify prospective small-molecule kinase inhibitors. For each given kinase, INKA performs a four-component analysis by determining the phosphorylation status of the kinase itself, its activation loop and all its possible substrates. INKA assigns a nonzero score to kinases with both kinase-centric and substrate-centric phosphorylation status.

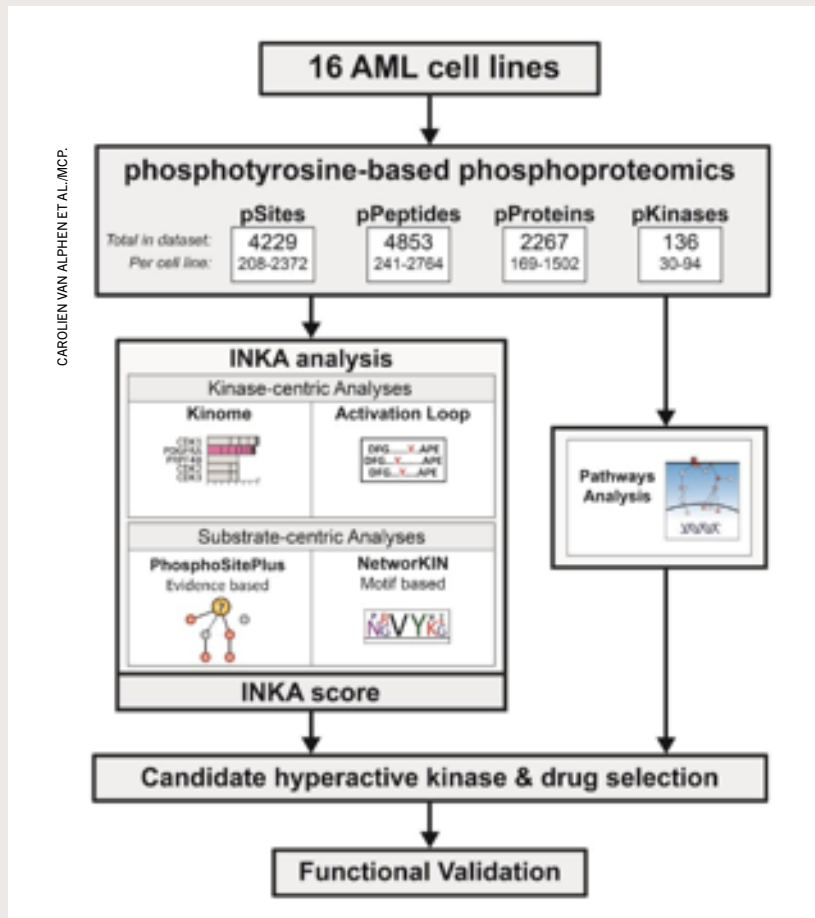
A panel of 16 AML cell lines was chosen for pY-phosphoproteom-

ics combined with INKA analysis to identify hyperphosphorylated active kinases. Due to the heterogeneous signaling in these cell lines, the analysis identified multiple phosphopeptides. INKA analysis of individual cell lines identified specific driver kinases, including PDGFRA, JAK2, KIT and FLT3. Using this approach, the researchers identified and functionally verified active tyrosine kinases in 10 cell lines. For the remaining six cell lines without a tyrosine kinase driver, they identified MAPK signaling as a potential drug target.

The authors concluded the study by applying their analytical strategy to clinical samples. Despite the lower amount of input sample, phosphoproteomic and INKA analysis identified similar driver kinases in patient samples to those in the cell lines. The in-depth analysis performed in this study provides a basis for future clinical applications for personalized treatment of AML patients.

DOI: 10.1074/mcp.RA119.001504

—Himanshi Bhatia



This schematic representation shows INKA analysis for a panel of acute myeloid leukemia cell lines.

in the gene encoding UbiA prenyltransferase domain-containing protein-1, or UBIAD1. The disease is characterized by inhibition of the SCD-associated UBIAD1 degradation via the endoplasmic reticulum-associated degradation pathway. This significantly contributes to the dysregulation of cholesterol synthesis. A new study published in the **Journal of Lipid Research** sheds light on the SCD etiology and its importance in improving the efficacy of cholesterol-lowering statin therapy, for which the major limitation is the UBIAD1-mediated dysregulation of cholesterol synthesis. A multidisciplinary team at the University of Texas Southwestern Medical Center led by Dong-Jae Jun postulates that accumulation of SCD-associated UBIAD1 via sequestration in the ER results in a buildup of cholesterol. Identification of agents that accelerate the degradation of SCD-associated UBIAD1 may help to prevent cholesterol accumulation and the corneal opacity associated with SCD.
DOI: 10.1194/jlr.RA119000551

(Laser)-capturing the substantia nigra proteome

Many challenges hinder the analysis of tissue sections, including their heterogeneous nature and limited cell numbers in distinct cell populations. Laser capture microdissection, or LCM, is a technique that purifies small cell populations from mixed samples. In a study published in the journal **Molecular & Cellular Proteomics**, the authors present a

detailed workflow for LCM-based proteomic analysis of the substantia nigra, a region of the brain rich in dopaminergic neurons and implicated in Parkinson's disease. The authors have unraveled the substantia nigra proteome using limited quantities of tissue samples.

Eva Griesser and colleagues at the University of Dundee, U.K., first optimized their protocol for isolating proteins from tissue samples. They performed comparative analysis for testing LCM efficiency in five healthy donors who each provided intact tissue and 3,000 cells, which were isolated with LCM. Bioinformatic analysis identified neuron-specific proteins and gene ontology, or GO, cellular components to be enriched in the microdissected samples.

Application of this optimized protocol to the substantia nigra from 15 healthy donors identified 5,677 protein groups with GO terms ranging from substantia nigra development and neurotransmitter secretion (high intensity) to lysosome and trans-Golgi network (low intensity). This methodology will facilitate proteomic analysis of different brain regions in the course of neurodegenerative disorders.
DOI: 10.1074/mcp.RA119.001889

Promiscuous binding in motor neuron disease

Arginine-based dipeptide repeat polymers, or DPRs, are a unique characteristic of motor neuron disease, or MND. Among the abnormally expressed DPRs in patient

brains, proline-arginine, or poly-PR, and glycine-arginine, or poly-GR, exhibit greater levels of cellular toxicity. The toxicity has been attributed to repeat-associated non-AUG-initiated translation that results in production of abnormal translation products of varying lengths. While it is reported that these polymers stall the ribosomal translation machinery and ribosome biogenesis, not much is known about the identity of the affected proteome. For a recent study published in the journal **Molecular & Cellular Proteomics**, Mona Radwan and colleagues at the University of Melbourne, Australia, performed whole proteomic profiling to probe the interacting partners of these toxic polymers of varying lengths.

Using a combination of immunoprecipitation, mass spectrometry and green fluorescent protein-labeled peptides, the authors identified multiple cellular pathways through which Arg-rich polymers manifest cellular toxicity. The affected protein machinery for poly-PR and poly-GR ranged from cytoskeletal proteins to arginine methylases PRMT1 and PRMT5, which was in striking contrast to the partners of inert polymers like poly-GA. The effect was further pronounced with varying lengths of these polymers, with 101x DPRs inducing marked ribosome stalling and toxicity. These insights into the multiple pathophysiological mechanisms inherent in MND pave a path for deeper understanding of neurodegeneration.
DOI: 10.1074/mcp.RA119.001888

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How to catch and kill a coronavirus on a doorknob

By John Arnst

More than two months after the World Health Organization declared the outbreak of the new coronavirus a global pandemic, we lather and scrub our hands — singing Happy Birthday, twice, or maybe the chorus to Mr. Brightside — to wash away the possibility that we'll bring the virus into our mouths and lungs from a contaminated handrail or doorknob. To cut off these routes of indirect transmission, researchers at Miami University in Ohio are developing polymer coatings for public surfaces that have the potential to capture and inactivate SARS-CoV-2, the virus that causes COVID-19.

