Vol. 19 / No. 8 / September 2020

# ASBMB TODAY

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

## A zest FOR synthetic biology

### Why are metabolic engineers so interested in limonene?

ASBMB '21
ANNUAL MEETING

# The 2021 ASBMB Annual Meeting will be virtual!

## Learn more at asbmb.org/annual-meeting

EB
Experimental Biology

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

# CONTENTS

## NEWS




## FEATURES

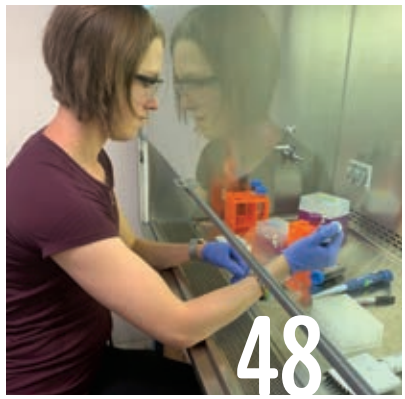


**COVER PHOTO: OKEYKAT/ UNSPLASH**




## PERSPECTIVES



ASBMB TODAY

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



ASBMB
American Society for Biochemistry and Molecular Biology

**www.asbmb.org/asbmbtoday**
**PRINT ISSN 2372-0409**



## EDITOR'S NOTE

# A time for reimagining

*By Comfort Dorn*

At the height of the strange summer of 2020, I read an article, "How pandemics wreak havoc and open minds," about the ways in which the bubonic plague of the 14th century marked the end of the Middle Ages and beginning of the Renaissance.

The COVID-19 pandemic is unlikely to reach Black Death dimensions, but as we all avoid social interactions, we have plenty of time to sit on our couches and reconsider the way we operated in our personal and professional lives until last March. For many of us, the notion of working from home was pretty far-fetched; now, it's hard to imagine a return to daily commuting. Did it occur to us that the essential employees would be delivery drivers and grocery clerks? That we'd be valued for mask making and sourdough?

In addition, coronavirus research has taken off at a gallop, with an accompanying deluge of scientific papers, calling into question the ponderous traditions of academic publication. The pandemic and coinciding Black Lives Matter protests have highlighted flaws in the highly competitive (and often non-inclusive) systems of biomedical research.

I offer these examples because two writers have done more than fret about them. Ken Hallenbeck and Chris Pickett lay out blueprints for change on pages 40 and 43. They reimagine these hidebound structures.

What can you reimagine?

The world will be a different place next spring — a year after COVID-19 began to shutter much of the planet. Why not make this a time for rethinking these structures in ways that are more sensible and just? We want your ideas for how to do that. We will dedicate our June/July 2021 issue to the theme of reimagining, and we want your contributions. Read the two essays mentioned above. Think about the systems around you. Can they be improved? Should they be replaced? What would make them better?

I asked our ASBMB Today editorial advisory board for some food for thought — a few prompts to get you thinking and writing: Bill Sullivan wonders if science communication should have a more central role in academia and if the tenure process needs to be revamped. Melissa Vaught suggests a shift toward institutional systems that accommodate and support people during challenges and disruptions both large and small. She also wonders about the central role of conferences in professional networking. Binks Wattenberg wants to rethink the relationships that institutions have with their surrounding communities.

We don't have room for all of their ideas here; I'll share more at asbmb.org/asbmb-today.

Maybe you have ideas for reimagining some of these systems — or others. We invite you to write them down. Good ideas come in all sizes, so your submission can be anything from 250 to 1,500 words. Please email it to asbmbtoday@asbmb.org. Deadline is March 15, 2021.

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

# Society to name fellows

*By Angela Hopp*

The American Society for Biochemistry and Molecular Biology is launching an honorific program to recognize members who have made outstanding contributions to the field through their research, teaching and mentoring, or other forms of service.

About two dozen scientists will be inducted into the ASBMB Fellows Program each year. Nominations will come from the membership, and the ASBMB Council will make the final selections.

"The ASBMB fellows will be expected to embody the society's core values and serve as role models by performing excellent research, taking teaching and mentoring to new levels, advancing diversity in the field and giving back to the community by participating in society programs or publications," Barbara Gordon, ASBMB's executive director, said.

Nominees must be regular, industry or emeritus members. (Student, affiliate and early-career members are ineligible.) Nominees must also have a history of service to the society, such as committee work, event organizing or editorial board service.

"The fellows program is intended not just to honor those who are recognized, but also to illuminate, through their stories, the variety of ways in which our membership as a whole enriches our profession and the people whom it serves," said Peter J. Kennelly, a professor at Virginia Tech and a member of the ASBMB Membership Committee, which conceived of the fellows program.

Nominations are being accepted now through Jan. 4. Once the nominations are in, the ASBMB Membership Committee will narrow the list to 25 candidates for the ASBMB Council to evaluate. The first class of fellows will be contacted in mid-February, and a public announcement will follow soon thereafter. The fellows also will be honored at the 2021 ASBMB Annual Meeting, which will be held virtually.

"The ASBMB has been the professional home for and nurtured the careers of many great scientists," said Bettie Sue Masters, a member of the ASBMB Membership Committee and a faculty member at the Duke University School of Medicine. "The ASBMB Fellows designation will recognize the contributions of those members who have excelled in research, education, advocacy and mentorship of future scientists and contributed to the mission of the society. This honor will recognize their commitment to their profession."

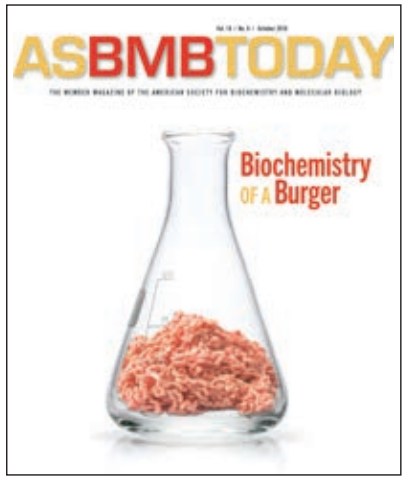
To learn more about the program or to nominate a member, visit asbmb.org/about/asbmb-fellows.

# ASBMB Today wins awards

*By ASBMB Staff*

*ASBMB Today* staff and contributors were recently honored for their work in the magazine.

Former senior designer Lisa Schnabel won a silver EXCEL award from Association Media and Publishing in the category of magazine cover–manipulated media for the cover of the October 2019 issue, a beaker full of ground beef illustrating the article Biochemistry of a Burger.




Contributing writer TL Jordan won a bronze EXCEL award in the editorial/opinion piece category for their essay "What I wish people understood about being a trans scientist," published in the October 2019 issue. Jordan graduated with a M.Sc. in immunology from the Mayo Clinic Graduate School of Biomedical Sciences this year and completed the ASBMB Advocacy Training Program in 2018.

Contributing writer Amanda Koch won second place in the 2020 Bio-Rad Science Writing Competition for a version of her essay "Out of my comfort zone: How I use science to influence policy," published in the June/July 2020 issue. Koch is a Ph.D. student at Colorado State University in the biochemistry and molecular biology department.

EXCEL Awards recognize excellence in media, publishing, marketing and communications for nonprofit and for-profit associations.

Bio-Rad's writing competition invites life science Ph.D. students to share something that they have learned during their studies with the wider scientific community.

## Regev wins Lurie prize


REGEV

**Aviv Regev**, the departing chair of the faculty and a core member at the Broad Institute of the Massachusetts Institute for Technology and Harvard University, has won the Foundation for the National Institutes of Health's 2020 Lurie Prize in Biomedical Sciences. Earlier this year, she announced she was be leaving the Broad to become Genentech's research and early development chief in August.

Established in 2013, the Lurie Prize recognizes outstanding achievement by a promising scientist who is 52 years old or younger. The prize includes a $100,000 honorarium, made possible by a donation to the FNIH by philanthropist Ann Lurie, president of the Ann and Robert H. Lurie Foundation.

Regev's laboratory at the Broad Institute, MIT and the Howard Hughes Medical Institute studies how complex molecular circuits function in cells and between cells in tissues. The award recognizes her work in laying the groundwork for the field of single-cell genomics, spearheading leading-edge technologies that enable a sharper perspective on human cells and applying them to revolutionize understanding of biology and disease.

"Her innovative work has made a major contribution to scientific understanding, highlighting an astonishing diversity in the activities and types of cells," said Maria C. Freire, president and executive director of the FNIH. "Applying those revolutionary techniques to cataloguing every cell in the body promises to have a vital impact on the future of diagnosis and therapy."

Regev won the American Society for Biochemistry and Molecular Biology's Earl and Thressa Stadtman Young Scholar Award in 2014.

## Gierasch wins Outstanding Achievement Award for research

**Lila Gierasch**, a distinguished professor of biochemistry and molecular biology at the University of Massachusetts Amherst and editor-in-chief of the Journal of Biological Chemistry, was one of two scientists recognized with the UMass College of Natural Science Outstanding Achievement Award in research.


GIERASCH

The award recognizes the college's faculty, staff and students who have made important contributions to their disciplines, departments, college and university.

Gierasch, a 1986 Guggenheim fellow and member of the National Academy of Sciences, is known for her work focused on protein folding and chaperone function in vitro and in vivo.

She won the ASBMB's Mildred Cohn Award in Biological Sciences in 2014.

## Alrubaye wins teaching, mentorship award

**Adnan Ali Khalaf Alrubaye**, a research assistant professor of biological sciences and poultry science at the University of Arkansas, has been awarded the 2019 John and Lois Imhoff Award for Outstanding Teaching and Student Mentorship by his university's teaching academy. The Imhoff award, presented annually to a member of the UA faculty, recognizes Alrubaye's excellence in teaching the department's introductory microbiology course and mentoring students.


ALRUBAYE

When not teaching microbiology, Alrubaye studies the pathogens that cause bone infections in farmed chickens, and he has published on antibiotic-free methods, such as selective breeding and nutrient supplementation, to improve chicken husbandry.

Alrubaye has been a member of the UA faculty since earning his Ph.D. and M.Ed. there in 2013. His previous teaching awards include the Fulbright College Master Teacher Award, the University of Arkansas' Collis Geren Award for commitment to graduate education, and the Most Outstanding Faculty Member award from the university's student government.

## Cameron assumes ASV presidency

**Craig Cameron**, virologist and chair of the department of microbiology and immunology at the University of North Carolina at Chapel Hill, has assumed the presidency of the American Society for Virology.

Cameron, who studies RNA-dependent RNA polymerases and RNA-binding proteins and is an associate editor at the Journal of

CAMERON

Biological Chemistry, was named ASV president-elect last summer. He moved to UNC last year after 25 years at Pennsylvania State University.

In addition to his role with the ASV, Cameron is a fellow of the American Association for the Advancement of Science, a member of the National Science Advisory Board for Biosecurity, Molecular Genetics B Study Section and a former chair of the ASBMB Minority Affairs Committee.

"With his outstanding track record of research, service, and leadership, it is no surprise that Craig Cameron has been elected to lead the American Society for Virology," said Blossom Damania, vice dean for research at the UNC School of Medicine. "We are extremely fortunate to have Craig at the helm during the time of a global COVID-19 pandemic, and we congratulate him on this highly deserved honor."

## Brenner moving to City of Hope

**Charles Brenner** will be moving to the City of Hope National Medical Center in Southern California to chair its new department of diabetes and cancer metabolism.

Brenner, a former chair of the American Society for Biochemistry and Molecular Bioogy's Publications Committee, former chair of the editorial advisory board of ASBMB Today and the 2016 winner of the ASBMB Award for Exemplary Contributions to Education, currently serves as the Roy J. Carver chair and head of biochemistry at the University of Iowa.

During his 11 years at Iowa, he hired eight faculty members into the department and oversaw the creation of the university's high-throughput screening facility and the trans-collegiate, trans-disciplinary Obesity Research & Education Initiative.

Brenner is among the world's experts in NAD metabolism and developed quantitative targeted NAD metabolomics. He has discovered many conditions in which the NAD system is disturbed at the transcriptional and metabolomic levels by metabolic disturbances.

BRENNER

At City of Hope, he plans to expand his program on genotype-specific approaches to cancer, to dissect the systems biology of NAD (i.e., to determine how particular tissues distribute NAD precursors to other tissues, especially as a function of metabolic disruption). He also aims to utilize what has been learned about the activities of nicotinamide riboside in the context of diabetic and chemotherapeutic neuropathy, fatty liver, postpartum, and viral infection to improve human health.

"The fit between what I do in NAD biology and what City of Hope wants in this unit is outstanding," Brenner said. "In addition, we will do strategic hiring in our new department to make it a home for creative, rigorous metabolism scientists."

## AACR: Kadoch receives award; Langer, O'Malley inducted as fellows

**Cigall Kadoch**, an assistant professor at the Dana-Farber Cancer Institute and at Harvard Medical School and a member of the Broad Institute, has received the 2020 American Association for Cancer Research Award for Outstanding Achievement in Basic Cancer Research, which recognizes achievements in basic research into cancer by faculty 45 years old or younger.

Kadoch studies ATP-dependent chromatin remodeling complexes known as SWI/SNF complexes. Named for the phenotypes they contribute to in yeast, where they were first discovered, these multiprotein complexes alter gene expression by modifying the position of nucleosomes along a strand of DNA. As a graduate student, Kadoch discovered that a specific SWI/SNF protein mutation found in a subtype of sarcoma can change the composition and genomic targeting properties of the complex, ultimately upregulating oncogenic gene expression to support tumor development. As a professor, she has led further investigation into the mechanisms by which disruption of SWI/SNF complexes contributes to the development of various types of cancer and neurodevelopmental disorders.

KADOCH

During its annual meeting, the AACR also announced the election of a new class of fellows of the AACR Academy, a group that recognizes and honors distinguished cancer researchers. Among this year's fellows are two ASBMB members:

• **Robert Langer**, a professor at the Massachusetts Institute of Technology, for developing synthetic polymer systems that can be used both for controlled drug delivery and as substrates for tissue engineering for regenerative medicine;


LANGER

• **Bert O'Malley**, chancellor and chair of the molecular and cellular biology department at Baylor College of Medicine and associate director of basic research at that college's comprehensive cancer center, for basic research into the role of intracellular hormones and cofactors in cancer cell metastasis.


O'MALLEY

## Ramachandran named Pew–Stewart Scholar

University of Colorado cancer biologist **Srinivas Ramachandran** has been named one of five 2020 Pew–Stewart Scholars.

Ramachandran, an assistant professor in CU's department of biochemistry and molecular genetics, is working to develop liquid biopsies for early detection of cancer by examining unique signatures from cell-free DNA shed by tumors.


RAMACHANDRAN

"Our long-term goal is to use knowledge from the basic biology of how our genomes are packaged to understand the tumor processes without having to do a biopsy," Ramachandran said, "then use that information to identify cancer biomarkers."

For more than 15 years, the Pew–Stewart Scholars Program for Cancer Research has supported promising early-career scientists whose research will drive discovery and accelerate progress to a cure for cancer. As a Pew–Stewart Scholar, Ramachandran will receive a four-year grant to further his research.

## Lamb to serve as chair of chemistry at UTSA

University of Kansas professor **Audrey Lamb** is moving from Lawrence to San Antonio to chair the chemistry department at the University of Texas at San Antonio.

Lamb is a full professor in the department of molecular biosciences at KU, which she joined in 2003 after doctoral training at Vanderbilt University and a postdoc at Northwestern University. She directs the university's graduate program in chemical biology and recently spent a year serving as the interim dean of graduate studies.


LAMB

The Lamb laboratory studies microbial uptake of iron and other metals from the environment. Bacterial pathogens use metallophores, secreted natural products that bind to and chelate metals for uptake, to supply the metals they need for many cellular processes, including respiration. The synthesis of these natural products, many of them derivatives of peptides, is not dependent on the ribosome; because such enzymes are not found in humans, they are a promising class of potential drug targets. The lab is also studying the biosynthesis of riboflavin (vitamin B2). The lab's research focuses on the enzymology of specific steps in biosynthesis in pathogens such as Pseudomonas aeruginosa and Staphylococcus aureus.