Rick Page and Dominik Konkolewicz, who specialize in protein biochemistry and polymer chemistry, respectively, recently received \$181,849 from the National Science Foundation for this work. They plan to develop protein-polymer materials that can use peptides to either capture the virus by grabbing onto its spike proteins or inactivate the virus by disrupting its outer lipid layer, or do both.

“We’re taking two reasonably different areas of chemistry and putting them together to make advances on both sides,” Page said. “Neither of us would be able to do this on our own.”

Page and Konkolewicz have been collaborating for more than six years and have worked on applying functional groups that can disrupt vesicles and other lipid layers to polymer coatings. They investigate both how synthetic macromolecules behave in



Rick Page



Dominik Konkolewicz

contact with biological species and how biological membranes interact with the polymers, as sticking macromolecules to a synthetic surface can cause changes in the combined 3-D net-like structure that affect the performance of both materials.

“We can change how closely we pack the net elements and where we place different groups,” Konkolewicz said. “If we change the structure in a systematic fashion, how does that impact the material’s performance?”

The researchers also intend to evaluate the overall durability of the polymer-protein coatings once they’ve been applied to a surface; a coating that rubs off the first time someone touches it would be of little practical use.

“We can put the peptides (right) on surfaces ... but there’s very little chance that the peptide would stay on the surface for the length of time that we want it to. So if we’re looking at a doorknob, and you touch the doorknob, the peptide’s gone,” Konkolewicz said. “On the other ex-

treme, we can make purely synthetic materials that have an incredibly long lifetime but don’t have any biological function.”

According to Page, another challenge will be ensuring that functional groups remain active in the environment where the materials are tested.

“We typically think of them acting in water, but we’re going to be putting them on a surface where they may very well be getting dried,” he said. “(We’re) trying to figure out how much of these we need to put on the surface and if we can keep the groups functional so they are still able to sequester a virion.”

Like researchers at most universities, Page and Konkolewicz have had their labs — which are around 1,400 square feet each — closed since mid-March. However, they recently received approval to begin working on their NSF-funded project in June, which will entail researchers working in shifts and maintaining appropriate distance from one another.

“I think it’s going to start off with a few graduate students coming back,” Page said. “We’re doing all of the intro work that we can (for the COVID-19 project) at home ... to try to get things ready to go so that come June 1, we can hit the ground running.”

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On the front lines of CORONAVIRUS CARE

Recent months have been challenging, tiring and exciting for Mike Gillette, an ICU physician and Molecular & Cellular Proteomics associate editor

By John Arnst

More than two decades ago, Michael Gillette noticed that patients being treated in the intensive care units at Massachusetts General Hospital for the same condition responded differently to the same drugs. Reasoning that different molecular processes underlay common syndromes, he became interested in better aligning the treatment with the specific pathology — what we now call precision medicine. Since then, he has juggled his work at Mass General with translational and biomarker research at the Broad Institute of the Massachusetts Institute of Technology and Harvard and teaching duties at the hospital and Harvard Medical School. But with the outbreak of COVID-19 in Massachusetts, the critical care physician has spent all of his working hours, and most of his waking ones, treating coronavirus patients in the now single-purpose intensive care units.

Gillette's professional path was more circuitous than most. After graduating from Carleton College in Minnesota with a B.A. in biology and philosophy, he attended Oxford University as a Rhodes scholar, where he earned master's degrees in philosophy and experimental psychology and in human biology. He then earned both an M.D. and a Ph.D. from Harvard Medical School, going on to train at Mass General with a specialization in pulmonary and critical care medicine.

A longtime colleague of Molecular & Cellular Proteomics Deputy Editor Steven Carr, Gillette became an MCP associate editor in 2018. He recently spoke with John Arnst, an ASBMB Today science writer, about working in the intensive care unit at Mass General during the pandemic. Earlier this year, they talked about how Gillette came to work in proteomics. These interviews have been edited for clarity and length.

How has working in the intensive care units been since the coronavirus outbreak hit Massachusetts?

Well, next to New York and New Jersey, Massachusetts has had a particularly difficult time with the pandemic. The state is now approaching 100,000 confirmed cases and 7,000 deaths, but we're fortunately on the downward slope, at least until the impact of trying to reopen things is fully realized.

The intensive care unit that I work in most of the time, the main medical intensive care unit, is an 18-bed unit. And there's another mixed medical–surgical intensive care unit I often attend on that typically has an additional 10 or 12 medical ICU patients.

We will sometimes occupy several beds in the cardiac intensive care unit, particularly in the winter in the middle of flu season. So, when things are bad, we might have 32 or 34 beds for medical ICU patients. We got up to more than 180 at our peak occupancy in April.

Our cardiac intensive care unit became a COVID-19 unit. Our neuro ICU became a COVID-19 unit. Our burn unit became a COVID-19 unit. We had adult COVID-19 patients being managed in the pediatric intensive care unit. Half of the postoperative acute care unit was a COVID-19 unit.

Two general floors in one of our buildings have the appropriate physical infrastructure — gas lines, electrical panel, stuff like that — and were converted to COVID-19 units. And that's just accounting for the critically ill patients. A number of hospital floors were dedicated COVID-19 floors for those who just needed general supportive care and supplemental oxygen.

All kinds of doctors and nurses were stepping in outside of their normal roles and their normal practice to



After graduating from Harvard Medical School in 1995, Gillette did his residency, then a fellowship, at Massachusetts General Hospital, where he continues to work today.

assist — nurses who don't normally do critical care were doing critical care; physicians who don't normally do critical care were doing critical care. We've had surge staffing in place now for several months, which is supposed to be five days on and five days off, although the five days off is often interrupted with time on.

What did that look like for ICU docs?

The ICU-trained docs were trying to put together detailed protocols to guide other practitioners and were consulting across all the units. Even ICU triage, which is normally a little side role when you're on service in the intensive care unit, became a dedicated role, and it took a critical care expert working full time to keep up with where patients were, what the capacity was, how to redistribute them and how to load balance across hospitals.

It's really been an extraordinary time — lots of people stepped up in other ways, even within their domain of expertise. For instance, these critically ill patients often need a fair number of procedures done; they need central line access and arterial lines and things like that.

Normally, that's all part of our practice. But when you're as busy as we have been, it's really difficult to be admitting and managing critically ill patients all over the hospital and getting the procedures done and supervised. And that's especially true given that we usually rely on residents to be stepping in and doing some of these lower-level procedures once they're trained; but there was a real objective, especially earlier on in the epidemic, to try to keep trainees out of direct patient-contact situations. Attending-level surgeons and other expert proceduralists formed a specialized team to get this work done quickly and safely.

Another thing that has been really striking is the degree to which the pandemic is revealing the fracture lines in our social fabric. You read these things in the newspaper: "This is another manifestation of systemic racism and class disparities." But it's really evident in the hospital because the things that are associated with severe disease — hypertension, diabetes, obesity and heart disease, and to a lesser degree, actually, lung disease — are disproportionately represented in black and Latino populations where the health care needs have historically been systematically under-addressed.

How is the surge in COVID-19 patients affecting the rest of the hospital's operations?

There was a time when, whichever intensive care unit you walked into, everybody was critically ill from COVID-19. And that was it.