Lamb, who is a member of the American Society for Biochemistry and Molecular Biology Council, was set to start her new position at UTSA in August.

## Drennan receives mentorship award

**Catherine Drennan** is one of 12 faculty at the Massachusetts Institute of Technology who received the university's 2020–2021 Committed to Caring mentorship award in June.

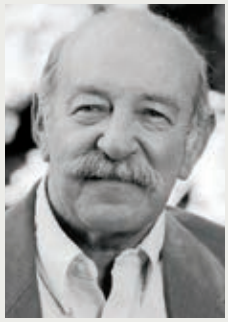
The award recognizes professors who have prioritized the well-being of their graduate students, helped to develop scholarly excellence and supported inclusion and equity in the research community. Recipients are nominated by their graduate students and selected by a committee of graduate students and staff members.


DRENNAN

Drennan, a professor of chemistry and biology at MIT and a Howard Hughes Medical Institute investigator, is a former member of the American Society for Biochemistry and Molecular Biology Education and Professional Development Committee. Her pedagogical work includes research into best practices for active lectures and developing research-based modules for undergraduate courses on biochemistry.

In addition to education research, Drennan studies the structural biology of metalloenzymes. Her lab's targets have included multiple enzymes that depend on metal cofactors, such as ribonucleotide reductase, an early enzyme in DNA biosynthesis. In March, she won the Protein Society's Dorothy Crowfoot Hodgkin Award, and in May, she was inducted into the American Academy of Arts and Sciences.

## Kivie Moldave



The American Society for Biochemistry and Molecular Biology recently learned that ribosome biologist and University of California, Irvine emeritus professor Kivie Moldave died in December. He was 96.

Born in Kiev in 1923, Moldave came to the United States in 1937. He published his first paper in the Journal of Biological Chemistry in 1952, as a graduate student with Richard Winzler at the University of Southern California. At this early stage of his career, he studied amino acid metabolism in the brain and in cancerous tissues. This interest led him to investigate aminoacyl tRNA synthesis, mechanisms of protein translation and the composition of the ribosome. As a mainstay in the field of translation regulation, Moldave participated in the 1985 Santa Cruz workshop that contemporaries credit with planting the seed for the Human Genome Project, which was officially launched five years later.

Moldave's career took him to biochemistry departments across the U.S., beginning at Tufts University in 1964. He moved to the University of Pittsburgh School of Medicine to chair its biochemistry department in 1966 and then to the UC Irvine Medical School in 1970. Though he later moved to the University of California, Santa Cruz to act as academic vice chancellor, UC Irvine would remain his scientific home; he held an emeritus position there after retiring from UCSC in 1992. He also spent time as a visiting professor at Cornell University and at universities in Copenhagen, Jerusalem, Mexico City, Vancouver, London and Paris.

From 1983 to 2005, Moldave was the serial editor of the textbook "Progress in Nucleic Acids Research," and he served several terms on the editorial board of the JBC. He was a member of numerous societies including the ASBMB, held leadership roles in the biological chemistry division of the American Chemical Society and was a member of advisory committees of the American Cancer Society. In his later years, he served on the executive committee of the UC Irvine Emeriti Association.

Moldave received the United States Public Health Service Career Award in 1963, the UCI Distinguished Faculty Award for Research in 1982 and the Distinguished University Service Award from the UCI Emeriti Association in 2008.

He is survived by his wife, Rose, to whom he was married for 70 years and his daughter, Ayn, and son, Peter.

## David H. MacLennan

David H. MacLennan, a Canadian biochemist and geneticist who studied the regulation of calcium in muscle, died June 24. He was 82.

Born in Swan River, Manitoba in 1937, MacLennan studied plant science at the University of Manitoba, then earned an M.S. in plant pathology and a Ph.D. in biology, both at Purdue University. He was a postdoctoral fellow and assistant professor at the Institute for Enzyme Research at the University of Wisconsin before joining the department of medical research at the University of Toronto in 1969, where he remained for the rest of his career, serving as department chair, J. W. Billes professor of medical research and university professor.

An early interest in mitochondrial electron transport components and the mitochondrial proton pump led MacLennan to study the sarcoplasmic reticulum calcium pump, including the mechanism of ion transport and storage and release of calcium that powers muscle contractions. He helped demonstrate that mutations in a regulator of the calcium pump can cause cardiomyopathy, and he led teams that defined the genetic basis for human skeletal muscle diseases, malignant hyperthermia, central core disease and Brody disease. He also identified a calcium release channel mutation that causes porcine stress syndrome.

MacLennan was a fellow of both the Royal Society of Canada and Royal Society of London and a foreign associate of the U.S. National Academy of Sciences. His many honors included the Canadian Biochemical Society's Ayerst Award and the Biophysical Society's National Lectureship Award, the Gairdner Foundation's International Award, the Canada Council Izaak Walton Killam Memorial Prize in Health Sciences and the Glaxo–Wellcome Prize. In 2001, he was appointed an officer of the Order of Canada. He was a member of the Journal of Biological Chemistry editorial board from 1975 to 1980 and 1982 to 1987 and an associate editor for the Canadian Journal of Biochemistry from 1972 to 1976.

# Herbert Tabor (1918–2020)

## The longtime editor-in-chief of the ASBMB's Journal of Biological Chemistry was a beloved figure in the field

*By John Arnst*


ASBMB

**Herbert and Celia Tabor had a long marriage and scientific collaboration.**

Dr. Herbert Tabor, longtime editor-in-chief of the Journal of Biological Chemistry, died Aug. 20 at his home on the National Institutes of Health campus. He was 101.

Tabor led JBC from 1971 to 2010 and oversaw the journal's expansion from 1,000 to 4,500 published articles per year and transition to online publishing in 1995. He continued to investigate the function of polyamines and their role in health and disease into his late 90s.

"Herb left a legacy like none other in JBC's history," said Lila Gierasch, editor-in-chief of JBC. "Were it not for Herb, I don't know what the journal, and the molecular bioscience he helped it shepherd, would look like today."

Born in New York City in 1918, Tabor graduated from Harvard College in 1937. He then enrolled at Harvard Medical School, where, during his final year as a medical student, he worked with A. Baird Hastings on the ionization of magnesium phosphate. The subject would become the subject of Tabor's first paper in JBC in 1943.

Tabor's blooming interest in biochemistry followed him through his medical internship. After graduating with an M.D. in 1941, he interned at Yale New Haven Hospital and worked concurrently in the lab of John Peters on a carbon monoxide method for measuring blood volumes. While there, he assisted in the first administration of penicillin — staving off a deadly case of streptococcal septicemia — in the United States. In 1943, Tabor joined the war effort as a medical officer on a Coast Guard cutter escorting Atlantic convoys before being transferred to the National Institutes of Health, where he joined Sanford Rosenthal's team to study treatment for burns and traumatic shock.

In 1946, Tabor married Dr. Celia White, whom he had met on a Boston streetcar through a mutual friend six years prior; she had just concluded her medical residency at Vanderbilt University Medical School Hospital. In 1949, the Tabors moved into commissioned officer housing on the NIH campus in Bethesda, Maryland. In 1952, Celia Tabor joined the Rosenthal lab, starting a collaboration with her husband that would continue until her retirement in 2005. In 1954, JBC published the Tabors' first of more than 80 joint articles, "Purification of amine oxidase from beef plasma," 19 of which appeared in the journal.

In 1961, Herb Tabor joined the editorial board of JBC, becoming an associate editor in 1968 and editor-in-chief in 1971. In 1977, Herb Tabor was elected to the National Academy of Sciences. Over the following decades, he and colleagues demonstrated the role that polyamines play in the growth of normal and cancerous cells.

After four decades at the helm of JBC, Tabor stepped down in 2010, continuing his involvement as a co-editor. In 2011, the journal established the Herbert Tabor Young Investigator Awards to honor Tabor's

scientific and editorial legacy and to recognize early-career first authors of standout JBC papers for their creativity and scientific excellence. The Herbert Tabor Research Award, established in 2004, honors senior investigators.

In 2018, the county council of Montgomery County, Maryland, marked Tabor's contributions to science by designating Nov. 28 as Herb Tabor Day in an official proclamation, and the state of Maryland honored Tabor with a governor's citation. Friends and family also feted Tabor in a virtual celebration of his 100th birthday.

"Herb was an inspiration to us all," said Barbara Gordon, executive director of the American Society for Biochemistry and Molecular Biology, which publishes JBC. "That he was able to do what he loved for so long, and leave such a mark on the scientific community and the society, was just amazing. We loved him, and we're going to miss him dearly."

Tabor is survived by his daughter, Marilyn, and his sons Edward, Richard and Stanley. He was preceded in death by his wife, Celia, who died in 2012.

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

## Celebrating Tabor's legacy

**In 2018, the Journal of Biological Chemistry published a thematic minireview series (jbc.org/site/thematics/polyamine) about the wide-ranging biochemical effects of polyamines in celebration of Herbert Tabor's 100th birthday. A year later, the journal published a collection of articles (jbc.org/site/thematics/tabor) that showcased the long-lasting impacts of Tabor's research and editorial leadership.**

COURTESY OF WILLIAM SMITH

**Herbert Tabor, shown here in San Antonio, joined the editorial board of the Journal of Biological Chemistry in 1961, became an associate editor in 1968 and became editor-in-chief in 1971. He served in that role through 2010, at which point he became co-editor, a position he held until his death.**

# A career in metabolism research and a drive to mentor minority students

*By Nuala Del Piccolo*

Claudio Villanueva is a born researcher. "As a child, I was always interested in science and wanted to learn more about the natural world," the UCLA associate professor said. "I would take toys apart, so that I could look inside to see how they worked."

However, Villanueva's childhood had limited exposure to careers in science. His family immigrated to Ontario, California, just east of Los Angeles, from Nicaragua when he was 9 years old. He attended schools with limited resources and struggled as a student.

"Looking back on it, I really lacked focus and a vision for how hard work in the classroom would lead to a career later," Villanueva said. "My parents didn't understand the U.S. education system, so my siblings and I had to figure it out for ourselves."

High school was a turning point for Villanueva. First, he took a test to match his interests and skills with career options. "The test told me to pursue a career in manual labor," he said. "I was really disappointed and felt like I had better options."

Second, during a schoolwide athletic and academic awards ceremony where he was recognized for his achievements on the wrestling team, Villanueva saw his classmates being honored for their work in the classroom with college admissions letters and scholarships. "The awards ceremony was a real wake-up call for me," he said. "I got a T-shirt, but I knew that my classmates' academic awards were much more meaningful."

COURTESY OF CLAUDIO VILLANUEVA

**Claudio Villanueva is an associate professor in the department of integrative biology at UCLA, where he studies lipid metabolism and adipocyte development. He also volunteers his time with organizations that promote diversity and inclusion in the sciences.**

He changed his trajectory and started working harder in his classes, Villanueva said. "I also started setting goals for myself, and quickly realized how much more effective I was at reaching an end point when I had a goal in mind. This lesson has actually carried me through my whole career — college, grad school, postdoc appointment, and now a faculty position."

After high school, Villanueva attended Chaffey College, a community college near his hometown, thinking he'd eventually go to dental school. When he transferred to California State University, San Bernardino, to finish his undergraduate degree, a professor encouraged him to apply to the McNair Scholars Program, which prepares students from underrepresented groups to attend and complete graduate research programs.

As a McNair scholar at CSUSB, Villanueva participated in a summer program that included preparation for the GRE graduate school entry exam, development of science communication skills and a lab placement. He worked in a biology lab, where he studied subcutaneous sodium transport in leopard frogs. At the end of the program, he traveled to Penn State to present his research and discuss science with fellow McNair scholars from around the country.

"In this simple model (leopard frogs), I learned how to design experiments and the technical aspects of measuring sodium transport using a voltage clamp," he said. "The research conference connected me to fellow young scientists and opened my eyes to the exciting possibility of a career in research."

## Finding a research focus

Villanueva abandoned his dental school plans to pursue research and a Ph.D. at the University of California, San Francisco. In Robert Farese Jr.'s lab at the Gladstone Institute, he studied lipid metabolism, with a focus on the role acyl-CoA:diacylglycerol acyltransferase, or DGAT, enzymes play in fatty liver disease. His results

COURTESY OF CLAUDIO VILLANUEVA

**Villanueva and the University of Utah's SACNAS Student Chapter are pictured at the 2017 national SACNAS conference in Salt Lake City, where they handed out sunglasses at their University of Utah recruitment table.**

showed why mouse models missing the enzyme DGAT1 are protected against obesity, fatty liver disease and diabetes.

**Spurred to research by a program for undergrads from underrepresented groups, UCLA's Claudio Villanueva pays it forward.**

"Mice that lack the DGAT1 enzyme can't store triglycerides efficiently and actually burn fat more quickly," he said. "These mice are actually leaner than wild-type mice, even though they eat more food."

Villanueva returned to southern California to complete his postdoctoral training with Peter Tontonoz at UCLA. He continued to study lipid metabolism but shifted his focus to the genetic level, with a specific focus on transcriptional regulation of the enzymes involved. Humans have two types of adipocytes, or fat cells, he explained; white fat cells store energy in the form of lipids and are associated with obesity, while thermogenic (brown and beige) fat cells quickly break down fatty acids to generate heat.

"I examined gene transcription in white and thermogenic adipocytes, and identified a gene — TLE3 — that attenuates thermogenic adipocytes," he said. "Inhibition of TLE3 shifts white fat cells to so-called 'beige fat cells,' a process that enables exclusively lipid storing cells to start burning energy."

In 2012, Villanueva launched his own lab at the University of Utah to study the molecular mechanisms that regulate adipocyte biology and lipid metabolism. "We are interested in understanding how cells sense and control metabolism in response to stressors like temperature," he said. "This requires an understanding of integrative metabolism and physiology."

"Our lab explores the molecular mechanisms that promote energy expenditure. These studies will provide opportunities for intervening in metabolic diseases that are associated with obesity."

## Promoting diversity

At Utah, Villanueva began mentoring students in the lab and the classroom. He found joy in mentoring students. "It's a lot of fun to see trainees learn and grow as scientists," he said.

He was discouraged, however, by the scarcity of minority students, who at the time made up just 6% of the incoming graduate students in the Bioscience Graduate Program at Utah. "The U.S. population is changing rapidly, and the scientific work-

force needs to reflect those changes in order to reliably serve the public," he said.

To address the issue, Villanueva and a few trainees started a local chapter of the Society for Advancement of Chicanos/Hispanics and Native Americans in Science. The mission of SACNAS is to help members of these underrepresented groups attain advanced degrees, careers and positions of leadership in science, technology, engineering and mathematics fields.

The new SACNAS chapter quickly gained popularity, and as involvement increased, so did minority recruitment. By 2019, 30% of incoming graduate students were members of minority groups. Villanueva credits this rapid growth to SACNAS's involvement with the process and hiring Jeanette Ducut–Sigala, who was involved in recruitment. "Prospective students feel welcome at universities when they see themselves represented in the current student body," he said.

Villanueva encourages current students to attend SACNAS's annual conference, which includes both professional development workshops geared toward undergraduates, grad students and postdocs and opportunities to speak with recruiters from major academic institutions, large private companies and government agencies.

"For me, the highlight of the conference is interacting with students interested in science," he said. "Many students come to the SACNAS conference not realizing how many people of diversity are actually doing science, since numbers are so limited at individual institutions. The conference is a really incredible experience because students realize, 'Wow, there are people with stories similar to mine doing science!' On top of that, lots of faculty members at the conference are really invested in student success and actively seeking to mentor and encourage the next generation. It's a unique experience."

The conference also includes cultural programs such as a powwow, songs, dances and art displays. Each year, the organizers take care to feature traditions from the original inhabitants of the host location (recent examples include Honolulu, San Antonio and Washington, D.C.).

Inspiring keynote speakers discuss diversity in the sciences and the relationship between science and society. These speakers often identify as minorities and hold leadership positions in STEM; recent speakers have included Nobel Prize winner Dr. Mario Cappechi, President of the Republic of the Marshall Islands and climate action leader H.E. Hilda C. Heine, and then-U.S. Secretary of Energy Dr. Ernest Moniz. Villanueva encourages young scientists seeking inspiration to listen to these speeches, which have been archived on YouTube.