And they all have the same stories. There's basically one narrative: seven days of malaise, myalgias, a fever and dry cough. Then progressive shortness of breath that brings them to the hospital, where some of them stabilize and others relatively quickly worsen and end up needing to be intubated for acute respiratory distress syndrome.

Part of what was so strange is that we normally are very busy and have full intensive care units without patients with COVID-19 and ARDS. The conditions we normally treat didn't disappear with the onset of COVID-19. So the question became: Where were they all? It really can't be a good thing that all of the critically ill patients that I would normally be taking care of weren't there.

There have been a lot of COVID-19 deaths where we'll never know, because of a lack of testing, whether

they were directly attributable to COVID-19. But there is a still larger impact of people who delayed seeking care for other conditions and then came in later than they normally would, sometimes past the point when you could actually help them anymore.

Now that COVID-19 cases are starting to ratchet down, we're starting to see the patients with liver failure and the patients with strokes, the patients with heart attacks showing up again, so it's just really clear that people were laying low and deciding that it was better to suffer at home than to go in and risk being infected if they weren't already infected. And that's a scary thing.

A lot of these COVID-19 patients who are now getting better from their critical illness are going to need sustained periods of rehab. Those numbers are huge, and I don't think the rehab capacity really exists for that. It's like a wave; it just keeps going to the next level of care and the next level of care and the next level of care.

What about accounts of people who have recovered from COVID-19 but are now experiencing pain or loss of sensation in their extremities?

There's just a lot we still don't really understand about the disease. But one thing has been pretty clear: The patients who get critically ill and have respiratory failure have needed ventilatory support for quite a long time, even relative to severe cases of ARDS.

Regular influenza can sometimes cause severe ARDS, but for the most part, it'll be a bacterial infection or pancreatitis or something similar that sets it off. And we're treating the underlying cause at the same time that we're supporting the patient through the ARDS. But if you don't have anything that actually treats COVID-19 — I mean, we've got encouraging news about remdesivir but not enough remdesivir to be giving it to everybody — if you aren't treating the underlying disease, then it's going to continue to drive the illness for a longer period of time.

The longer you're critically ill and the longer you're intubated, the more debilitated you're going to be. And so, even without these other strange complications of coronavirus infection that we're just beginning to understand and tally, there are going to be patients who need a long time to recover.

As you're scaling back in the hospital, do you feel like you're better prepared for when things ramp back up in a few months?

I think there's the direct answer, and then there's a sort of caveat. The direct answer is: absolutely.

The foresight and the leadership at our institution were amazing, partly because they had forewarning that New York didn't have, partly because they were learning

from that experience. I think the playbook really is there — how you develop that kind of surge capacity quickly — and there are going to be a lot more practitioners who are familiar with the drill, if you will.

Without wanting to seem strange and macabre, it was kind of exciting to be dealing with this in the early going. I was working really long hours, but I would not have wanted to be doing anything else. I felt like this was stuff I'm trained for.

But the caveat to that is that I do think practitioner fatigue is going to be a pretty serious issue, in addition to the existing concerns about stress and mental health in the general front-line community. While that's not something that personally I deal with, I am getting tired. If we get a month off and then the cases start to uptick a little bit and then by fall we're back to this full-surge programming again, that's going to be hard. Even though we'll have the playbook, I think that's going to be, in many ways, harder than the first time.

How did you become interested in proteomics and biomarkers?

We have syndromes that we treat, like severe sepsis. Severe sepsis means that you have either a strong suspicion of an infection or evidence of an infection, and some sort of multisystem organ dysfunction. That has all kinds of different manifestations and different molecular underpinnings in terms of the host response. It remains a relatively lethal condition.

Although progress has been made because of improvements in supportive care and our deployment of critical early interventions, it's still something where, depending on the center, 25% to 40% of patients who present with severe sepsis succumb to it during their hospital stay.

With those kinds of numbers, as you'd imagine, pharmacologic interventions have been investigated and proposed, and a lot of drugs have gotten into various clinical trials, with some of them in advanced clinical trials. At this point, there are no drugs that are FDA approved for severe sepsis. There was one, Xigris, that became FDA approved and made it into clinical use; it has since been withdrawn for a lack of efficacy and concerning side effects.

The issue is probably not that we have never had drugs that might work but that we have never known the patients to give them to. I was really interested, from that perspective, in precision medicine before it was a kind of buzzword. So 20 years ago, I came over from Mass General and started working at the Center for Genome Research, which became the Broad Institute.

I wanted to work on understanding the molecular underpinnings of disease so that we could stratify patients

and could begin to say, even if it's a retrospective analysis, that there are subgroups that we can define molecularly with biomarkers.

How has your background as a physician informed that research?

I think having a clinical sense of where the important questions lie and what a clinician would want to know is really central, particularly on the biomarker side of things but probably also on the biological discovery side of things.

I find that when I'm working with my proteomics colleagues, my clinical perspective is constantly valuable in helping make sure that people are thinking about the right sorts of samples that we'd want to collect, what the right sort of controls are and which relevant variables we're going to manage throughout the course of a treatment or project.

Was cardiopulmonology, or being a physician in general, something you thought you were going to do from a young age?

No, it wasn't one of these things where I grew up having any idea what I was going to do.

I'm a little bit, dispositionally, a dilettante. I had a biology/philosophy double major as an undergraduate. I have a master's degree in philosophy and experimental psychology, and I have a master's degree in biological anthropology. I have an M.D., and my Ph.D. is in neurophysiology. I thought coming out of college that I was either going to do environmental law or marine biology.

I had a friend who was going to medical school while I was at Oxford at the time I was collecting these random degrees. During a trip, we were literally sitting on top of Mount Kenya, and it was a gorgeous morning. We were exhausted, and I was getting increasingly concerned in the background about what I was going to do when I left Oxford because I really hadn't made up my mind at all.

JENNIFER GILLETTE



In less demanding times, Gillette and his wife Jennifer — with whom he has two sons and recently began fostering a third — enjoy hiking, fishing and skiing, among other hobbies.

And he said, "I think you should go to medical school because biology and medicine are cool." He was going to go to medical school. And so I just decided, sitting up there in the thin atmosphere, "Medical school sounds really interesting; I'll bet I'd really like that." And I was probably in my second year of medical school before I started to grapple with the idea that, as things would naturally progress, I was probably going to end up being a doctor. I was very interested in brain and mind stuff that combined all of my interests in biology, philosophy and experimental psychology.

I ended up doing a Ph.D. in neuroscience in the middle of medical school, and I expected to do neurosurgery and combine that with neurophysiology, but I couldn't line up enough surgical rotations early enough to actually do a surgical internship without postponing a year. And I thought, "Well, I'm going to get on with it; I'll do a medical internship and then I'll apply in surgery." In my early rotation as a medical intern at Mass General, I was in the intensive care unit, and the people there were great and the physiology was really cool. And I liked the combination of really sick patients and fascinating ethical problems. So a lot of circumnavigation to get where I ended up.

Do you have any advice for early-career scientists who are starting out?

I would say it's important to really be assertive and advocate for yourself. I also think you should, at all stages, focus on working with the people you're excited about and working on problems that you're passionate about.

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If you want to find interesting enzymes, a carnivorous plant is a really good place to look," said UCI professor Rachel Martin, who has applied her lab's expertise in cysteine proteases from sundew plants to study the cysteine protease of SARS-CoV-2.

Pivoting from carnivorous plants to COVID-19

UCI professors team up to seek protease inhibitors

By Laurel Oldach

You might not think that research into how carnivorous plants digest their meals would be remotely useful in responding to a pandemic. But that's the thing about basic research: Its applications are unpredictable.