## Moving forward

Last year, Villanueva relocated his lab to UCLA. He was attracted by the university's strong consortium of labs focused on metabolism research (including the Tontonoz lab) and the corresponding opportunities for collaboration.

Villanueva also appreciates that UCLA is not complacent about diversity issues but is constantly seeking to innovate. "The university provides workshops for faculty about pedagogy as it relates to diversity and inclusion. Now, we are engaged in active discussions about how to create classroom environments that are more supportive of minority students," he said. "Organizations like SACNAS have been instrumental in increasing diversity in the sciences by making people feel supported, less isolated and alone. I hope we can create a similar environment at UCLA."

The move has been productive so far, though in-person lab work has been curtailed by the COVID-19 pandemic. For now, Villanueva and his students are spending time analyzing data, learning the computational skills needed to analyze next-generation sequencing results and planning future experiments. Villanueva said he looks forward to returning to the lab fully when public health officials deem it safe to do so.

"Ultimately, at the core," he said, "I'm fascinated by the natural world and love the fact that I have a career where I can make new discoveries and share them with the world."

### ABOUT THE RESEARCH SPOTLIGHT

The American Society for Biochemistry and Molecular Biology's Research Spotlight highlights distinguished biomolecular and biomedical scientists from diverse backgrounds as a way to inspire up-and-coming scientists to pursue careers in the molecular life sciences. Eligible candidates include Ph.D. students, postdoctoral fellows, and new or established faculty and researchers. To nominate a colleague for this feature, contact us at asbmbtoday@asbmb.org.

**Nuala Del Piccolo** (ndelpiccolo@ucdavis.edu) is a postdoctoral scholar in the biomedical engineering department at the University of California, Davis. She earned her Ph.D. in materials science and engineering at Johns Hopkins University.

# Science and medicine

## Connecting the known and the unknown

*By Adriana Bankston*

Tian "Sally" Zhang got an early introduction to scientific publishing. When she was a high school junior working as a research assistant at the University of British Columbia, she studied how efficiently a peptide killed biofilm bacteria. The research was published in 2016 as a first-author paper in PLoS One. Through this work, Zhang said she "began to be interested in biology," leading to her subsequent college major and interest in medicine as a career.

Now a senior at Emory University majoring in biology and minoring in physics, Zhang is the president of the school's American Society for Biochemistry and Molecular Biology Student Chapter, which she worked to start in fall 2018. The following spring, the chapter surveyed students on trends related to career development, started a mentorship program, and engaged members in outreach and science advocacy initiatives.

The chapter's advocacy activities focused on a letter-writing campaign urging policymakers to fund research and science, technology, engineering and math programs. A volunteer outreach program sent undergrads to local elementary schools to demonstrate chemical reactions by combining an acid and a base to propel a plastic bottle modified to look like a boat. The mentoring program matches grad students and students in the school of medicine with undergrads to discuss career development and various educational paths.

After the COVID-19 outbreak, the Student Chapter slowed its activities, but members engaged in a few virtual events last spring. They plan to continue hosting new activities online in this school year, Zhang said. "We have been working to implement novel policies … to serve the student population in a remote format."


COURTESY OF SALLY ZHANG

**An internship at Harvard Medical School and Boston Children's Hospital let Sally Zhang to think about becoming a physician.**

With all her Student Chapter activities, Zhang has not neglected her research. Working in the Center for Neurodegenerative Diseases at Emory, she was an author on a paper about protein interactions in Alzheimer's disease, using proteomics to study human brain tissue. During an internship at Harvard Medical School and Boston Children's Hospital, she worked on a clinical report about a rare disease in infants.

Over time, these experiences led Zhang to think about becoming a physician. "Medicine makes a connection between what is known and what is unknown," she said, adding that she enjoys the "interactive nature of patient care."

While shadowing a clinician as part of her Alzheimer's research , Zhang said she saw how much a physician can do for patients by using personalized treatment strategies and being empathetic. Examining clinical trials data during her Harvard internship, she saw inside the patient–physician dynamic and really enjoyed it.

Zhang's goal is to become an academic physician. She plans to attend medical school, become a doctor and potentially run her own laboratory someday. Ultimately, she would like to pursue a career where she can both see patients and do bench research.

**Adriana Bankston** (abankston81@gmail.com) is principal legislative analyst at the University of California Office of Federal Governmental Relations. This post represents the writer's personal views and not the views of her employer. Follow her on Twitter @AdrianaBankston.

JLR | JOURNAL OF LIPID RESEARCH

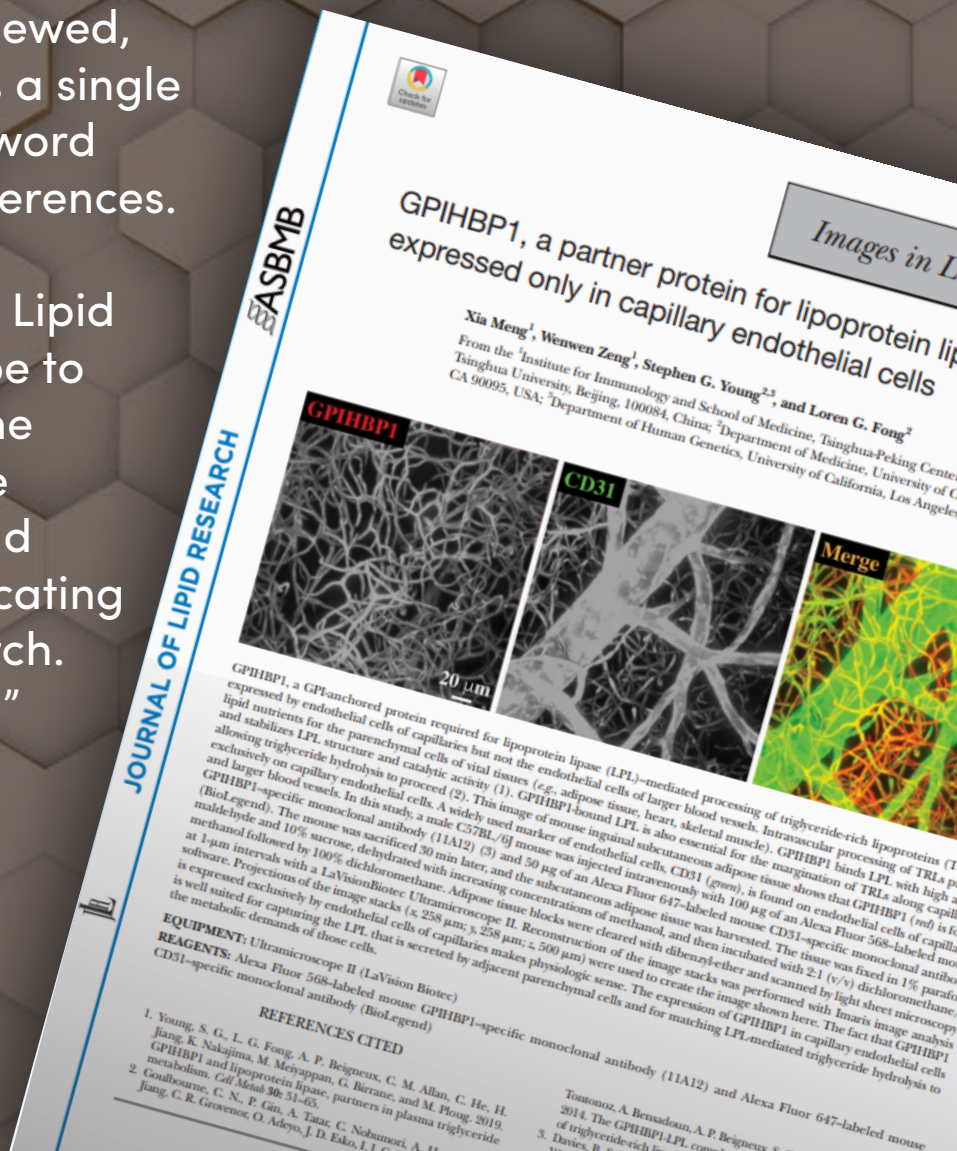
# Images in Lipid Research

## A new article format in the Journal of Lipid Research

The editors of the Journal of Lipid Research are pleased to announce the adoption of a new article format: "Images in Lipid Research." Each peer-reviewed, one-page article contains a single horizontal image, a 400-word caption and up to four references.

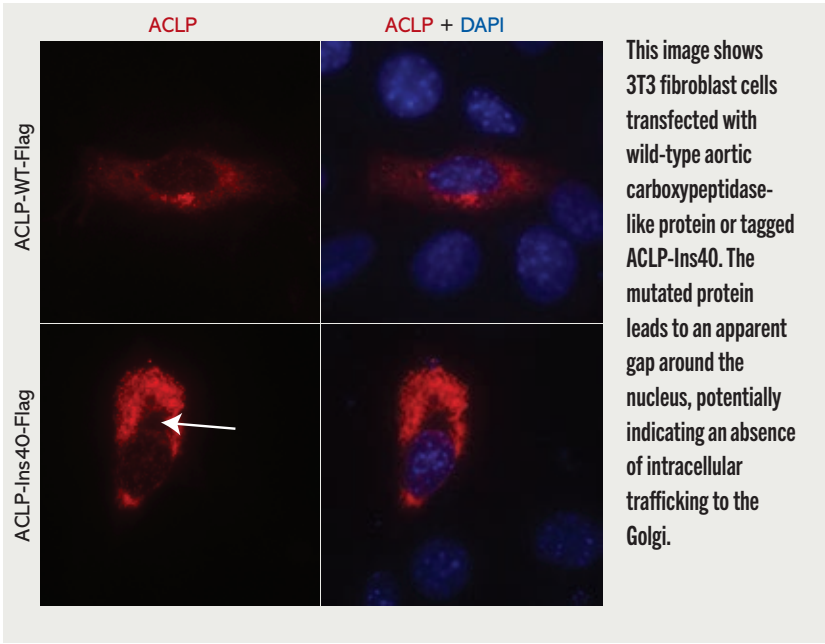
In creating the "Images in Lipid Research" format, we hope to celebrate scientists and the images they create. These articles will be easy to read and effective in communicating discoveries in lipid research. "Images in Lipid Research" will appear in PubMed and will be citable.

**Learn more at jlr.org.**



# A disorder of disrupted proteins

*By Nicole Lynn*




LAYNE LAB/JBC

This image shows 3T3 fibroblast cells transfected with wild-type aortic carboxypeptidase-like protein or tagged ACLP-Ins40. The mutated protein leads to an apparent gap around the nucleus, potentially indicating an absence of intracellular trafficking to the Golgi.

Composed of proteins, fibers, cells and other substances, connective tissues attach, stabilize and reinforce the structure of human bodies. While there are many causes of connective tissue disorders, Ehlers–Danlos syndrome, or EDS, involves the disruption of collagen or collagen-regulating proteins by means of genetic mutations.

EDS, which affects as many as one in 2,500 people, is an inherited disorder that weakens connective tissues, specifically affecting the skin, joints and blood vessels. Researchers recently have found that some EDS-presenting families share mutations in the adipocyte enhancer binding protein 1, or AEBP1, gene, which encodes for the aortic carboxypeptidase-like protein, or ACLP, found in collagen-rich connective tissues including the skin, ligaments, tendons and vasculature. Individuals with AEBP1 mutations develop a subtype of EDS called EDS-classic-like-2, or EDSCLL2, which is characterized by joint hypermobility, abnormal scarring, delayed wound healing and vascular ruptures.

Medical student Neya Vishwanath, then a second-year master's student in the medical sciences program at the Boston University School of Medicine, and colleagues in Matthew Layne's lab were interested in investigating mutations in AEBP1 and the processing mechanisms for ACLP. Their goal was to examine mechanisms of protein secretion and collagen fiber stability for these proteins in the context of EDS.

"In all my biology courses, we were always taught how integral connective tissue is to a healthy body," Vishwanath said. "In the Layne lab, (we) wanted to better understand the importance of ACLP in connective tissue health and figure out how mutations in ACLP could cause human disease."

In a recent paper in the **Journal of Biological Chemistry**, Vishwanath and colleagues highlight a specific mutation found in EDS patients called ACLP-Ins40. They found that this mutation, which causes an insertion of 40 amino acids in the collagen-binding region of ACLP, results in the improper exit of ACLP from cells and leads to cellular stress. The researchers also mapped and identified the specific amino acids required for proper ACLP secretion.

The team also identified novel protein processing mechanisms critical in ACLP secretion. Specifically, they demonstrated how glycosylation, or the addition of sugar groups to ACLP, is necessary for the proper cellular exit. When sugar groups are unattached to ACLP, the result is in-cell retention of ACLP and increased cellular stress.

Research with two other labs focused on the potential for ACLP to contribute to collagen fiber mechanics, specifically highlighting ACLP's role in mechanical strength, Vishwanath said. "Our collaborative studies with Michael Smith and Joyce Wong's laboratories at Boston University determined that ACLP contributes to the mechanical strength of collagen fibers that make up numerous connective tissues including ligaments, tendons, and cartilage."

Vishwanath and her colleagues hope insights from this work will contribute to a greater understanding of the mechanisms involved in connective tissue structures and provide scientists with targets for pharmacological interventions to treat connective tissue disorders such as EDS.

*DOI: 10.1074/jbc.RA120.013902*

**Nicole Lynn** (nalynn@g.ucla.edu) is a graduate student at the University of California, Los Angeles, in the chemistry and biochemistry department.

# Spit-stimulating natural compounds could end dry mouth

*By John Arnst*

Dry mouth might not seem like a pressing concern in the middle of a pandemic. However, the condition affects between 10% and 30% of adults and seniors — most often as a side effect of radiation therapy for head and neck cancers or as a symptom of autoimmune diseases such as Sjögren's syndrome — and can increase a patient's risk of developing dental decay, tooth demineralization and oral infections.

In a step toward developing drugs that might treat dry mouth, or xerostomia, researchers at King's College London performed a nonbiased proteomics analysis of the effects that various natural compounds have on the channels of chemesthetic transient receptors, also known as TRP channels, expressed on the mucosal membrane that lines the inside of the mouth. They published their findings detailing the compounds' influence on the flow and protein composition of saliva in the journal **Molecular & Cellular Proteomics**.

The proteomics analysis was the product of a collaboration between Jack Houghton, now a postdoctoral researcher at a University of Cambridge proteomics facility, and the lab of Gordon Proctor, a professor of salivary biology at King's College London.

"The group has been studying dry mouth from a number of different angles for several years," Houghton said. "But ultimately, it's quite an open question still because it's not just a lack of saliva, it's also the quality or the content of the saliva that changes, and these changes cause differences in how flavors adhere to the mucosal surfaces in the mouth."

BARBARA KOSULIN/UNSPLASH

**Nonivamide is one of the active compounds in chile peppers and is more heat-stable than capsaicin.**

Where saliva comes from is also a key distinction. The human mouth contains three major salivary glands — the parotid far behind the molars, the sublingual below the tongue and the submandibular beneath the mandibles — and close to 1,000 minor glands dotted across the tongue, palate and lips.

"There are hundreds of minor salivary glands in the lip — you can kind of feel them if you rub your tongue against your lip, the little hard, circular balls," Houghton said. "We are interested in these minor glands because they are within the mucosal surfaces where we thought that we might see differences or changes in how this saliva adheres."

Houghton and colleagues applied multibatch quantitative mass spectrometry to saliva collected from volunteers who had rinsed their mouths with a TRP agonist. They found that nonivamide, a capsaicinlike agonist of the TRPV1 channel that is naturally found in chile peppers, and menthol, an agonist of the TRMP8 channel, both caused an increase in the secretion of digestive proteins and the flow of saliva in all parts of volunteers' mouths, including the minor glands. As both compounds are alkaloids, they would not carry the same risks as acidic tastants that stimulate salivary secretion but erode enamel tissues.

This expands on previous findings that agonists of salivary channels such as piperine, an alkaloid found in black peppers, and capsaicin, the active compound in chile peppers that has been explored for its role in mitigating obesity, high blood pressure and neuropathic pain, are able to increase the flow of saliva in patients' mouths.