Before the COVID-19 pandemic, Rachel Martin, a biophysical chemist at the University of California, Irvine, studied diverse proteases, including from the carnivorous sundew plant, for a different purpose, to explore ways to break down harmful, protease-resistant aggregates such as amyloid plaques.

Now, Martin is leading many of the labs in her department in a research consortium that aims to design new protease inhibitors specific for the coronavirus protease. Working six feet apart in the lab or from home using software for virtual screens, the team hopes to contribute to a future arsenal of antivirals against SARS-CoV-2, the virus that causes COVID-19.

A hunt for protease inhibitors

Proteases play an important role in COVID-19 infection. The novel coronavirus translates much of its RNA genome into two long polyproteins. It requires a protease called MPro, or the main protease, to cleave that long polyprotein into 16 individual active

units that replicate the viral genome, hijack the host cell's immune response and carry out other nonstructural roles.

Protease inhibitors have been successful treatments for other viral infections, such as HIV. Drug repurposing studies such as the World Health Organization's Solidarity Trial are testing the HIV protease inhibitors ritonavir and lopinavir in patients with COVID-19 to see whether they give clinical benefit.

But existing drugs developed for other viral proteases may fail to block MPro. Even if they do work, there's a possibility that their effect will be limited or that widespread use will promote viral resistance. In all likelihood, cocktails of multiple antivirals will be needed, so scientists around the world are racing to find compounds that inhibit MPro activity and might become, or inspire, future drugs. That's where Martin, vice chair of the chemistry department at UCI, comes in: A protease expert whose lab is conversant in both computational and biochemical studies, she saw an opportunity to contribute to the hunt for protease inhibitors.

Proteases from carnivorous plants

Martin studies the biophysics of protein aggregation, which is linked to human diseases such as Alzheimer's. One possible strategy



University of California, Irvine, chemistry professor Rachel Martin in her lab.

COURTESY OF RACHEL MARTIN



COURTESY OF RACHEL MARTIN

Marquise Crosby, a graduate student in Martin's lab, has shifted from studying sundew to producing protease.

“The stereotype of a lab scientist is somebody who's socially maladjusted and has no friends, but that's not how it works at all. Experimentalists are very social!” says Rachel Martin.

to reverse harmful aggregation would be to introduce new proteases. To find proteases with new functions, Martin and colleague Carter Butts sequenced the genome of the sundew *Drosera capensis*, a plant that traps and slowly digests insects that land on its sticky hairs.

“If you want to find interesting enzymes, a carnivorous plant is a really good place to look,” Martin said. Unlike animals, which break down food mechanically and digest it in specialized organs, she said, a carnivorous plant “has to perform all of its digestive functions right out in the open, where it's in competition with bacteria and fungus. ... All it has are really amazing enzymes.”

Once Martin and her team identified 44 new cysteine proteases in the sundew genome, they needed to predict each protease's substrate selectivity to decide where to focus their biochemical resources.

After using a program called Rosetta to predict the structure of each protease and refining those predictions manually, the team used molecular docking simulations and machine learning to predict the substrates each enzyme might be able to bind and cleave.

When COVID-19 struck, Martin said, she realized that the pipeline her team used to search for substrates could be converted to seek inhibitors instead. After all, she said, “If you think about it, an inhibitor is just a substrate that doesn't do the chemistry.”

Martin knew her lab could contribute. As most of the UCI campus prepared to shut down, she prepared her team to launch a socially distanced research project. James Nowick, a chemistry professor in a neighboring lab, was ticking through a shutdown checklist when Martin stopped in to ask that he leave the shared ultrapure water system on—she was going to need it. Nowick said, “It was like a lightbulb went on — that biomedical scientists should be putting all hands on deck to solve this problem.”

He wasn't the only fellow professor to sign up to help; the consortium quickly grew to ten labs. Martin said, “Basically every colleague that I told about it said, ‘What can I do?’”

An assay for robust inhibition

The consortium includes two computational labs and six experimental labs in addition to Martin's from the UCI chemistry department. The team has two research goals; the first is to find one or more inhibitors that specifically inhibit the SARS-CoV-2 main protease.

Much like the sundew protease project, the work starts with computational modeling. The team takes a structure — the European protein database currently lists 124 reports on the structure of the protease, including many in complex with ligands — and uses molecular simulations to predict other possible conformations. Then, they dock ligands numbering in the thousands from libraries curated by DrugBank, UC Irvine and other academic institutions around the world to see which are best able to bind to the enzyme's active site. This lets them narrow down the dizzying list of potential molecules to strong candidates to be tested in the wet lab.

To test how well the modeled chemicals work in a test tube, the consortium needs huge quantities of purified protease, which Martin's lab is producing and characterizing, and adequate amounts of each of the promising compounds, which the department's synthetic labs are producing. They also need to monitor how active the protease is in the presence of each candidate inhibitor. Researchers in Nowick's lab synthesized a probe that had been published, but was not yet available for sale. When the protease cleaves the probe, it fluoresces, allowing high-throughput testing of candidate inhibitors in a 96-well plate format.

Mapping mutational landscapes

The consortium is pursuing a second goal in tandem with the first: to identify inhibitors or combinations that make it difficult for the virus to develop resistance.

The team has started by working to understand what Martin calls the mutational landscape of the protease in circulating coronavirus strains. If there is already a strain

in circulation that can resist a candidate protease inhibitor, that's crucial information for moving forward. Similarly, if resistance is just a mutation or two away, the scientists would like to know that.

Every day, undergraduate T.J. Cross, who joined Martin's lab just days before the university shut down, and graduate student Gemma Takahashi comb an epidemiological sequencing database in search of new mutations to the protease. Each time a laboratory submits a sequence to the Global Initiative on Sharing All Influenza Data, or GISAID, that includes a new protease mutation, the team uses molecular dynamics simulations to model how it affects the protein's shape, movements and interaction with selected compounds. In May, the team posted a preprint analyzing 79 known variants of the protease.

"Right now, we are simulating every single one," Martin said. "And yes, it is expensive. Yes, we're doing it. We know that it may not be sustainable long term ... but we're going to do the best we can for a while."

Logistics of a big consortium

Martin's salary, those of her faculty colleagues and their students and postdocs, are funded by grants, and she said that program officers have been happy to support their pivot to COVID-19 research. Covering the cost of reagents and computer time has been more of a challenge. The university has dedicated some discretionary funding and led crowdfunding efforts to support the project, but to keep it going long-term, the group will need more funding. That's a challenge, as grant cycles move much more slowly than this project has.

Martin has led research consortia before, but never one that came together so fast. Within eight weeks of conceiving of the project, she was supervising the first positive control assays remotely. Soon, she said, the team hopes to test its first candidate compounds.

At the same time, she added, because just two people can safely work in the lab



Undergraduate T.J. Cross helps monitor a global epidemiological sequencing database for new mutations to the SARS-nCoV-2 protease.

at a time, the work seems to move achingly slowly. Every stint at the bench must be carefully coordinated in the lab's Slack channel. Members of the lab also miss sharing ideas, technical advice and the simple pleasure of each other's company.

"The stereotype of a lab scientist is somebody who's socially maladjusted and has no friends, but that's not how it works at all," Martin told the audience of a recent webinar. "Experimentalists are very social!"

Martin has also stayed in close contact with other teams working on protease inhibitor development. Around the world, teams at the University of Hamburg, the University of Science and Technology of China, the Swiss Federal Institute of Technology, and the University of California, San Francisco, and other international consortia are working to develop protease inhibitors.