Houghton and his colleagues plan to examine the mechanisms the TRP agonists use to modify the rheological properties of saliva. Fortunately, the saliva they'll be analyzing was collected two years ago – long before the COVID-19 pandemic limited access to both research labs and willing volunteers.

"The next steps have already been carried out, but haven't been published yet," Houghton said. "They are essentially further investigations into the direct stimulation of the saliva gland cells by the TRP agonists."

*DOI: 10.1074/mcp.RA120.002174*

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

# Health journey helps researcher teach old mice new tricks

*By Laurel Oldach*

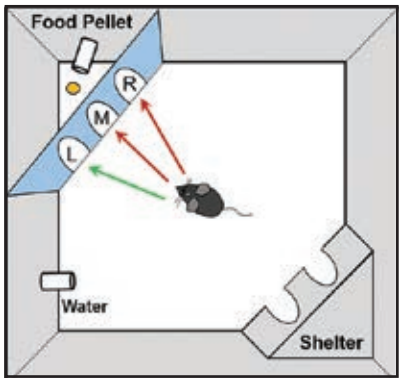
Eileen Parks' diagnosis led to hours of midnight reading, years in the lab and, recently, a discovery that improves our understanding of cognitive changes with age.

"I have a very specific type of epilepsy," the Oklahoma University graduate student explained. "My seizures are controlled now by medication. But my science brain wanted to understand (why) … I can only have a seizure during the second or third day of my menstrual period."

For about one in three women with epilepsy, the odds of having a seizure fluctuate in synchrony with their menstrual cycle — more specifically, with progesterone. Parks calls progesterone "the master hormone" because enzymes can convert it into other hormones and metabolites with diverse biological activity. One of those, allopregnanolone, piqued her interest.

"If I'm curious about something, I will literally spend all night on my computer reading everything I could find out about it," Parks said. She learned that allopregnanolone tends to suppress seizures because it binds to and affects the activity of a receptor for the neurotransmitter GABA, or gamma-aminobutyric acid. GABA-responsive neurons, which generally inhibit other neurons' activity, can help dial back the excessive stimulation thought to lead to epilepsy.

Her dogged curiosity carried Parks into a graduate research fellowship in the lab of Bill Sonntag, an Oklahoma University Health Sciences Center professor who studies the impacts of aging on the brain. Parks' interest did not fit perfectly into the lab's research,




PARKS ET AL/JLR 2020

**This schematic shows a cage designed to test memory extinction and relearning. A mouse is trained to pass through a certain door in the corner to earn a food pellet; when the experimenter changes which door is preferred, old mice are especially slow to adapt to the new conditions.**

but Sonntag told her she had a legitimate question; very little was known about how allopregnanolone alters during aging.

"It's reduced in all these disease models: epilepsy, PTSD, Alzheimer's," Parks said. "But only a few studies have really investigated its levels in normal aging." None, she added, had looked at the regulation of allopregnanolone synthesis in the aging brain.

By the end of a mouse's two-year lifespan, it becomes as forgetful as a human many decades older. An old mouse takes longer than its young peers to learn where it can climb out of a water maze or which of three doors it must pass through to receive a food pellet. Parks, Sonntag and colleagues showed that that decline in sharpness correlated with a decline in allopregnanolone.

Younger mice learned faster; older mice more slowly. But when the older mice received a booster dose of allopregnanolone, that gap shrank. The team then found that giving young mice an infusion of the inflammatory cytokine interleukin-6 or blocking its activity in older mice also could reduce the gap.

That meant the changes were caused by increasing inflammation. As they grew older and accumulated the inflammatory molecule interleukin-6, mice made less of the enzymes that convert progesterone to allopregnanolone. Meanwhile, they made more of the enzymes that convert progesterone into corticosteroids associated with stress — another known facet of aging. "This is a phenomenon we're aware of that happens with age," Sonntag said. "The increase in glucocorticoids has been investigated a lot" and linked to inflammation.

In their recent paper in the **Journal of Lipid Research**, the team left open the question of how allopregnanolone improves cognition. But they have hypotheses: Perhaps, by altering GABA receptor function, allopregnanolone affects the birth of new neurons, which require GABA. Or the hormone might alter the way that neurons use energy, as it's known to affect mitochondrial function.

In any case, asking about allopregnanolone worked out. "I have one of those personalities where I get really fixated on things," Parks said. "In this case, it paid off."

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

# From the journals

*By Gabriela Contreras, Anand Rao & Rajamani Selvam*

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

## Toggling to a third state to treat malaria

About 228 million cases of malaria and 405,000 malaria deaths occurred globally in 2018, according to the World Malaria Report 2019, and the parasite Plasmodium falciparum is responsible for more than three-quarters of malaria cases worldwide. The cGMP-dependent protein kinase G, or PfPKG, is essential for the parasite's life cycle, and the use of allosteric kinase inhibitors such as cyclic GMP analogs to interrupt PfPKG activity represents a promising anti-malarial strategy. However, researchers know little about the mechanisms underlying PfPKG inhibition.

Jung Ah Byun of McMaster University and an international team used comparative nuclear magnetic resonance analyses of a key regulatory domain of PfPKG to demonstrate that the cGMP derivative 8-NBD-cGMP effectively antagonizes the enzyme. The authors showed that 8-NBD-cGMP accomplishes effective inhibition through an intermediate third state that is unlike the traditional active versus inactive two-state equilibrium.

The discovery of this third state, reported by the team in a recent paper in the **Journal of Biological Chemistry**, provides new insights into enzyme allostery and may be useful for therapeutic development for malaria.
*DOI: 10.1074/jbc.RA120.013070*

## Creating a neural signaling roadmap

Neurotransmitters transmit chemical signals from synapses to facilitate cell–cell communication. Impairments in synapse function play a key role in the pathology of neurological diseases such as Parkinson's, schizophrenia and epilepsy. Synaptosomes, which are stable and functional nerve terminals that can be manipulated for various processes, are employed to understand molecular processes of communication. These processes include post-translational modifications, or PTMs, which are important for protein function.

In a recent paper in the journal **Molecular & Cellular Proteomics**, Inga Boll and a team from the University of Southern Denmark write about the role of a PTM, sialylation (the addition or removal of sialic acid), in N-linked glycopeptides in rat synaptosomes. The researchers have made a large-scale comprehensive map of sialic acid–containing glycosylation sites. Protein kinases, proteases and phosphatases carry these sialylated glycosylation sites.

Brief depolarization of the synaptosomes allowed the researchers to identify changes in site-specific sialylated and desialylated N-linked glycoproteins. These changes occurred on essential synaptic proteins such as ion channels, transporters and synaptic vesicle proteins and are as dynamic as post-translational phosphorylation. This study unravels sialylation, a novel modulator that alters the neurotransmitter release in response to depolarization. The researchers have identified the need to establish state-of-the-art techniques to study the implications of the molecular functions of sialylation.
*DOI: 10.1074/mcp.RA119.001896*

## A potential target against mycobacteria

Mycobacterium tuberculosis, the bacteria that causes tuberculosis, has a unique cell wall characterized by the presence of mycolic acids. These are lipids that play a key role in the pathogenesis of TB, the world's top infectious killer, which causes 1.5 million deaths each year, according to the World Health Organization.

Nguyen-Hung Le and colleagues at the universities of Toulouse and Montpellier in France have learned that mycolic acid biosynthesis is regulated by kinase-mediated phosphorylation. In recent research published in the **Journal of Lipid Research**, they used lipidomic and phosphoproteomic analysis of a Mycobacterium strain with altered Ser/Thr phosphorylation. The authors discovered that a Ser/Thr protein kinase, PknB, plays a key role in maintaining cell wall integrity and regulates synthesis and transport of mycolic acids. Overexpression of PknB affected growth and enhanced susceptibility to antibiotics in mycobacteria .

The authors also identified the mycobacterial membrane protein large 3, or MmpL3, as the substrate of PknB, and this phosphorylation is the major regulator in mycolic acid trafficking and cell wall biosynthesis. Mycobacteria require MmpL3 to transport mycolic acids, and it is the proposed target of many anti-mycobacterial inhibitors under development.

These findings contribute to the understanding of mycolic acid biosynthesis, which is important to the development of new anti-mycobacterial compounds.
*DOI: 10.1194/jlr.RA120000747*

## A new role for an insulin receptor substrate

Insulin receptor substrate 2, or IRS2, is an adaptor molecule recruited by insulin receptors to facilitate insulin signaling. As such, IRS2 is implicated in diabetes mellitus and in breast and pancreatic cancers and neuroblastoma. IRS2 function is known to mediate signaling including lipid uptake and metabolism, and key checkpoints for its function are the ubiquitin ligases that can break down the proteins that help IRS2.

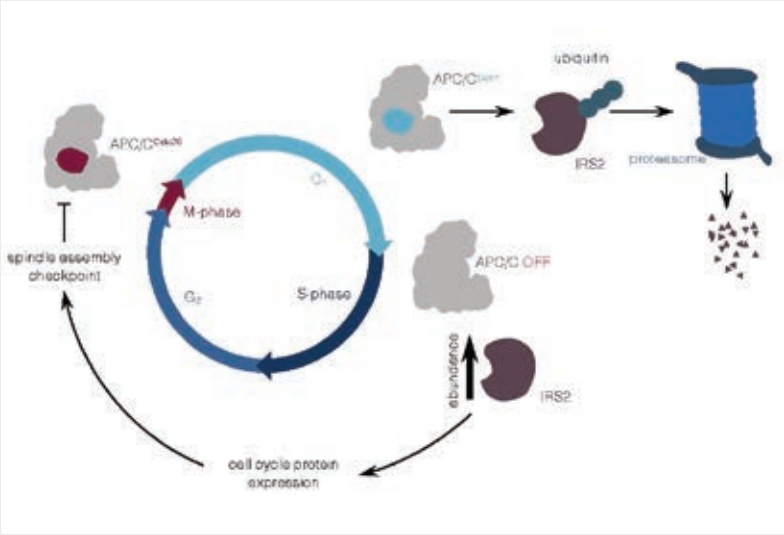
Though some researchers have reported ubiquitin ligases that target both IRS2 and other IRS molecules, none had reported ubiquitin ligases that specifically target IRS2. Sandhya Manohar and a team at Harvard Medical School addressed this question with a proteomic screen of anaphase-promoting complex/cyclosome, or APC/C, to identify potential substrates during the intermediate G1 growth phase of the cell cycle. The APC/C assists in the breakdown of proteins involved in the cell cycle, achieving this feat with the help of activators. In their recent paper in the journal **Molecular & Cellular Proteomics**, the authors provide evidence suggesting IRS2 is a direct substrate of APC/CCdh1, where Cdh1 is an APC/C co-activator during G1.

When APC/C was blocked and/or Cdh1 was knocked down, the researchers observed increased IRS2 levels. They also found that IRS2 depletion decreases the expression of cell-cycle regulatory proteins and perturbs the mitotic spindle checkpoint during the mitotic phase. The stabilization of IRS2 depends on a unique D-box motif present in IRS2, thereby establishing a new mode of regulating IRS2.

Together, these findings identify a ubiquitin ligase that targets only IRS2 and not the other main IRS protein, IRS1, and establish a new role for IRS2 as a cell-cycle checkpoint regulator. In addition to IRS2 roles in lipid uptake and metabolism, this study unravels a new role of IRS2 in cell-cycle regulation.

*DOI: 10.1074/mcp.RA120.002069*

SANDHYA MANOHAR ET AL./MCP




**Insulin receptor substrate 2 primarily targets for proteasomal degradation. When anaphase-promoting complex/cyclosome is inactivated, IRS2 increases. This increases the expression of cell-cycle proteins, which is important for normal progression through the mitotic phase of the cell cycle.**

## Amino acid sites play new roles in cell processes

Protein kinase B, also known as AKT1, plays a key role in cell survival and oncogenesis and is activated by the addition of a phosphate group to two amino acid sites, serine 473 and threonine 308. However, how the phosphorylation of one or both of these sites affects AKT1's function is unknown.

In recent work published in the **Journal of Biological Chemistry**, Nileeka Balasuriya of the University of Western Ontario and an international team mapped AKT1's preferred substrates when serine 473, threonine 308 or both regulatory sites are phosphorylated. Using programmable AKT1 variants and peptide libraries, the authors showed that each phospho-form of AKT1 has common and distinct substrate requirements.

These results demonstrate new modes of involvement of AKT1 in the regulation of cellular processes.

*DOI: 10.1074/jbc.RA119.012425*

## Solving the maize of plant defense proteins

By the year 2050, the world's population is expected to grow from 7.8 billion to an estimated 9 billion, and, according to the Food and Agricultural Organization of the United Nations, food production must increase by 70% to meet anticipated demand. Corn, or maize, uses sunlight effectively and can produce over 500 kernels from just one seed, making it a preferred crop to address growing hunger needs. However, approximately 10% of crop yield is lost to pathogens such as Ustilago maydis, a fungus that causes maize to grow large tumorlike structures. Understanding how plants defend against such diseases may help researchers develop fungus-resistant maize strains.

Kiwellin proteins are plant defense proteins that inhibit microbial effectors such as chorismate mutase Cmu1, but researchers have done few studies on how kiwellin proteins such as kiwellin 1 protein, or KWL1, and kiwellin protein homologs work together to coordinate their response against pathogens. In a recent paper published in the **Journal of Biological Chemistry**, Florian Altegoer of the Philipps University of Marburg and collaborators in Germany reported the structure of a maize KWL1 homolog, KWL1-b, in complex with Cmu1 and compared it with a previously reported Cmu1–KWL1 complex. They found that the structures of the complexes are similar, but KWL1-b is expressed at lower levels and shows a different pattern of tissue-specific expression. The authors also showed that KWL1-b, like KWL1, inhibits Cmu1 activity and is able to bind carbohydrates but shows different preferences for which carbohydrates it binds.

SEBASTIAN MACKIEWICZ

**Researchers are studying a plant defense system that could help develop fungus-resistant strains of the food crop maize, shown here growing in a field in Poland.**

The authors' data suggest that KWL1 and KWL1-b are part of a redundant, spatiotemporally coordinated defense system in plants and that minor structural divergences between two close homologs result in functional diversification, as seen by the differing carbohydrate-binding properties of the two KWL proteins. These findings could be important for developing fungus-resistant maize strains.
*DOI: 10.1074/jbc.RA119.012207*

## What ionizing radiation does to proteins

X-rays, gamma rays and ultraviolet rays are useful for disinfecting instruments and in diagnostic medical exams, but high doses of such radiation can damage tissues and lead to cancer. Cell death due to the production of reactive oxygen species, or ROS, such as hydrogen peroxide and superoxide can cause tissue damage. Researchers know that, at the DNA level, cells employ several strategies to avoid and repair DNA damage due to oxidation. However, the mechanisms involved in repairing the DNA damage are relatively unknown.

In a recent paper in the journal **Molecular & Cellular Proteomics**, Steven T. Bruckbauer and colleagues at the University of Wisconsin describe performing mass spectrometry on Escherichia coli cells that they had treated with ionizing radiation to identify the resulting oxidative modifications. The researchers determined that fewer than 10% of the proteins present in the organism were affected by radiation. The most common oxidative modification was hydroxylation, followed by dioxidation. Glyceraldehyde 3′-phosphate dehydrogenase, or GAPDH, is the primary target of oxidation by radiation.

Similar oxidation on GAPDH is also present in human breast carcinoma cells, suggesting that it is a critical player in oxidative damage from bacteria to eukarya. This work adds to our knowledge of the repertoire of cellular functions of GAPDH.
*DOI: 10.1074/mcp.RA120.002092*

## Hydrogen bonding and beta-amyloid aggregation

Alzheimer's disease is characterized by brain cells that wither and die, resulting in loss of memory and other mental faculties. Excessive

buildup of beta-amyloid is a hallmark of Alzheimer's, and researchers believe it contributes to the disease's pathology. The chaperone DnaJ heat shock protein family member B6, or DNAJB6, inhibits the formation of toxic beta-amyloid aggregates, but researchers don't know much about the mechanism by which this intervention occurs.