"We're keeping in touch to make sure that we're not duplicating efforts," Martin said. "Everybody I've talked to from all over the world ... has been very collaborative and eager to solve the problem."

"If you want to find interesting enzymes, a carnivorous plant is a really good place to look," says Rachel Martin.

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



ASBMB MID-CAREER LEADERSHIP AWARD

Corbett goes the extra mile to support young scientists

By Nivedita Uday Hegdekar

Anita Corbett understands firsthand how early influences can shape a young scientist's career path. A high school chemistry teacher named Mrs. Broadway encouraged Corbett's interest.

"I liked science and was good at it, but that was about it," she said. "However, she saw something special in me that I didn't. She appointed me as the captain of Science Bowl team and encouraged me to develop my leadership skills and scientific acumen."

As an undergrad at Colgate University, Corbett said, her conversations with Roger Rowlett helped her develop as a researcher and science advocate. "I was one of Roger's earliest trainees and loved working in his lab. He had confidence in my abilities and was such a positive influence."

While pursuing her Ph.D. in Neil Osheroff's lab at Vanderbilt University, Corbett learned to love teaching and mentoring. "His lab welcomed many undergraduate researchers," she said, "and I gained a lot of experience through training and mentoring people from different walks of life."

In 2003, Corbett was the first woman to receive tenure in the department of biochemistry at Emory University School of Medicine. She is now a professor in the biology department and co-director of several prominent programs at Emory University.

Corbett is passionate about increasing diversity and inclusion in science and goes the extra mile to support the career development of young scientists. She nominated the recipient of the 2019 ASBMB

Unraveling human diseases with systems biology research

Anita Corbett's research group focuses on understanding the molecular basis for diseases, particularly how missense mutations in proteins lead to distinct disease phenotypes.

Studies have shown that mutations in multiple genes encoding structural RNA exosome subunits are linked to disease. In one project, following a successful collaboration with clinicians, the Corbett group was the first to link mutations in a gene encoding one particular subunit of the RNA exosome, EXOSC5, to clinical outcomes (developmental delays, cerebellar hypoplasia and motor weakness).

In a recent study, the Corbett group collaborated to combine various genetic models, including budding yeast and zebrafish, as well as biochemical techniques to characterize how changes in the protein found in people with EXOSC5 mutations ultimately affected the function of the RNA exosome complex.

As the RNA exosome subunits are expressed ubiquitously in every cell, so are the pathogenic variants. Thus, the lab also further determines the requirement for the RNA exosome in specific tissues/cell types and provides insight into how defects in RNA exosome function contribute to specific clinical manifestations.



Anita Corbett

Young Investigator Award, Christine Dunham.

"When shortlisting seminar speakers at Emory University, I focus on inviting junior faculty, particularly women, whose careers would benefit from another invitation on their CV," she said.

Corbett describes the research in her lab as "model system fluid" because high school students, undergraduates, graduate students and postdoctoral fellows with expertise in various model organisms all collaborate on certain projects.

After 23 years as a professor, Corbett has this advice: "Always pursue an area of work that fulfills you; don't shy away from asking for help when required; and always, always

help your fellow researchers. The rest will follow through."

Anita Corbett is the inaugural recipient of the ASBMB Mid-Career Leadership Award recognizing an individual at the full professor or senior scientist level with a strong commitment to advancing the careers of women in biochemistry and molecular biology. This award will be presented at the 2021 ASBMB Annual Meeting in Indianapolis.

Nivedita Uday Hegdekar is a graduate student at the University of Maryland working toward a Ph.D. in biochemistry and molecular biology and an M.S. in patent law.



ASBMB EARLY-CAREER LEADERSHIP AWARD

Jura is inspired by her grandmother, a ‘true pioneer’

By Kerri Beth Boggs

When she was a child, Natalia Jura traveled from Krakow to northern Poland to spend the summer months with her grandmother. Her grandmother was a pharmacist, and she gave Jura small tasks to help serve her customers. Jura learned how to weigh and mix chemicals for her grandmother’s formulations. She became curious about how the medicines worked.

“I wondered, ‘How does she know what to mix so that people get better?’” Jura said.

Jura now considers her grandmother a true pioneer. After leaving university to have children, Jura’s grandmother returned to finish her degree and become a pharmacist. Her determination and ambition inspired Jura to take on new challenges.

“She would always tell me, ‘Your brain is your biggest asset,’” Jura said. “Growing up as a girl, that was an important message.”

Jura created a home laboratory. She tested acids and bases with pH indicators and observed the color changes. Her mind thrived on figuring out how things worked.

Jura’s scientific interests grew stronger throughout school, so she pursued a master’s in molecular biology from Jagiellonian University in Poland. Though the university had little funding, Jura’s professors carved out projects to give their students research experience. Jura learned that she could accomplish goals in science even when resources were sparse.

Jura earned her Ph.D. in molecular and cellular biology at Stony Brook University in New York. She then entered the world of structural

Chasing high resolution structures of elusive cell receptors

Natalia Jura aims to understand how cells communicate with each other and the environment. Her lab addresses this question by studying the structure of single-pass transmembrane proteins, which serve as cell surface receptors. Receptor tyrosine kinases, or RTKs, represent leading clinical

targets since they are often hijacked by cancers and viruses. The long-term goal of Jura’s lab is to develop therapeutic strategies to target these receptors in human diseases.

RTKs eluded structural investigation for many years because they are difficult to express and analyze via X-ray crystallography. Jura’s lab developed techniques to improve the purification of these receptors. They use cryo-electron microscopy to study different conformations of the proteins. One goal of Jura’s lab is to reconstruct the architecture of RTK signaling complexes to understand how they promote cell proliferation, division, movement and other crucial processes.

Jura’s lab also studies the molecular and structural mechanisms by which pseudokinases communicate signals. These highly conserved proteins evolved parallel to catalytic kinases, and they represent another important group of disease targets. Although pseudokinases are members of the protein kinase superfamily, they primarily utilize noncatalytic mechanisms for signaling. Jura hopes that understanding the structure and function of these proteins will open doors for development of inhibitors to target pseudokinases linked to disease.



Natalia Jura

biology as a postdoc at the University of California, Berkeley.

Now an associate professor at the University of California, San Francisco, Jura said she is grateful for the collaborations she has built since she started her lab in 2010.

“The ultimate beauty of science is when we team up and work together on something.”

Natalia Jura is the inaugural recipient of the ASBMB Early-Career Leadership Award honoring an individual who is an associate professor, assistant professor or equivalent with a strong commitment to advancing the

careers of women in biochemistry and molecular biology along with demonstrated excellence in research, discovery and/or service. Due to the cancellation of the 2020 ASBMB Annual Meeting, this award will be presented at the 2021 ASBMB Annual Meeting in Indianapolis.

Kerri Beth Boggs (kerri.slaughter@uky.edu) is a graduate student in the biochemistry department at the University of Kentucky. Follow her on Twitter @KB_Boggs.



What we've lost by closing our labs — and what we risk reopening them

By Audrey L. Lamb & Graham R. Moran

When our university campuses closed in March, we realized that, although we can adapt much of our instruction material to deliver it effectively via the web, the medium is wholly different from the classroom and cannot replace what students learn at the bench. The technical skills we teach in a laboratory simply do not translate, and the loss of experimental inquiry inevitably has significant impact to undergraduates, graduate students, postdocs and us, the faculty. All this uncertainty raises many questions, most of which we cannot answer fully at this stage. Scientists are natural planners, and not knowing how to develop a plan is the most frustrating aspect of this shutdown.