In a paper published in the **Journal of Biological Chemistry**, Nicklas Österlund and colleagues at Stockholm and Lund universities used a mass spectrometry–based approach to assess directly beta-amyloid oligomers formed in solution. The authors found direct evidence that oligomeric, not monomeric, forms of beta-amyloid are captured by DNAJB6. Moreover, they showed that this ability is dependent upon particular amino acids capable of hydrogen bonding, specifically serine and threonine.

These findings provide new details that improve researchers' understanding of beta-amyloid biology and may aid in the development of new Alzheimer's disease therapies.
*DOI: 10.1074/jbc.RA120.013459*

## Ceramide reduction could be used to treat alcoholic liver disease

Alcoholic liver disease, a condition in humans caused by alcohol overconsumption, progresses from alcoholic steatosis (fatty liver) to fibrosis and cirrhosis. In alcoholic liver disease patients, the liver ceramides

## An enzyme hops and scoots on the phospholipid bilayer

Phosphatidic acid phosphatase is an important lipid metabolic enzyme in eukaryotes. It converts phosphatidic acid, or PA, to diacylglycerol, which is needed for the synthesis of the neutral lipid triacylglycerol. The diacylglycerol can also be used for the synthesis of membrane phospholipids.

PA phosphatase lacks a transmembrane domain and is confined in the cytoplasm as an inactive phosphorylated enzyme. Activation occurs when the enzyme is dephosphorylated by a protein phosphatase complex at the nuclear/endoplasmic reticulum, or ER, membrane followed by its interaction with the membrane bilayer and substrate PA. Thus, PA phosphatase requires the membrane surface for catalysis.

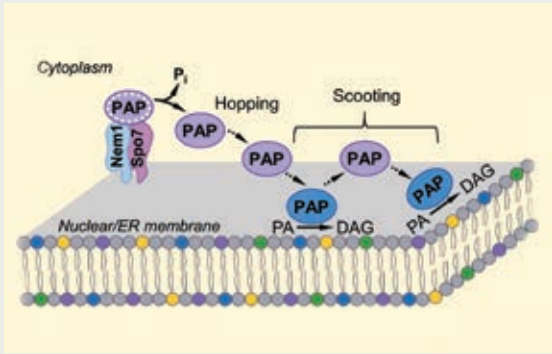
To evaluate PA phosphatase activity, researchers have used a system composed of detergent/PA-mixed micelles. However, this system does not simulate the membrane phospholipid bilayer. Joanna M. Kwiatek and George M. Carman at Rutgers University have developed a system that mimics the nuclear/ER membrane to assess the PA phosphatase activity. This recent research was published in the **Journal of Lipid Research**. As a model, the researchers used PA phosphatase of the yeast Saccharomyces cerevisiae. In this system, the substrate PA is incorporated into liposomes composed of the major ER membrane phospholipids.

The results revealed that the PA phosphatase activity depends on the phospholipid composition of liposomes, but the composition did not have a major effect on the enzyme and liposomes interaction. Moreover, the activity was dependent on both the molar and surface concentrations of PA in liposomes. These results suggest that the enzyme operates along the nuclear/ER membrane in the organism.

The authors propose a hopping and scooting model for the action of the PA phosphatase. The phosphorylated form of the enzyme is dephosphorylated by the Nem1-Spo7 complex at the nuclear/ER membrane. The dephosphorylated PA phosphatase hops onto the membrane surface. Then it scoots along the membrane, binds to its substrate PA and catalyzes the dephosphorylation of PA to produce diacylglycerol. The enzyme then scoots along the membrane and binds another molecule of PA to carry out another round of catalysis.

The system employed in this study has great potential to be applied to study other interfacial phospholipid synthetic enzymes.
*DOI: 10.1194/jlr.RA120000937*

KWIATEK AND CARMAN/JLR




**This illustration shows phosphatidic acid phosphatase, or PAP, in the yeast Saccharomyces cerevisiae hopping to the membrane surface, then scooting along the membrane to produce diacylglycerol, or DAG.**

are increased. Ceramides are lipids that promote apoptosis and impair insulin signaling and cell growth. Researchers previously have shown that the reduction of ceramide prevents alcoholic steatosis and glucose intolerance in mice.

Jason Correnti from the Carr lab at the University of Pennsylvania and a team from several U.S. universities have demonstrated that ceramide reduction improves alcoholic liver disease in a mouse model. In a recent paper published in the **Journal of Lipid Research**, the researchers write that they overexpressed acid ceramidase, by an inducible system, to reduce hepatic ceramides in chronically alcohol-fed mice. They observed that ceramide reduction reverses alcohol-induced insulin resistance and improves alcoholic steatosis. Ceramidase induction decreases hepatic ceramides, and reduction of ceramide promotes very low-density lipoprotein secretion and increases lipophagy, which is the autophagic degradation of intracellular lipid droplets. Moreover, they observed decreased oxidative and lipotoxic stress in the mice.

The authors observed that a hepatic-specific acid-ceramidase is induced in human alcoholic liver disease. Therefore, the overexpression of acid-ceramidase is relevant in this disease. The results suggest a potential role for hepatic ceramide inhibition in preventing alcoholic liver disease.
*DOI: 10.1194/jlr.RA119000446*

## Picturing the protein that stabilizes myelin stacks

Myelin is a lipid-rich substance that wraps around axons to insulate them and improve electrical signaling. Scientists believe myelin protein P2 stabilizes myelin as it forms these insulating layers around peripheral nerves, but researchers have not identified the underpinning molecular mechanisms that allow apposing myelin layers to pack tightly together.

Using cryo-electron microscopy, X-ray diffraction and atomistic molecular dynamic simulations, Salla Ruskamo of the University of Oulu and a European team revealed the role of P2 with unprecedented clarity. Using Escherichia coli liposomes as a model, the authors showed that P2 forms a 3D lattice between myelin bilayers, allowing them to be stacked and compacted as additional layers are added.

These findings, reported in a recent paper in the **Journal of Biological Chemistry**, further researchers' understanding of myelin sheath assembly and may be important in tackling myelin-related diseases.
*DOI: 10.1074/jbc.RA120.013087*

**Gabriela Contreras** (gicontrerasa@gmail.com) earned her Ph.D. in biology at Heidelberg University. Follow her on Twitter @gabiitca.

**Anand Rao** (arao@asbmb.org) is an ASBMB science communicator. Follow him on Twitter @AnandRaoPhD

**Rajamani Selvam** (rajamaniselvam@gmail.com) is an Oak Ridge Institute for Science and Education research fellow at the U.S. Food and Drug Administration in Maryland. Follow her on Twitter @Rajaman06539874

# Connect your community with a virtual scientific event

Interested in hosting a virtual event? The ASBMB is here to help. The ASBMB provides a platform to share scientific research and to discuss emerging topics and technologies in an interactive, virtual setting.

When you host a virtual event with the ASBMB, your event will:

- accommodate up to 500 attendees
- be marketed to the ASBMB's 11,000 members
- reach the ASBMB's network of journal authors and meeting attendees

Learn more about how to submit your proposal at asbmb.org/meetings-events

ASBMB
American Society for Biochemistry and Molecular Biology


A zest
FOR
synthetic biology

# Why are metabolic engineers so interested in limonene?

*By Laurel Oldach*

Orange zest wouldn't be quite so zesty without limonene. And home bakers and mixologists aren't the only ones who appreciate it. Limonene, which constitutes all but 5% of the essential oil of orange peels, is used industrially as a source of flavor for foods and of scent for cosmetics and household products. It also is used as a starting point for various pharmaceutical products and as a solvent and degreasing cleaner.

The limonene used in these applications is a byproduct of the juice industry. The Soudijin family of Bradenton, Florida, trades in limonene and about a dozen other citrus byproducts at their company, Florida Worldwide Citrus. According to product manager Matthew Soudijin, a grandson of the company's founder, the price of limonene has spiked around the world during the COVID-19 pandemic as surges in demand for cleaning products crash into delays in citrus harvests and processing caused by global shutdowns and slowdowns.

Business was already tough. Florida's orange harvest has plummeted in recent years as citrus greening, a bacterial infection spread by insect pests, spreads across the state. While Florida Worldwide Citrus once dealt mainly in local products, most of its supply now comes from growers in other countries. Unpredictable weather, on the rise worldwide, can damage crop yields further.

"The price tends to fluctuate with the harvest," Soudijin said, adding that these variations can make for unhappy customers. "If beverage and flavor companies are paying $2 a kilo, and then twice as much six months later, they see that as a problem."

To stabilize their production costs, those companies would prefer to use a reliable synthetic source. But although limonene is a simple molecule, it has a chiral hitch: a carbon whose bonds can be arranged in two ways, pro-

DVORTYGIRL/WIKIMEDIA

**Secretory glands in the outermost layer of citrus fruit rinds produce oil that, in oranges, is composed of up to 95% limonene.**

OKEYKAT/UNSPLASH

ducing either D- or L-enantiomers. Whereas citrus fruits produce only D-limonene, many synthesis methods produce a mixture of the two enantiomers. The mixture, called dipentene, works well enough for degreasing oil shafts, but it can't be used for fragrance and flavor purposes, because while D-limonene has a pleasant citrus odor, L-limonene smells like turpentine.

This is exactly the kind of problem that synthetic biologists like to solve using enzymes, which are stereoselective by nature. Industrial production of vitamins, penicillin, amino acids and many other chiral products depends on commercial-scale fermentation using microbes engineered to conduct molecular transformations that turn sugar from the media into more valuable molecules. But unlike many of those products, limonene is toxic to cells.

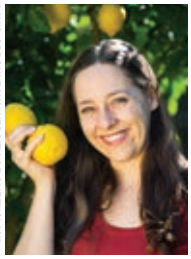
Sarah Reisinger, vice president for research and development in biotechnology at the flavor house Firmenich, told Perfumer & Flavorist magazine in April, "I believe, in the coming years, the pace of renewable biotech ingredient introduction will increase." She added, "I believe that biotech products, in addition to renewability, offer the reliability, consistency of product composition and cost that the industry needs."

Historically, limonene has been available so cheaply that overcoming challenges to producing it through fermentation wasn't worth the investment. But now, with a $300 million market at risk, could limonene become one of those biotech ingredients?

From tricks of the fermentation trade to entirely new approaches, researchers in academia and industry have developed a variety of ways to keep their organisms alive while also optimizing expression and production of limonene — and some new approaches whose proponents argue that "alive" is overvalued. They're getting better at making limonene and related molecules more efficiently. Whether these approaches will yield enough efficiency to bring biofermented limonene to market remains to be seen.

## Working toward monoterpenes

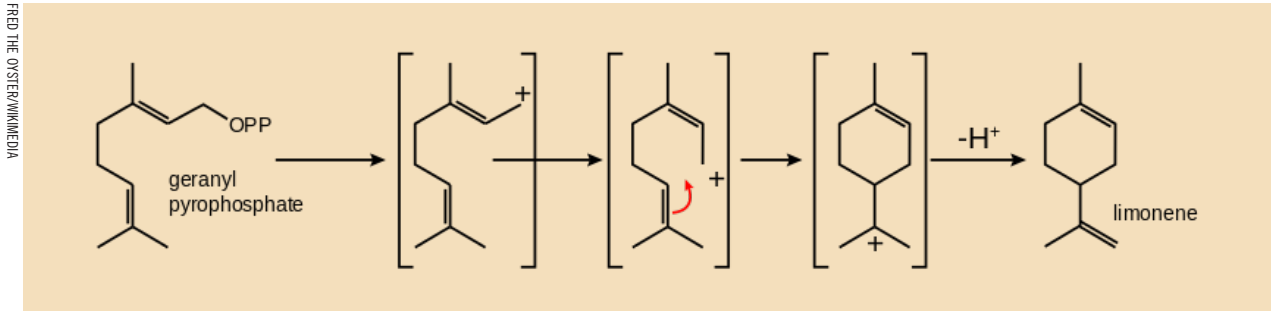
Modifying an organism to produce a novel molecule can be a challenge. New metabolic pathways may steal energy or building blocks from other processes that the cell needs to stay alive, putting stress on the organism. In some cases, at high enough levels, the desired product or its metabolites may even prove toxic to the organism.



DAVID SPROULE/ UNIVERSITY OF QUEENSLAND

CLAUDIA VICKERS

Claudia Vickers is director of the Future Science Platform in Synthetic Biology at Australia's Commonwealth and Industrial Research Organisation and also has a lab at the University of Queensland. She focuses her academic work on engineering microbes to generate monoterpenes, a class of molecules including limonene that are unusually difficult to produce.




FRED THE OYSTER/WIKIMEDIA

**Starting with the 10-carbon geranyl pyrophosphate, limonene synthase enzymes remove phosphate groups and cyclize the precursor to generate limonene.**

"What's interesting about (terpenes) is that they're modular," Vickers said. "They start with a five carbon product that has a prenylphosphate moiety, and there's a series of condensation reactions to make molecules with five, 10, 15, 20 (carbons)." After this concatenation of subunits, other enzymes use energy from the remaining phosphate group to make molecular transformations that diversify the terpenoid family: twisting the molecule into cyclic structures or oxidizing its double bonds to add methyl or hydroxyl groups.

Some 70,000 terpenes and terpenoids are known. Their functions are nearly as numerous. Plants use terpenes for defense against herbivores and as components of resins, hormones and cell membranes; the smallest, like limonene, are volatile and involved in intraspecific and cross-species recognition. Vickers, who trained as a plant biologist, said, "They're involved in almost everything."

All cells generate isopentenyl pyrophosphate and dimethyl pyrophosphate, the two five-carbon precursors, and most use them to make much larger lipids like sterols. But plants, somewhat unusually, are able to generate the 10-carbon molecules known as monoterpenes, such as menthol, limonene and pinene. Cajoling microbes to produce these molecules is a challenge, Vickers said.

The Future Science Platform keeps a catalog of DNA coding for enzymes with various functions from various organisms. Vickers calls it a parts repository, conjuring a hybrid between Addgene and AutoZone. Limonene is a popular target terpene among metabolic engineers because there is a part, an active and well-characterized enzyme, that makes it in a single step from a 10-carbon precursor called GPP.

In principle, it should be possible to express that enzyme in an organism that already makes GPP and then harvest the product. But Vickers cautions against such simplistic thinking.

THOR SWIFT/BERKELEY LAB

**Researchers at the Joint Bioenergy Institute's fermentation lab conduct prototype-size fermentation.**

"It's important to understand, you can't go in, massively upregulate everything, brush your hands and go, 'Right, job done,'" she said. "That often doesn't give you the product. It's often all about balancing flux in the pathway."

For example, in brewer's yeast, the enzyme that joins IPP and DMAPP subunits also immediately adds a second IPP subunit. Feeding in more precursors in hopes of boosting GPP production without modifying that enzyme would not increase the amount of limonene in the cell; it simply would result in more of the 15-carbon product. But removing the offending enzyme outright is not an option, because the cell requires metabolites later in its synthetic pathway to stay alive.

Vickers credits a postdoc in her lab with devising a solution involving conditional degradation of the enzyme that competes against limonene synthase. By combining inducible degradation with sensing of the required product, Vickers said, "We got a balance between healthy growth of the cells and channeling carbon off to the monoterpene."

Trial-and-error approaches like this are staples of metabolic engineering. Scientists introduce a change and

U.S. DEPARTMENT OF ENERGY/WIKIMEDIA

Engineers grow modified microbes in bioreactors such as this one, and harvest their products.

then use metabolomics to assess its effect on an engineered microbe and identify any bottlenecks upstream of the desired product.

Should someone find a way to produce high titers of limonene without cannibalizing another essential metabolite, there's another problem waiting: At a high enough concentration, limonene and other monoterpenes can kill microbes that produce them. The small, hydrophobic hydrocarbons are thought to incorporate into cell membranes and compromise the integrity of the cell.

"To date, most of the production of these compounds has not reached levels that are high enough to actually produce toxicity," Vickers said, "which is unfortunate, because we're trying to get to high levels!"

## Addressing toxicity

Synthetic biologists have found ways to remediate the harmful effects of natural products they wish to produce in bulk. After all, even ethanol kills microbes at a high enough concentration; that has not stopped humans from producing it by fermentation for millennia.