In the absence of experiments, scientific skills are abstract. We may be able to teach the concept of how to perform a titration online, but the skill of using a pipette to deliver accurate volumes requires intellectual and muscle memory synergy that can be imprinted only by tactile stimuli. Similarly, though students easily can grasp the concept of aseptic technique for microbiology, the elaborate choreography required to prevent contamination is only learned by doing. How many of us could learn to juggle without rhythmically lofting objects?

Remote work

When in-person instruction and research abruptly ceased in March, Audrey immediately had to adapt two active-learning classes to

emergency remote instruction. The first was a 75-student metabolism class for juniors and seniors taught via team problem-solving using white boards. She converted the material to individual problem-solving with flexibility to complete timed exams. While course evaluations indicated this was an acceptable solution, most students said they preferred in-person, team-based instruction. The second, a graduate class on professional development, adapted more readily to remote instruction, as it included outside speakers who already were slated to present remotely. Before the stay-at-home order, the speakers were the only people on a screen, but now everyone participated online.

Graham's lab scattered to a variety of locations (both nearby and distant from campus) and began working on the backlog of manuscripts. This proved to be a productive period, with six manuscripts prepared. However, two require confirmatory experiments and cannot be submitted until research activity resumes.

Both of us have been helping students prepare dissertations and serving on committees for candidacy exams and dissertation defenses. These exams are now fully online, which can seem impersonal, and explanation of data is limited when a student can't easily go to the board and show their thinking. We also have been reviewing manuscripts for academic journals, which requires a balancing act when considering the need for additional experiments: We don't want to hinder progress, yet the

science should be solid. With labs closed, requesting additional experiments may slow publication of good work by months or longer.

Our lab members

Our undergrads, living in the petri dish of dorms and community eating (buffets and food courts) were the most likely to spread the disease, not unlike people on cruise ships or in prisons. Therefore, they were evacuated first, leaving our campuses largely empty. Undergraduate researchers in both our labs no longer were able to pursue their projects. For seniors, this meant final experiments were not completed. Continuing undergrads are also unlikely to be able to resume their work safely in the coming semester as rules for reopening labs at both our institutions strictly forbid or severely limit undergraduate researchers. One set of guidelines actually states that the PI is responsible for "communicating expectations for behavior on and off campus" including requiring the student to agree to "Avoid violations of social distancing norms (e.g., attending parties that involve large groups and close contact)" and "Timely disclosure if roommates' contacts or behaviors increase the risk for exposure."

The most novice lab members need the closest supervision — they must learn laboratory safety risks — and frequently are not allowed in the lab alone until trained. The new restrictions will prevent individual undergraduates from conducting research and have additional conse-



quences for our disciplines. A student who can't experience the scientific process directly will have difficulty deciding to pursue higher degrees in the field, and graduate school admissions committees will have even more difficulty assessing the likelihood of success for students without lab experience.

From our perspective as professors, a graduate student may experience little consequence with a one-semester delay; however, this perspective is not shared by the graduate students. The young and ambitious perceive time differently. Nevertheless, all agree that a year or more would impede project progression, particularly for first- and second-year Ph.D. candidates. Graham has a very engaged first-year graduate student who had to halt research activity at

this critical stage. After providing instruction on the software the lab uses for analysis, Graham created mock data for the student to analyze. This activity filled eight weeks but now largely is exhausted. We both seek to find constructive ways to maintain involvement with laboratory projects and continue each student's learning.

We have concerns about the use of funds granted specifically to support the research activities of junior investigators. Both of us employ individuals who oversee many day-to-day laboratory functions and activities. These researchers present a unique set of problems. Once all writing opportunities are exhausted, is it correct and prudent to continue to pay their salaries? Morally, the answer is easy; they should be supported. But what does it mean for productivity within

the granting period if universities are less than fully operational in the near term? More importantly, will this limit future employment opportunities of these individuals, lengthen their career progression or both?

The prospect of reopening

Laboratories are hives of activity and interaction and were not designed to be left fallow and empty. Research labs must conduct experiments; the system requires that graduate students and postdocs in biochemistry and molecular biology develop technical skills and perform a body of experimental work. Publications remain the primary currency of the sciences, and we are funded to complete specific objectives. With grants running and experiments designed, we are keen to get back into the lab.



Audrey's research team has the green light to return to her laboratory, whereas Graham's is expected to return in a limited capacity in mid-June. However, the two of us are not in the first wave of people allowed to return to campus. Most universities have decided that people who predominantly work in offices (including professors) should continue to work remotely. Audrey is genetically predisposed to lung infections and therefore considered high risk. We have discussed at length the logistics of both conforming to the regulations set by our institutions and defining additional protocols within the lab to minimize the chance of community spread.

Limiting the number of people in the lab will slow productivity. We train our personnel, answer questions and help to solve problems in labs of about 12 people. Having one or two working at a time, with the faculty providing remote, discontinuous and iterative supervision, will be much less efficient. Slow is better than nothing but not what we expect for reasonable productivity.

Labs have thousands of surfaces, many of them touched by all group members and some that cannot easily be sprayed with an alcohol solution without damage (absolutely do not spray the microscope, for example).

Reopening will require additional training on COVID-19 transmission and proper use of personal protective gear (to prevent viral spread as opposed to providing experimental safety), establishing calendars to minimize or prevent overlap of personnel in the lab, and new guidelines for sanitizing workspaces between users. We have moved benches and equipment to put greater distance between workspaces. Some labs are installing plastic sheeting between back-to-back benches, akin to the sneeze guards now prevalent at drive-through restaurants and the grocery check-out. Can we be safe in a laboratory without community immunity? Even with all of our efforts to promote safety, we can't control all outcomes. Our lab colleagues will be at significant risk regardless of what we do to mitigate.

Collaborative work or common instrumentation compounds these dangers. Will that incubator that everyone borrows to grow bacteria become a node for viral transmission? The same is true for shared instruments and spaces such as the nuclear magnetic resonance or mass spectrometry lab or the cold room. Audrey's team is prioritizing projects that do not require the NMR but instead can be accomplished using equipment within the Lamb lab. Some grad students from other labs use our equipment regularly, and we have included them in the calendaring system as if they were full-time employees to reduce overlap.

The risks will be cumulative as each of us passes from home to work

repeatedly. Dangers also exist from and for our home lives. If Audrey's son rejoins his soccer team on the pitch, will she have to be isolated from him when he returns home? Graham worries about commuting home to Milwaukee, potentially carrying the virus from the higher risk population in Chicago. If he returns to work, should he not travel to see his family?

Social distancing is effective at reshaping the infection curve but, in the absence of a vaccine or a treatment, doesn't change the area beneath that curve. Avoiding contact with others ensures only that the number infected does not spike and overwhelm our capacity to respond. Obviously, we must all commit to less contact and stringent hygiene, but in doing so we dramatically prolong the threat. So the resumption of scientific activity worldwide appears to be contingent on the development of a vaccine or drug against COVID-19. Without such a remedy, we must weigh the value of our work against the potential cost to health and life.

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The COVID-19 pandemic is squeezing women out of science

By Marina K. Holz

In the early days of working from home during the pandemic, before everyone discovered virtual backgrounds, I noticed something peculiar. My male coworkers joined meetings from bookshelf-lined offices, while my female colleagues logged in from kitchen tables and living rooms. “My husband and I are both professionals who work from home, yet somehow, he is holed up in the upstairs office, while — as you can see — I am here in the dining room,” one of my coworkers remarked during a recent video conference.