Jay Keasling, a professor at the University of California, Berkeley, who founded the synthetic biology company Amyris, said, "I wouldn't say that they're all easy, but there are some tricks."

The most popular trick is to choose a new microbe, one with higher tolerance for the product. That works best if an easily engineered alternative organism tolerates the molecule better. If not, some labs use directed evolution, growing the microbe of interest in increasing concentrations of the desired product to select for mutations that yield more resilience.

Engineers also can take steps to mitigate the harmful compound's effects on the microbe: for instance, incorporating transporters to remove it from the cell, designing the pathway to sequester the product in an organelle that will keep the harmful molecule away from important cellular functions, or adding a modification such as a sugar that renders the molecule nontoxic and then is removed after isolating the product. Keasling's lab once achieved a 90-fold increase in limonene yield by outfitting E. coli with a metabolic pathway to boost production of a precursor molecule and a cytochrome that hydroxylated the limonene, preventing it from integrating into membranes.

There are also solutions completely external to the cell. According to Vickers, the most effective way to diminish the harmful effects of limonene is to grow the organisms producing it in an emulsion of a nontoxic organic solvent, which extracts the hydrophobic limonene. "The moral from that story is that we often, as metabolic engineers, try to look for fancy genetic solutions," she said. "But there might be a much simpler process solution."

Beyond rendering a new metabolic pathway survivable, some biologists say, there is a more fundamental conflict at the center of metabolic engineering. Michael Jewett, a professor and director of the Center for Synthetic Biology at Northwestern University, said that cellular systems'

Jay Keasling examines a small culture in a lab at the Joint Bioenergy Institute.

ROY KALTSCHMIDT/BERKELEY LAB


NORTHWESTERN UNIVERSITY

MICHAEL JEWETT

tendency toward homeostasis often clashes with the functions an engineer would like to introduce.

"I want to make a whole lot of something the cell doesn't care about," Jewett said. "So we end up in this tug of war … between what the cell's evolutionary and adaptation objectives may have led it toward and my engineering process objectives, which are titers, rates and yields."

Jewett's lab is one of a few that are working on an unconventional approach to resolve the conflict. "We just cut the rope," he said. "Rather than focus on the chassis organism itself, (we) focus on the molecular machinery — not only within the organism but outside of it."

## Synthetic biochemistry

Jewett's lab often works with cell-free production systems made from bacterial lysates, which he says offer some convenient features of a biological system but do not force the engineer to fight as hard against the cell.

"Cell-free systems … can produce molecules that are otherwise toxic to cells," he said. "They can actually use toxic feedstocks, like pretreated biomass; and we also look at it as a really exciting prototyping strategy."

By carrying out cell-free translation of enzymes in lysate from E. coli and then mixing the enzyme-enriched lysates in a process he compares to mixing a cocktail, Jewett's lab dodges the hurdle of tweaking the expression levels of numerous enzymes introduced into a genome.

"You can reduce the problem of synthesizing biosynthetic pathways to one of simply mixing solutions by liquid handling," he said.

The method keeps many of the beneficial aspects of a cell system; for example, in raw lysate, glycolysis constantly produces energy and enzyme cofactors from sugars. It eliminates any problems that may arise from a toxic product. In a recent paper on limonene biosynthesis, Jewett's lab reports on cell-free optimization of a synthetic pathway that converts glucose into limonene in nine enzymatic steps. By testing the efficiency of homologous enzymes from different organisms, they found that certain combinations unexpectedly produced dramatic improvements in yield.

"Frankly, we're limited only by the ability to analyze the samples," Jewett said. "We could make 100,000 different combinations of pathway enzymes, but that would take my grad student a long time with the (mass spectrometer)."

The research team regards their approach as a tool for prototyping in advance of engineering new strains; once the highest-yield pathway is found, they say, it can be introduced into a microbe.

## "Activities in a pot"

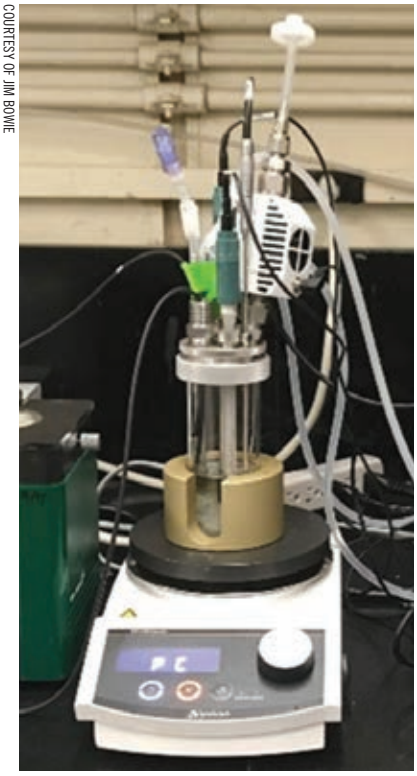
Even farther from a cell system is the synthetic biochemistry approach Jim Bowie, a professor at the University of California, Los Angeles, is pioneering in the lab and at the company he co-founded, Invizyne.


UNIVERSITY OF CALIFORNIA, LOS ANGELES

JIM BOWIE

"The idea is very simple," Bowie said. "We have a biochemical transformation that we want to perform, and a series of enzymes that carries out those steps. So let's just express those enzymes … and put those activities in a pot. And now we have a biochemical pathway."

This approach relies heavily on purification; the laboratory introduces only the enzymes and cofac-


COURTESY OF JIM BOWIE

A prototype-sized synthetic biochemical reactor runs in Jim Bowie's lab.

tors directly involved in conversion of glucose to a desired product into a stripped-down reaction mixture. Bowie argues that this approach is even easier than a system of lysates to tweak and optimize; it produces a simpler mixture of products, which makes for easier purification down the line. As in Jewett's method, toxicity is no object.

Of course, enzymes consume cofactors such as ATP and NADH in the course of their activity. Supplying a steady stream would be costly; this is one of the useful functions cellular homeostasis provides when it's present.

"The trick is cofactor recycling," Bowie said. But he doesn't hope for a system with perfect stoichiometric balance between cofactors added and consumed; setting up a system like that, he said, is "basically asking for a perpetual motion machine."

Instead, Bowie's lab devised what he calls a molecular rheostat for ATP that involves two competing glycolysis pathways that depend on the concentration of phosphate in the system. An enzyme borrowed from the Krebs cycle converts glyceraldehyde-3-phosphate into 3-phosphoglyceric acid, replenishing ATP. A second enzyme performs the same conversion but without generating ATP and tends to outpace the first enzyme when ATP levels are high and free phosphate is low. Together, the two competing reactions balance ATP level. Bowie calls a system designed on similar principles for NAD regulation a purge valve.

The approach adds a few layers of complexity back to a simplified system and costs more up front than relying on live microbes, because all the enzymes must be harvested and purified. Bowie argues that, with sufficiently stable engineered enzymes, the increased cost should amortize over time. Still, his approach has its detractors.

"I think that most people don't think it's realistic to put these complex systems together with free enzymes," Bowie said. But he's optimistic. "We already know that metabolic engineering is extremely challenging. We already know that. Why not give this approach a chance?"

"Frankly, it works surprisingly well," Jewett, who was not involved in the work, said about the molecular purge-valve system. Invizyne has landed small business innovation research funding and enjoyed some preliminary interest from flavor and fragrance companies, although they're more interested in the commercial possibilities of synthetic cannabinoids, which may command a higher price.

## Mechanismless optimization

Synthetic biochemistry involves tight control and design of a pathway; every component is planned and adjusted. Biologists, computer scientists and chemists are taking a radically different approach to optimizing biosynthetic pathways at the company Zymergen.

As flavor and fragrance companies contemplate producing limonene through biofermentation and academics explore how to do that, veterans in the synthetic biology industry are hesitant to jump aboard. Their reasons come down to economics and past experience.

MORITZ NIE / UNSPLASH

Zach Serber, co-founder and chief scientific officer of Zymergen, said, "If you have a microbe making a drop, a tiny amount of something interesting, that's tantalizing … but wildly insufficient for commercial production. You need to be making truckloads, train car loads of the stuff, efficiently."

Engineers cannot always reach that efficiency by tweaking the known components of a system, Serber said.

"You often fall short of your commercial goals. You reach a wall, whereby optimizing the known components of biology doesn't seem to be sufficient," he said. (See "Lessons from jet fuel" at right.) Serber argues that the challenge stems from biology's many unknowns.

"The vision of making biology like electrical engineering may come true. But it certainly ain't easy and has been slow in coming," he said. "Because unlike capacitors and resistors … the parts available to do biology have evolved; we don't usually know what they do, and they interact with one another in peculiar, unexpected ways."

At Zymergen, Serber said, instead of using analytical chemistry to hunt systematically for bottlenecks in a metabolic pathway, "We treat the genome of a microbe as an optimization landscape, a design space, where the phenotype you're trying to improve — the efficient production of a given biomolecule — is going to be affected by all the genes in the genome, in ways you can't necessarily predict."

## Outlook

Will limonene ever be made in commercial quantities by biofermentation? The answer depends not just on synthetic biologists' success in resolving technical problems but also on producers outside the lab, their output and pricing decisions, and whether demand for the molecule continues to grow.

Limonene is just one of thousands of natural products that may be at risk in a changing climate. And looking ahead, synthetic biologists envision producing chemicals that never have been observed before in a cell or carrying out blends of organic and inorganic reactions using enzymes.

Back in Florida, the Soudijin family of Florida Citrus Worldwide has adapted to the changing market. In addition to buying fruit from around the world to make up for shortfalls in locally harvested product, they've invested in a more elaborate flavor extraction and concentration lab to produce flavors themselves. Among other offerings, they sell extracts and essential oils to companies that want to adjust the flavor of their orange juice but still use only orange-derived ingredients.

Still, the Soudijins are looking warily at the next few years, wondering what the future will bring for their industry.

SAMANTHA GADES / UNSPLASH

### Lessons from jet fuel

**There was a time when synthetic biologists aimed to make biofuels, cheap ethanol and other products that could be burned as greener alternatives to petroleum-based fuel.**

**Back when Zach Serber was the director of biology at Amyris, the company focused on producing jet fuel wholly derived from sugarcane through fermentation. Though the company succeeded and gained regulatory approval for its fuel, the year that the greener fuel came to market, the price of crude oil dropped by almost half, making it impossible for Amyris to turn a profit on its product. The company dropped the product and survived by refocusing on more expensive chemicals, but the experience has scarred the industry.**

**According to Serber, scientists in the biofuels industry "went tilting at windmills. We went head to head against petroleum, trying to come up with transportation fuel based on biology and found that, especially when the price of oil collapsed, it couldn't compete on price."**

**Now, much of the industry regards the attempt to produce biofuels as a cautionary tale for anyone aiming at large-scale production of relatively inexpensive commodity chemicals.**

**"There's no way you're going to get a venture capitalist to put money into a biofuel at this point," Jim Bowie of UCLA said. "A ton of people lost their shirts."**

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

# Running a journal in a pandemic

*By John Arnst*

**Months before almost everyone in the scientific community was using Zoom to traverse the spaces created by the COVID-19 pandemic, Kerry-Anne Rye and Nicholas O. Davidson were discussing the goings-on of the Journal of Lipid Research across a staggering distance.**

COURTESY OF NICHOLAS O. DAVIDSON

Before they were named co-editors-in-chief, Nicholas O. Davidson and Kerry-Anne Rye started as associate editors with the Journal of Lipid Research in 2011 and 2008, respectively.

Rye and Davidson recently spoke with ASBMB Today science writer John Arnst about the ups and downs of running a scientific journal in the middle of a global pandemic and the journal's move, along with all journals published by the American Society for Biochemistry and Molecular Biology, to open access publishing later this year. The conversation has been edited for length and clarity.

COURTESY OF KERRY-ANNE RYE

Kerry-Anne Rye runs the lipid research group at the School of Medical Sciences in the Faculty of Medicine at the University of New South Wales Sydney.

**It's been an unprecedented year for all of us. How are both of you holding up with the duties of being editors-in-chief and continuing your own research while balancing the temporary realities of life during a pandemic?**

**Kerry-Anne Rye:** We're coping. It's not easy; things have changed. But I find the work I do with the journal is nice and different and a bit of relief at the end of every day after dealing with a lot of unprecedented issues. I look forward to looking at manuscripts, which takes me right into another zone.

**Nick Davidson:** I'm doing okay. It was a challenge not being able to come into the office, doing everything from home. But like Kerry, I look forward to having a chance to think about things other than COVID-19 patients coming into the emergency room of our hospital and worrying about the people in our research labs who are furloughed or laid off. We're getting back to something closer to normal now, but I think it's been a struggle for everybody.

**Has the pandemic affected the number of papers being submitted to the journal?**

**Davidson:** At the onset of this, Kerry and I anticipated that we would see a big decrease in the number of submissions. And that didn't happen.

**Rye:** It's actually the reverse; the submissions went up. I think this is fairly commonplace, and we think it's largely because people had a whole lot of half-finished stuff sitting on their to-do list. They were stuck at home and without a lot of other distractions, at least in the beginning, so they finished all these things off. For us it was great, because we got some really, really nice submissions.

I was very surprised because we kept saying, "We're going to have a contingency; we're going to see a reduction in submissions." It was like a broken record, and it didn't happen. But in the last couple of weeks, submissions have been down a little bit. We don't know if it's just noise or if it's real; it's too early to tell. But it could be that all the things that were on the to-do lists have been largely done, and with laboratories still not being fully open, work has slowed down.

**Davidson:** On our end, I think research has slowed down, but elsewhere research is starting to ramp back up again. We're all very worried about this new continuing surge of COVID-19. And you know what that's going to mean for the fall — we're all pretty much in a wait-and-hold pattern. It's a bit of a crazy time, and it is totally unprecedented. I don't think any of us can predict how this is going to impact science, but it has surely created some opportunities in COVID-19 research.

> "We're two people like chalk and cheese — we're very different. And it just kind of works; we've got a good system going. The one thing that no other journal in the world has is that we have 24-hour access to an editor-in-chief, because when I'm awake, Nick's asleep, or vice versa. It's pretty damn good."
>
> KERRY-ANNE RYE

**If researchers can pivot to working with COVID-19, as many have, some journals are scooping that right up.**

**Davidson:** Right.

**Rye:** With lipids, it's not as logical a move. I'm doing a couple of things with COVID-19, but I don't know that they're going to have an impact on how people view things. Just about everyone I know is looking for opportunities to do research involving the virus. For example, my institution totally locked down the staff except for anyone working with it. It's opened up a little bit since then, but the opening up has now reached a plateau.

That makes a big difference in the way you do things. You lose opportunities, because the casual conversations where you're having a cup of coffee and you talk to someone about what you're doing and you exchange ideas just don't happen anymore.

Proper COVID-19 research is also challenging because you need PC-3 facilities, at least in Australia (Author's note: This is the equivalent of a biosafety-level 3 lab in the U.S.). We have this one facility one floor above where I work that everyone's fighting over, and there's one other facility in the Sydney area. They're very, very expensive to maintain.

**When the two of you were announced as the incoming editors-in-chief, you developed a plan to broaden the scope of the journal to include additional clinical research with a focus on a number of lipid-related diseases and disorders. How has that gone so far?**

**Davidson:** We're seeing a lot of interest from the community in mechanistic research as well as in research that has translational applications; in complex disorders like atherosclerosis and peripheral vascular disease; in metabolic diseases such as Type 2 diabetes, obesity and nonalcoholic fatty liver disease; and also in neurodegenerative diseases like Alzheimer's — things that may be influenced by environmental interactions with polymorphisms in genes that regulate lipid metabolism. I'm very gratified. I think we've had a very robust response.

**Rye:** I agree. We look very closely at every submission, and the thing that strikes both of us, I think, is that the quality of what we're publishing is very good. We get Google Analytics sent to us monthly, so we can look at some of the stats to do with the journal, and it's very informative because one of the things it talks about is the potential impact of newly published papers.