In the last two decades, we have achieved remarkable gains in equalizing the standing of women in science. The numbers of women as lead authors on research papers and recipients of major research grants, in the senior ranks of the tenured professoriate, and in academic leadership have been on the rise. I am one of these success stories, being the first female dean at my institution, one of many to come. There is still much progress to be made, but we started 2020 with great hopes for the new decade. The pandemic abruptly caused research laboratories to shutter, and working from home became the new normal for most academics. “Great, we will finally have the time to write all the papers we always wanted,” the scientists hopefully proclaimed.

But startling posts shared on social media by journal editors suggest that the share of papers submitted by female scientists has dropped significantly during the last two months.

The professional slide for women in science has started to emerge.

While many male scientists, unencumbered by their usual travel and other distractions, have hit their productivity peak, a disproportionate number of women have experienced a productivity deficit — women overwhelmingly picking up the household responsibilities associated with caring for children and aging parents under the dictate to shelter in place. Women scientists were surprised how swiftly this happened to highly educated, self-aware professionals who have long advocated for equity in science but fell into the all-consuming role of the caregiver in their own homes. To be clear, many of us acknowledge that our wonderful spouses, who have been supportive of our careers, shouldering the burdens along the way, did not exactly force us into this domestic role. It just happened that they took over the home office and shut the door.

Institutions across the nation gradually are reopening their research programs, and scientists with school-aged children are scrambling to come up with child care solutions, as daycares and summer camps will not return to business as usual this summer. Running a backyard child care operation while managing a lab is not an option. Hiring a nanny on a graduate student stipend or a postdoc salary is impossible. Scientists are notoriously nomadic as they progress from grad school to postdoc and faculty positions, leaving them without a local network of reliable

family and friends. It is clear that the majority of the child care burden will fall on the female heads of household, who will remain at home while their male colleagues return to their offices and labs reenergized. Summer, one of the most productive seasons for scientists, effectively is canceled for many women in science.

It truly would be revealing to see the gender breakdown of grant applications to the National Institutes of Health (the primary federal funder of research) submitted for the June and July deadlines. The adverse effects on female scientists’ productivity — fewer papers, fewer grants — likely will have long-lasting and wide-ranging consequences. Papers and grants are the main currency for competitive fellowships, tenure-track appointments, promotions and awards, the lack of which will affect women scientists disproportionately.

While men return to the active practice of science in all of its glorious forms, a large fraction of women will not, perhaps permanently. Whether or not academic institutions and research funders urgently address this issue now will determine the professional futures of women in science for decades to come.

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



Out of my comfort zone: How I use science to influence policy

By *Amanda Koch*

Once had a meeting with a senator's staff member while he walked down a hall to another meeting.

The staffer came out of his office, looked at me, asked my name and then said, "follow me" as he turned into the hall. Frazzled, I gathered all my things; I was carrying too much and not wearing the right shoes for hurrying to catch up with someone. But I caught up. Wordlessly, the staffer opened his hand, clearly expecting something from me. I put my sweaty palm into their open hand and then realized he were not expecting a handshake. A business card! Right. As I dug around in my oversized bag for my card, he said, "Sorry, but another important meeting came up. We are going to have to chat on my way."

I was there to tell the staffer why the senator should support funding for scientific research. I had to do it in three minutes.

From what I've seen as a senior Ph.D. student, many scientists avoid policy issues. But government leaders make policy decisions that directly affect scientific research. Every year, Congress creates a federal budget that includes science funding. As scientists, we need to step up and talk to policymakers who may not see the importance of our research.

My motivation to advocate for science came during the 2016 elections. At that time, I was studying hard for my qualifying exams, developing a thesis project, conducting experiments that seemed to fail constantly and all the while trying

to understand what was happening in the political world. Watching the news and the presidential debates, I realized that government officials often do not make evidence-based decisions and many do not support science. I decided then that I wanted my scientific voice to be heard in politics.

Over the past 50 or so years, there have been times the government increased science funding because a policymaker thought a certain area of research was important. President John F. Kennedy wanted Americans to be the first to the moon — NASA received increased funding. Vice President Joe Biden's son died of cancer — the National Institutes of Health increased funding for cancer research. But scientists don't have to convince the president or vice president of the United States that scientific research is important. Advocacy can start at a city council or a state capitol.

And it doesn't have to be a solo endeavor. Scientists can form coalitions to advocate collectively. I know I work better in a group, so with my new passion for science advocacy I reached out to my fellow Ph.D. students and professors (also motivated to take action from the 2016 elections) to form an advocacy group. Together we brainstormed, learned about federal and state budgets, and developed an advocacy game plan. First, we created a tight and trustworthy network within our university. We locked down funding for our advocacy group and garnered

support from the university administration. Then we talked to our city council members about how we, as scientists, could best serve them. We developed relationships with our state senators and representatives so we could share our scientific opinions on current legislation. We also started keeping our eyes open for legislation at the federal level and discussed it with our senators' local staff members. For example, our group recently has been advocating for a federal bill, the Scientific Integrity Act. To encourage a "yes" vote on this bill, we met multiple times with the staffs of Rep. Joe Neguse, D-Colo., and Sens. Cory Gardner, R-Colo., and Michael Bennet, D-Colo. Our advocacy worked. The bill since has passed the House and is now in the Senate to be discussed.

At first, science advocacy seemed daunting, but it ended up being straightforward and fun, especially with a great group and a growing network.

Here, I'll walk through my advocacy protocol and describe actions I've taken to push myself out of my lab and make my voice heard in the policy world.

Be part of a group

This means leaving the lab for a few hours to connect with people. I started by having conversations with people I worked with who were politically aware or already engaged. Those conversations evolved into forming a university organization for graduate students and postdocs



around science policy and communication. A group with similar goals may exist already on your campus. In that case, do not start an identical group; a bigger collective voice is more powerful than scattered voices.

Develop a message

When you go into a meeting with an elected official, what's the ask? This can be challenging; it's hard to keep up with the news and decipher complicated legislation. I started with letter-writing campaigns encouraging my senators to support science funding and to seek out scientific experts when making policy decisions. Both of these asks align with most scientific disciplines. To develop more specific asks, I partnered with national science policy organizations.

Most scientific societies, including the American Society for Biochemistry and Molecular Biology, have advocacy initiatives and policy experts on staff. These groups provide amazing resources and are important allies. They will train you, explain the policy issues and give you needed empowerment.

Be clear and concise

In developing an ask, I've learned to avoid complex terminology. The message must stick with the policymaker, and science jargon is not the way to do that. Also, be aware of how much time you have. In the three-minute meeting described above, I covered these six steps.

- The thank you. "Thank you for your time. This shows support

from the office for science."

- The ask. "I am here today to ask that you encourage the senator to continue supporting science by voting to maintain (or increase) the budget for scientific agencies such as the National Institutes of Health and the National Science Foundation."
- The funding. "I am a Ph.D. student from Colorado State University and have been funded through the NIH and NSF for the past four years."
- The basic idea of the research. "Through that funding, I study how viruses replicate within host cells."
- The 10-year goal. "This work can be used to test which drugs stop a virus from spreading without

As scientists, we may feel removed from policy issues. But I believe science can and should inform policy. That's why it is critical, especially during this election year, to step out of the lab and be the voice for science.

hurting the cells' normal activity.”

- The wrap-up. “Thank you again for your time and for your and the senator’s continued support for science funding and for science in general.”

The overall message must be concise: fund science. To make the specific ask memorable, I say it at both the beginning and end of the conversation.

My final recommendation for developing a message, which will come easily to scientists, is to do background research. Knowing about a policymaker’s past decisions helps me formulate my message with confidence and makes the conversation go more smoothly.

The follow-up

Once my nerves settle after a meeting, I always send a quick email thanking the person for their time and offering further support on the topic if needed. Sometimes, after meeting with a senate staff member, I’ll send them additional resources that they can pass along to their senator. They also follow up with me to let me know how the senator has voted (usually when the senator votes for what I was advocating) or

simply that my concerns were passed along. Maintaining contact builds a relationship with the policymaker or staff member.

As scientists, we may feel removed from policy issues. But I believe science can and should inform policy. That’s why it is critical, especially during this election year, to step out of the lab and be the voice for science.

Amanda Koch

(amandakoch231@gmail.com) is a fifth-year Ph.D student studying biochemistry and molecular biology at Colorado State University. Outside of research, her passion is science communication and advocacy. In her free time, she enjoys backpacking, skiing, rock climbing and being with her family.



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‘We will not be silent’

Dear ASBMB members,

We, as members of the ASBMB Minority Affairs Committee, believe in the dignity of all human beings and have chosen to shine a light on injustice, advocate for diversity and equity, and ensure that all voices are heard.

We are sickened. Hundreds of years of wealth, housing, and health-care inequality and environmental racism have resulted in Black and other communities of color being disproportionately affected by the COVID-19 pandemic. And yet these workers have disproportionately been the ones picking and processing the foods, delivering the household staples, and providing the services that allow the rest of the nation to stay home and be safe.

We are grieving. Last fall, Atatiana Jefferson, a 28-year-old Black woman, was shot by police in her home while playing video games with her nephew. Earlier this month, Ahmaud Arbery, a 25-year-old Black man, was killed by white men while jogging. Breonna Taylor, a 26-year-old Black woman who wanted to become a nurse, was shot by police in her own home while sleeping. Last week, the graphic killing of George Floyd by police and his haunting final words echoed those of Eric Garner in 2014: “I can’t breathe.”

We are exhausted. Institutionalized racism, housing discrimination and educational inequality have prevented African Americans, Latinx, Native Americans and other minority groups from joining our ranks in scientific research and medicine. As a scientific society, we create events and programs to remove barriers and attract minority students to our ranks.



CLAY BANKS/UNSPLASH

PERSPECTIVES

We try to educate, advocate and serve as role models.

We are angry. The systemic biases, racial profiling and inequalities in access make our goals almost unattainable. The events of the past several months have shaken our belief that the better angels of our nature will prevail. As we watch and participate in the protests against police killings of Black people, we understand that hundreds of years of racism and oppression, starting with the sin of slavery, have culminated in what is currently gripping our nation. In this country, we still struggle to show that Black lives indeed matter.

We are united. Together, as scientists and leaders in our communities, we cannot sit silently. We need to channel our despair and anger. If you are not a member of a minority community, become an ally. Offer support, listen, amplify their voices, and educate your peers. In the words of Angela Davis: “In a racist society, it is not enough to be nonracist, we must be antiracist.” We call on all members of the ASBMB to step up, speak out

and intervene, even if our voices shake, for it is only in just actions that we will start correcting some of the historical wrongs that our nation has imposed upon communities of color.

We will not be silent. Dr. Martin Luther King Jr. is often quoted* as having said: “There comes a time when silence is betrayal. Our lives begin to end the day we become silent about things that matter. In the end, we will remember not the words of our enemies, but the silence of our friends. Only in the darkness can you see the stars.”

We must work together. The force of American history has crushed the lives and hopes of the Black community. We should not act surprised that finally the cauldron has boiled over, as, for too many years, our nation’s top leaders have not only ignored our plight but have added more fuel to the fire. We look to our elected leaders to provide the beacon that lights the path to an equitable future. For the first time in many years, the lights of the White House are dark.

We must walk together. Abra-

ham Lincoln, quoting the Bible, said, “A house divided against itself cannot stand.” As a scientific society, let us not wait for a beacon, but, through our engagement and actions, shine a light on inequities and light a path for everyone to walk on toward a just and equitable future. We must light up the darkness together.

Sincerely,

Sonia C. Flores, Chair, ASBMB
Minority Affairs
Committee
Vahe Bandarian
Ruma Banerjee
Suzanne Barbour
Carlos Castañeda
Joseph Chaney
Adela Cota-Gomez
Kayunta Johnson-Winters
Carlos Lopez
Deborah Neely-Fisher
Lana Saleh
Gustavo Silva

*These likely were not MLK’s actual words but rather a synthesis of parts of his speeches.

Cast your vote in the 2020 ASBMB Election!

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asbmb.org/membership/election

Deadline: July 1

 ASBMB

CLASSIFIEDS

Research Specialist, Protein Structural Biology Howard Hughes Medical Institute Austin, Texas, United States



We are currently looking for a highly motivated Research Specialist to support the lab of Dr. Keiko Torii at the University of Texas at Austin in Austin, Texas. The Torii lab has a long-standing interest to unravel how plant stem cells function and contribute to growth and development, with specific emphasis on signal transduction pathways and underpinning genomic/epigenomic mechanisms. In addition to harnessing chemical and synthetic biology, we are designing and building synthetic signal transduction circuits to control plant growth and development suited for a changing climate.

<https://careers.asbmb.org/job/research-specialist-protein-structural-biology/54075741/>

Assoc. Director/Director, Process Development Cue Biopharma Cambridge, Massachusetts, United States



In this newly introduced position at Cue Biopharma, the Director/Senior Director of Process Development will be tasked with improving and developing robust and scalable manufacturing processes, scientifically sound specifications, and associated analytical methods for our unique biologics. This role will be expected to support both internal research activities as well as work carried out through CMOs. Further, this individual, having demonstrated expertise and leadership in the field, will have the opportunity to build a small team to support upstream, downstream, and assay development activities. This position will report to the Vice President of Protein Therapeutics and will collaborate closely with the Head of CMC.

<https://careers.asbmb.org/job/assoc-directordirector-process-development/54168502/>

Postdoctoral Associate University of Pittsburgh Pittsburgh, Pennsylvania, United States



A postdoctoral position is currently available at the Soft Tissue Biomechanics Laboratory (STBL) in the Department of Bioengineering under the direction of Professor Jonathan Vande Geest. The STBL is currently developing a novel platform to study the mechanobiology of the optic nerve head in primary open angle glaucoma that seamlessly integrates state of the art techniques in regenerative medicine, 3D bioprinting, and intravital imaging. The long term goal of the STBL is to utilize this novel platform to improve the mechanistic understanding of how optic nerve head extracellular matrix remodeling is linked to retinal ganglion cell death and vision loss and if this understanding can be leveraged to discover the next generation of novel therapeutic targets for glaucoma.

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

Technology and Application Consultant Mettler-Toledo AutoChem, Inc. REMOTE, New Jersey, United States



The Technical Sales department of METTLER TOLEDO AutoChem (www.mt.com/autochem) needs a self-motivated, ambitious team player to fill our Technology and Application Consultant role, ideally located in New Jersey. We are looking for people who love science and technology, and excel at building dynamic relationships with people and are interested in expanding their commercial and business skills. Ideal candidates are problem solvers with a strong chemistry, chemical engineering, or biochemistry background who will accept challenges, ask questions, research, and engage our customers. This position will be responsible for providing world class technical sales consulting services to potential and existing customers in the optimization and improvement of particulate process and applications, particularly crystallization. As a recognized expert, you will establish strong peer based relationships with scientists and engineers in the field, while ensuring sustainable sales growth of the business in their region.

<https://careers.asbmb.org/jobs/view/technology-and-application-consultant/54168494/>

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