It used to be that one or two papers were potentially going to have high impact and the rest were low impact, and now almost all of what we're publishing is coming up as potentially high impact. Hopefully, this will increase the number of citations. I think we're probably publishing a little bit less, so in terms of impact factor, that's going to have a positive effect as well. I think the journal is tracking very, very nicely. I'm really pleased with it.

**That's great. Also, what about the training program with the four junior AEs and having them to help reach into the clinical community?**

**Davidson:** It's been a really rewarding experience. We brought on four new junior associate editors: Two of them are underrepresented women investigators, both physician–scientists, and two of them are Ph.D. basic lipid researchers. They are very active and have transformed what used to be our in-person AE meetings, though I'm not sure if we'll go back to those

anytime soon. They've been very busy as reviewers, especially in terms of soliciting minireviews on their own. So I would say this inaugural cohort of four junior AEs has been spectacularly successful. We've just begun our solicitation for new junior associate editors for consideration later this year, so from my perspective, it's gone spectacularly well.

**Rye:** Yeah, it's fantastic. The one thing that has really struck me is that the junior associate editors have a very different view of the world from us, and they're right on top of things that we're not particularly engaged with, like social media, and they can have very different perceptions than we do about what is important and what's not. We take a whole lot of notice of what they say, and it makes a big difference.

## Speaking of later this year: The journals are moving to open access in December. How is that progressing?

**Davidson:** We're eagerly awaiting this transition to open access, and we're all really excited to see what that migration is going to look like. Elsevier has a lot of capacity to help with the analytics for the journal, between tracking papers more efficiently and promoting the journal with their databases on where potential submissions are more likely to come from.

**Rye:** It's going to be interesting. I've been really impressed with what I've seen so far from the platforms that Elsevier has. We'll be working with a dedicated team of people when the transition happens, and they've been very responsive. I think they're pretty flexible and nimble in terms of being able to accommodate just about anything.

We also get access to a much wider pool of submissions; some will come to us from other journals where they're not a particularly good fit, but they might be a good fit for us. In the current mode where ASBMB self-publishes, that just doesn't happen. I think it's going to open up quite a lot of doors, which could be really important, because it gets back to what I was saying earlier, that we might be seeing a COVID-19–related drop in the number of submissions, and I'm seeing that in a few other journals as well.

COURTESY OF NICHOLAS O. DAVIDSON

**Nick Davidson is division chief of gastroenterology and director of the Digestive Disease Research Core Center at Washington University School of Medicine in St. Louis.**

## Any last thoughts about running the JLR?

**Davidson:** We're having a blast.

**Rye:** We've two people like chalk and cheese — we're very different. And it just kind of works; we've got a good system going. The one thing that no other journal in the world has is that we have 24-hour access to an editor-in-chief, because when I'm awake, Nick's asleep, or vice versa. It's pretty damn good.

## Yeah, literal around-the-clock editorial access. That's great.

**Rye:** We've got to find a way we can advertise this.

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

# Meet Luke O'Neill

## The immunologist shares his thoughts on inflammation research and the novel coronavirus

*By Jack J. Lee*

LUKE O'NEILL

Whenever we get injured, our immune systems come to our rescue via the inflammatory response. While redness and swelling around a cut might cause discomfort, the coordinated response of immune cells — orchestrated by inflammation-promoting signals like cytokines and prostaglandins — defends our bodies from foreign bacteria and viruses.

Luke O'Neill, a professor in the School of Biochemistry and Immunology at Trinity College Dublin, has been exploring the molecular and genetic underpinnings of inflammation and the innate immune system for over three decades. More recently, he's begun investigating the roles of metabolic pathways in immune-cell activity — a research area known as immunometabolism.

He also has been examining inflammation's unexpected potential role in causing human diseases like Alzheimer's, Parkinson's and sepsis. O'Neill has co-founded several companies that are working to translate his research findings into possible drug treatments for these and other diseases.

His lab also is tackling the novel coronavirus. His group has started a few projects on COVID-19, such as testing out anti-inflammatory drugs on macrophages. These white blood cells contribute to excessive inflammation that has caused severe illness and death in infected patients.

In addition to his scientific work — which has led to numerous accolades and election as a fellow of the Royal Society in 2016 — O'Neill is a devoted science communicator. He's written two general science books, "Humanology" and "The Great Irish Science Book," with a third book on the way. He's also been on radio and television programs, answering questions about the novel coronavirus and teaching people about how to protect themselves.

O'Neill is even the occasional front man for the Metabollix, a band composed of doctors and scientists. They play cover versions of old favorites and have performed at scientific conferences including a few Keystone Symposia.

I spoke with O'Neill, a former associate editor for the Journal of Biological Chemistry, to learn more about his scientific journey and his thoughts on COVID-19. The interview has been edited for length and clarity.

### Q: What's it been like as an immunologist during the COVID-19 pandemic?

I became aware of it back in early January, but we never thought it was going to explode into this massive thing. We thought it might be like SARS at worst, which was contained very quickly. And then it began to grow and grow. When you're an immunologist, everybody's asking you about it. Suddenly, I'm on the radio and the TV talking about it.

My lab works on inflammation and cytokines, but I went to a conference back in January with some SARS people, just by coincidence. About six weeks later, I was contacted by a collaborator, and I began to think about experiments. As an immunologist who works on inflammation and cytokines, this is front and center to

TRINITY COLLEGE DUBLIN

**Luke O'Neill holds a model coronavirus in his lab in the Trinity Biomedical Sciences Institute in Dublin on the day in early July when the government awarded 5 million euros to support the institute's research into COVID-19.**

what we do. We've been studying the anti-inflammatory effects of a metabolite called itaconate.

### Q: How does inflammation fit in with COVID-19?

I've had a long interest in septic shock. We've known for 50 years that you get a massive inflammatory reaction during sepsis. Macrophages get activated, cytokines get made and you get multiorgan systemic inflammation.

When COVID-19 emerged, it was very clear it was like other viruses that affect the airways: It would cause an inflammatory reaction in the lungs. All the things I work on were found in the lungs of COVID-19 patients: cytokines like IL-1 and IL-6, macrophage infiltration. When you die of COVID-19, what you're dying of effectively is a sepsis-type scenario, where you get a multiorgan inflammatory reaction in the body.

### Q: Taking a step back, what got you into this area of study in the first place?

Do you mean years ago? We've got to go back to the Dark Ages. (Laughs.)

When I was doing biochemistry as an undergraduate, my final project was about Crohn's disease, an inflammatory bowel disease, and prostaglandins. Drugs like aspirin, ibuprofen and acetaminophen all block prostaglandins; that's why they're anti-inflammatory. Then I did a Ph.D. on cytokines because they drive prostaglandins.

I got more and more biochemical and began to work on the mechanisms of signaling and receptors. And then I got into transcription factors and Toll-like receptors. My whole scientific focus has been trying to get the underlying mechanisms in inflammation.

Recently, we've been working on

TRINITY COLLEGE DUBLIN

**Luke O'Neill speaks at Schrödinger at 75: The Future of Biology conference organised by Trinity College Dublin in September 2018; five Nobel Prize winners spoke at the event, along with other leading scientists from around the globe.**

metabolism, because you get a strange metabolic shift during inflammation as well. Macrophages begin to ramp up glycolysis, for instance.

It's like one big puzzle. What are the component parts? What are they doing? How can they go wrong? It's been always a journey toward understanding mechanism.

### Q: I've seen that some of your research has spun off into companies. What's that been like?

One company, Inflazome, is developing inhibitors of NLRP3, a very important inflammatory factor involved in a number of diseases. Another company, Sitryx, is developing inhibitors and various metabolic modulators for use in inflammatory diseases.

It's tremendous because they've taken our discoveries and they're trying to turn them into medicines.

> With COVID-19, we want to see treatments. There are trials happening with anti-inflammatories, so I'm waiting with bated breath to see what those trials tell us.

### Q: What are you looking forward to in the inflammation and immunology fields?

All these years of effort — not just my lab, of course, thousands of people — we're all trying to discover ways to treat these diseases. We work on Parkinson's, Alzheimer's and sepsis. Even with rheumatoid arthritis, where there are treatments, there's a big need for new anti-inflammatories that work better.

With COVID-19, we want to see treatments. There are trials happening with anti-inflammatories, so I'm waiting with bated breath to see what those trials tell us. There are also anti-virals, vaccines, antibody-based therapy. If a single one of those things works, the game changes because now there's hope.

### Q: You're also heavily involved in science communication. What inspired you to write "Humanology" and "The Great Irish Science Book"?

I'd be asked questions on Irish radio, and it began with immunology stuff I know about. But then the radio hosts go, "Oh, can you comment on this?" And that might be slightly outside my comfort zone. But then they said, "Oh, you're quite good at this" — so I began to get roped into it more and more and got to enjoy it. It's a bit of a thrill.

Then a publisher said, "You want to do a book based on your radio stuff?" They encouraged me, and I wrote "Humanology" about the scientific basis for what it is to be human. And then they said, "Do you want to do a book for kids?" Because there was a gap in the Irish market. There are loads of general science books for kids, of course, but there wasn't a specifically Irish one. In "The Great Irish Science Book," I give examples from Ireland: Geology will be Irish rock, say. And I give examples of Irish scientists, like chemist Robert Boyle; mathematician William Rowan Hamilton; and biologist William Campbell, who won the 2015 Nobel Prize in chemistry for the anti-parasite drug ivermectin.

### Q: Back to the pandemic: Will we eventually get out of this?

In Ireland, there's been great compliance with the lockdown and a gradual reopening. And, remember, we escaped every other pandemic. We got AIDS under control, the swine flu went away, the Black Death went away eventually. So the history of infectious diseases tells us that humans do get over it. Because of modern medicine, we can get over this. It's just a question of what's going to work.

There are loads of things happening: There are more than 120 vaccines in development now. There are anti-virals, anti-inflammatories, and antibodies as a therapy as well. So I'm optimistic because there are so many shots on goal.

**Jack Lee** (jlee636@ucsc.edu) is a graduate student in the science communication program at the University of California, Santa Cruz. Follow him on Twitter @jackjlee and read more of his work at jackjleescience.com/writing/.

# The COVID-19 deluge: Is it time for a new model of data disclosure?

*By Ken Hallenbeck*

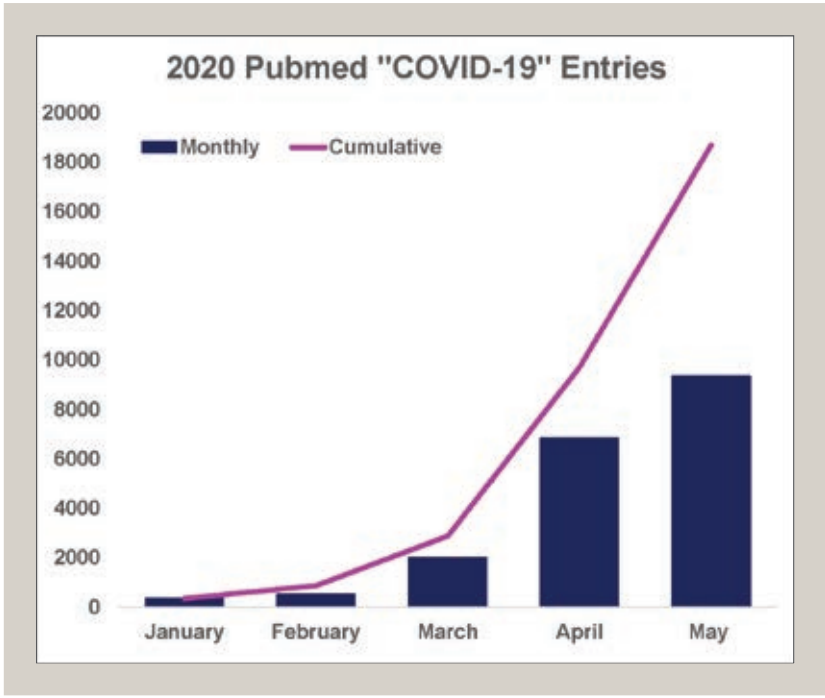
In the first five months of 2020, PubMed indexed 11,580 results for the keyword "COVID-19." The number of articles in the National Center for Biotechnology Information's archive increased steadily from 224 in December 2019 to nearly 7,000 in May. This deluge of scientific papers related to the pandemic provides a unique opportunity to review the core assumptions of the modern publication model.

As scientists turn their attention to understanding the novel coronavirus that causes COVID-19, the publishing system has adapted to rapidly disseminate COVID-19–related findings. For example, the first scientific report of a COVID-19 infection in the U.S. was published online in the New England Journal of Medicine on Jan. 31, just one day after the final clinical data were collected. Researchers and public health officials around the country needed these data to prepare for the outbreak; the work was cited more than 1,400 times in the four months after it was posted.

Rapid disclosure of data should not be limited to international health crises. The scientific community can use data only after they are disclosed, so why do months or years elapse between when data are collected and when they are shared? The benefits of reducing this delay are obvious in the case of COVID-19, but the same principle applies to all data.

The path to a scientific literature that rapidly and consistently captures all the data we generate is far from clear. In seeking such a path, I've looked at the success of preprinting in accelerating manuscript disclosure.

KEN HALLENBECK




**NCBI PubMed search results for "COVID-19" in 2020. Counts were identified by searching for articles with publication dates in each month.**

## Rebalancing to make room for data

Uploading manuscripts to preprint servers such as bioRxiv and chemRxiv speeds up the communication of work headed to peer review and publication. Preprinting also reframes the value of manuscripts: By disseminating submission drafts, authors acknowledge that the work therein is worth sharing with the scientific community regardless of peer review outcome. What preprinting accomplishes for manuscript drafts is also possible for stand-alone data.

Successful data-centric efforts within the life sciences include depositories such as the Protein Data Bank and Sequence Read Archive as well as publishing reform efforts such as Wellcome Open Research and the Structural Genomic Consortium's Open Lab Notebooks. But the idea that data can be collected and reported without a pitch about the data's implications has not been adopted widely. What would it look

like if we shifted to reporting data for its own sake rather than solely in the framework of story-driven manuscripts?

## Introducing data disclosure articles

I envision a future when results of experimental work can be preprinted or published separately from traditional journal articles. These new manuscripts would consist of polished data from a single study or related research questions. They could report the results of compound screens, preparation of valuable or challenging reagents, the structural model for a protein, bioinformatics tools, sequencing efforts or any field-specific minimum publishable unit of research work. These data represent additions to a field regardless of whether they motivate future studies or ever are included in traditional journal articles.

Data disclosure articles would not require peer review because they would not include discussion about the implications of the work. If not falsified or manipulated, data have objective value. While removing peer review from scientific publication is controversial, the scientific community can learn something even from poorly executed and communicated experiments; this often occurs regardless of peer review. While the threat of a reviewer's close inspection may motivate more robust experiments, data articles would not be generated in a vacuum: They also would become pieces of traditional peer-reviewed journal articles. With this model, however, data disclosure does not wait for authors to generate an analysis.

Peer review evaluates whether a traditional journal article's claims are supported by the data the authors include and cite. In my proposed model, the data can be preprinted and are not under review; rather, when a paper is submitted, the claims based on the data will be reviewed. By separating peer review from data disclosure, readers will see more clearly that the data and the claims based on those data are interacting but independent.

Reporting data in smaller, separate manuscripts has several advantages:

1. These reports could appear in real time as larger projects advance. Others in the field could provide feedback on ongoing studies rather than retroactive analysis of work completed over many years.

2. Data articles would be free from conjecture and meta-analysis as well as from the bias introduced by a journal's reputation.

3. Lowering the barrier to data disclosure would allow what are now unpublishable projects, such as replication studies or good ideas that didn't pan out, to reach the broader scientific community.

4 . Reducing the time to disclosure might motivate pharmaceutical companies to share data that is tangential to their drug-discovery pipelines.

## Potential pitfalls

Scientific literature is inundated with over 2 million unique manuscripts per year. Some people might argue that lowering the barrier to data disclosure only will increase this volume and could lead to publication of incomplete or poorly executed work. Without analysis by authors and reviewers, impactful data could be lost in the noise. In highly competitive fields, authors might hesitate to report results before a journal guarantees publication of the related article. To protect against these pitfalls, researchers will need to work toward a collective understanding of the minimum publishable unit and agree that preprinted data articles represent meaningful contributions to the scientific literature. Individual fields may need to develop new tools to curate and index data articles to aid in dissemination. These are challenging barriers, but if authors integrate this new model for data disclosure with the existing publishing mechanisms, their audience will be able both to gain access to data quickly and to appreciate novel findings.

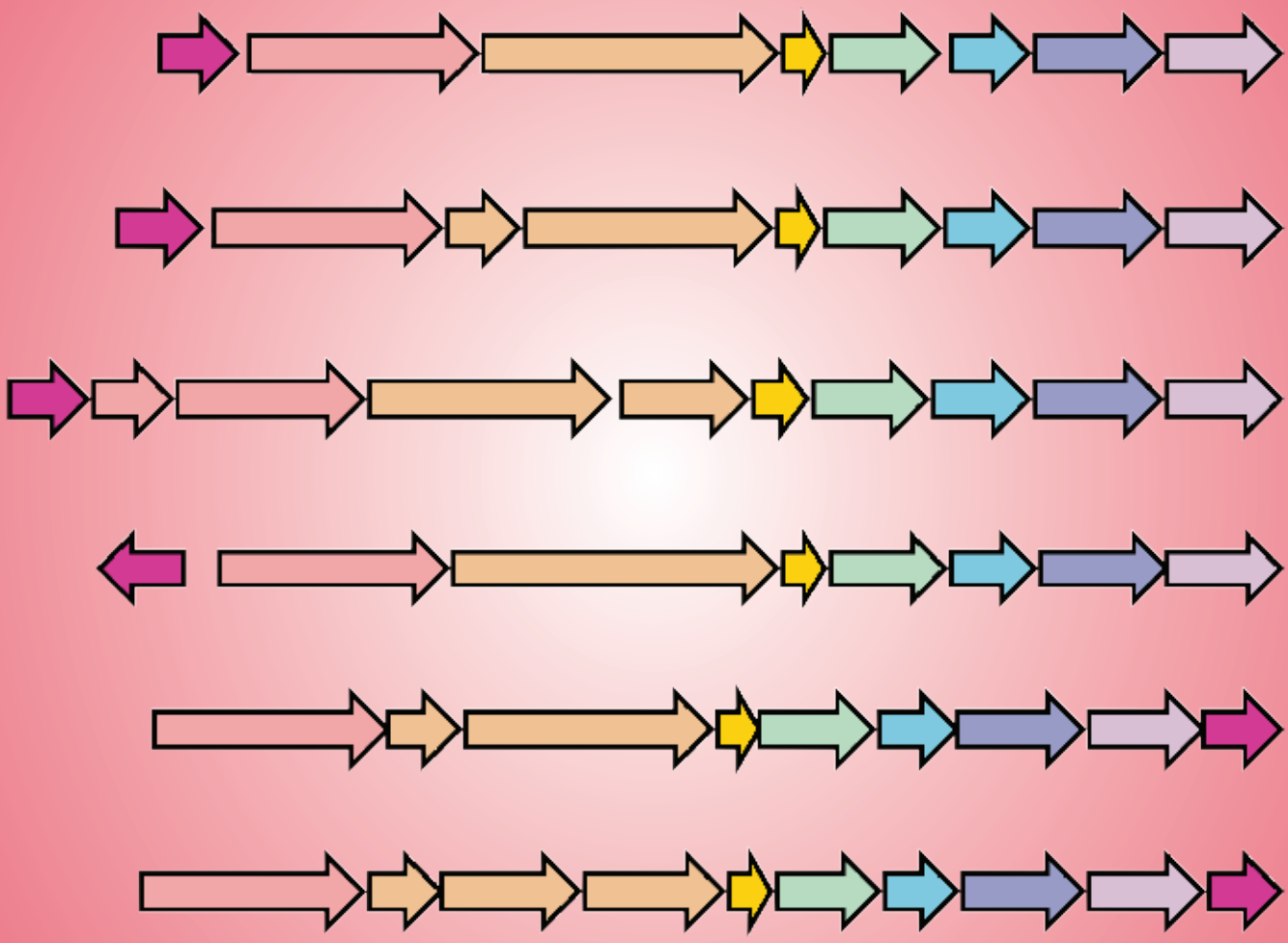
## First steps

To begin adopting this new model for data disclosure, I suggest authors preprint concise articles with an emphasis on the data presented. This will build momentum toward a publishing environment that encourages data disclosure as a necessary and independent scientific achievement. In this environment, all researchers, and the scientific enterprise, could function more effectively.

Scientists produce two things of separate but equal value: data and interpretation of that data. There is no reason our publication system should emphasize one of these at the cost of the other.

**Ken Hallenbeck** (k.hallenbeck@gmail.com) earned a Ph.D. in pharmaceutical sciences from the University of California, San Francisco, and now works in the department of early discovery biochemistry at Genentech Inc. in South San Francisco. He also serves on the board of directors of Relmagine Science, a nonprofit focused on empowering scientists to work toward a better research community.

JBC | JOURNAL OF BIOLOGICAL CHEMISTRY



# Women in biological chemistry

jbc.org/site/vi/women_in_jbc/

ASBMB PUBLICATIONS

# The time for change is now

*By Chris Pickett*

The U.S. biomedical research enterprise is riddled with systemic flaws that slow the progress of research. These flaws, and the disproportionate strain they put on different parts of the research workforce, have been put into stark relief during the COVID-19 pandemic. While it is understandable that most researchers want to find a way to return to some semblance of normal before considering reforms, that thinking is wrong.

The time for reform is now. Right now.

Returning to the status quo — ramping up research programs without significant policy changes — is an attempt to return to a system that worked for the privileged few. Now is the time to think critically about reforming departmental culture and enacting real, long-lasting reforms to make the research enterprise more just and equitable.

COVID-19 provides a window to consider reforms, and the research stoppage provides the space and time to implement them. Universities and departments should consider implementing long-term solutions to long-standing problems.

In late April, I convened a discussion series to delve into the systemic issues in biomedical research and how those issues were amplified by the pandemic. During four sessions, the 11 speakers talked about the challenge of trying to keep a research career going at a distance while caring for family members. Concerns about research evaluation, funding and career progression all figured prominently in their remarks. Just as prominent were concerns that departments and universities would fail to recognize and respect the disproportionate effects COVID-19 is having on the careers

of women and people from underrepresented backgrounds.

From these discussions, I drafted a white paper listing 17 recommendations universities and departments should consider to enact long-term change.

For example, more than 300 universities have paused tenure clocks due to COVID-19. Rather than stop with this short-term change, they should take this opportunity to revise how they evaluate a researcher's contributions to the university community, irrespective of the pandemic.

Similarly, departments should revise graduate admissions standards in a way that is broadly inclusive and applicable once the pandemic is behind us.

In the wake of the recent Black Lives Matter protests, universities made clear commitments to make their campuses more equitable and inclusive. These commitments are similar to previous performative commitments to equity and inclusion.

Only through intentional hiring, retention and promotion of BIPOC (Black, indigenous and people of color) scholars can universities actually live up to their commitments.

Departments should work immediately on how search committees will implement established protocols to prioritize hiring BIPOC postdocs into faculty positions once hiring freezes are lifted, and how they will revamp retention and promotion policies to value the typically underappreciated community service done by these faculty members.

Additionally, the pandemic and the Trump administration have pushed the scientific community to vocally defend foreign-born researchers working in the U.S. However, universities and departments could make real, beneficial reforms to demonstrate their commitment to nearly 50% of the biomedical trainee workforce by equalizing the pay of trainees regardless of national origin and enact policies that prevent faculty members from threatening a trainee's visa status to extort labor.

These recommendations are forward-looking, and most are intended to make long-term positive changes. If the pandemic has convinced universities and departments to make accommodations for their current crop of trainees and faculty, then they have the space to make permanent changes as well.

The biomedical research enterprise was not perfect before COVID-19, but we have a chance to install a better system for all members of the biomedical research enterprise for years to come.

The opportunity is here. The time is now.

**Chris Pickett** (clp3@princeton.edu) is the director of Rescuing Biomedical Research. He is a former ASBMB policy fellow.

# The mind of a public speaker

*By Blaise J. Arena*

KANE REINHOLDTSEN/UNSPLASH

Some years ago, I was waiting my turn to speak at a big technical conference in Hyderabad, India. There were more than 600 scientists and engineers in the audience. I noticed an Indian army soldier carrying a machine gun on his shoulder appear just a few feet from me. I glanced around and saw another dozen soldiers around the enormous room.

*Are they here for my protection? Probably not. Are they expecting a terrorist attack? Well, maybe.*

Actually, it turned out that there was a high-level government minister in attendance, and they were there for his protection. I was unmoved. I gave my talk to the biggest audience I'd ever addressed and took some written questions afterward. All went well.

I reflected on the experience later that evening and thought about how far I'd come. Early in my research career, I would have been terrified by the prospect of presenting to a huge audience (or a small one). But I had looked forward to this and had delivered a smooth, well-received talk, unfazed by machine guns. I had made a consistent, long-term effort to develop my presentation skills and overcome stage fright.

I was motivated by two things:

1. The research organization I had joined put high value on communication skills. It wasn't enough to do good research; you had to explain and convince effectively.

2. I did not want to suffer forever from any anxiety associated with giving a talk.

My approach to developing my presentation skills may help you.

## What can make or break a presentation?

### Make (you'll know it when you see it)

- The speaker is smooth, at ease.
- She is enthusiastic but explains at a comfortable pace. She highlights transitions when moving to new topics.
- The speaker admits to some blind alleys and surprises; there are bumps in any research road. She explains how she adjusted and learned. Being candid makes a more personal and interesting story.

### Break

- Slides are too hard to decipher.
- The speaker switches tracks without warning.
- He is too slow or fast, or uncertain.
- The speaker gives a chronological account of every single one of his experiments. This is monotonous and confusing. It prevents the audience from seeing the big picture, if there is one.
- The speaker ridicules others in his field. I have seen this only a handful of times. Don't do it, as it leaves a horrible impression. Instead, acknowledge inspiration from others.

## Preparation

Preparation will get you 75% of the way toward a good presentation. Too often, people dismiss this and think, "I'll just wing it." Some seasoned presenters can get away with this, but for most of us, it is a mistake. It's lazy and will lead to trouble. Some advice:

**Begin preparing well in advance.** Take the time to make a thoughtful presentation — and refine it. Throw it together the night before, and everyone will know it. But if you have no choice but to do a rush job, all of these suggestions, condensed in time, will help you. As will becoming more experienced.

**Know your audience.** Are they unfamiliar with your area? Do they already know your work; that is, are you just giving an internal update? You must design your presentation accordingly. I once saw a world-class paleontologist give a presentation (dinosaur cladistics!) about his work to a large audience of research chemists. We were all mesmerized. When done well, crossover talks can be a thing of beauty.

**Tell a story.** The beginning-middle-end format has been used for thousands of years because it works. Decide what your core message is and develop a narrative around it. Highlight mysteries and struggles and reach a resolution. If you have engaged the listeners, they will feel a stake in your success.

**Choose key experimental results to illustrate your points, without regard to chronology.** If you find yourself saying, "And then we did this, and then we did that," stop and revise. This is absolutely not the same as cherry-picking your data. In fact, it's fine to show some outliers. This is a matter of presenting relevant information — not showing how much work you did.

**Show an agenda slide and tell the audience what will be covered.** Refer to it as you move through the story. This keeps your audience with you, and that is what you need. I always have done this, and it really helps everyone, including me, stay on track.

- **Practice your presentation a couple of times, but don't memorize it.** Memorized talks are wooden. By practicing, you become familiar with the flow of your story and can check the length. You may notice areas that are a little rough; refine them.
- **Prepare your introductory remarks.** You've said good morning — now what? Write a sentence or two to keep in your pocket to get you going. Maybe some background on your work or a big-picture remark about its relevance to the world. Anything to get you off to a comfortable start.
- **Your slides can make your presentation and are worth lots of effort.** They will help both your audience and you. They must be readable from the back row. Don't jam a slide with so much text and imagery that the viewer struggles to decipher it instead of listening to you. Generally, less is more.
- **Here is one of my pet peeves:** The speaker presents an elaborate or unfamiliar graph. He has studied it a hundred times, but it's new to you. He blows through it, assuming it's obvious to everyone. While the viewer is still trying to decipher it, he moves on. I've seen this mistake many times; good speakers don't do this. Instead, they stop and walk the audience through an unfamiliar plot. Here's where you put your laser pointer to good use — focus on key features and orient the audience.

**Show an agenda slide and tell the audience what will be covered. Refer to it as you move through the story. This keeps your audience with you, and that is what you need. I always have done this, and it really helps everyone, including me, stay on track.**

## Giving your presentation

Stick to your time allotment. It shows respect for the audience and other speakers. If you run over, it means you haven't prepared adequately. I once attended a talk by a prominent, crusty professor who kept talking past his 45-minute slot, undeterred by pleas from the session leader to wrap it up. He used his time twice over and then announced, "I'm sure you will agree that my work was so interesting it was worth the extra time." It wasn't.

**Be animated.** Point, gesture, walk around a little. Make casual eye contact with the audience; don't just stare into space. Enjoy yourself.

**Stick to your time allotment. It shows respect for the audience and other speakers. If you run over, it means you haven't prepared adequately.**

**It's usually a good sign if you get questions.** You can anticipate some of them and be prepared. If you don't know the answer to a question, say so.

## Stage fright

Most people suffer from this, some severely. There are famous performers who have been incapacitated by stage fright. Don't let it make you miserable. Let's try to manage or overcome it.

Preparation is essential. Beyond everything I've already said, preparation should also moderate stage fright. Being ready helps!

I'll add my tips and tricks to the mountains that already have been written on this subject.

**The audience is with you.** They want you to succeed. Believe that.

**Visualize!** It really can help to imagine yourself in front of the audience, being interesting and cool. It's far more effective than visualizing fear and failure. Try it. You can even think of yourself as an actor on a stage.

**Train yourself to speak at a comfortable pace.** Nervous energy can make you race, leaving the audience wondering what happened.

I once co-authored a paper with an experienced, very articulate colleague. The paper had been accepted by a prestigious chemistry symposium, and we agreed that my colleague would give the talk. I was surprised by how this confident person let the large audience unnerve her. She rushed through. It was a missed opportunity.

The lesson here is that this can happen to anyone, including me.

Something I've done for years is to write on my notebook, in large letters: "Go slowly, teach." I stare at it in the minutes before my talk. Yes, you are a teacher, an explainer. You must calm down and move at a moderate pace.

**If possible, do a little advance work.** If you are to speak in an unfamiliar venue, check it out. Scout out the room during a break, even wander on the stage to get the feel of it. Chat with a few attendees beforehand. This will make you feel part of the scene instead of like an outsider.

**You have important experiences to draw on — use them.** Everyone has faced some life challenges that threatened to overwhelm them. A serious health problem, the death of a loved one or some other tragedy. Keep your public speaking challenge in perspective. No doubt you have overcome far worse things. You can do it.

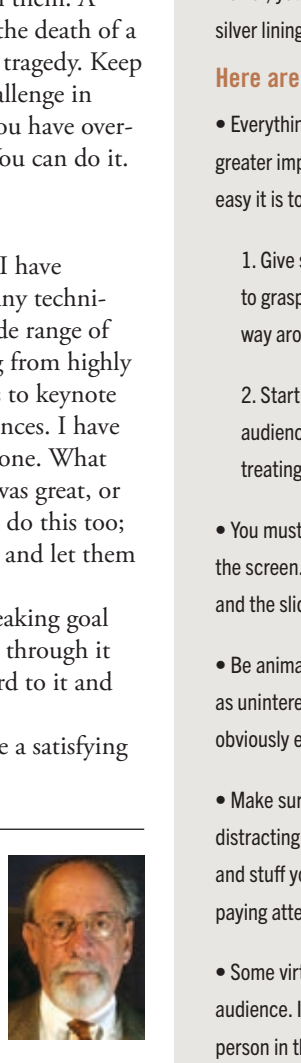
## Conclusion

Over my long career, I have been fortunate to see many technical presentations in a wide range of disciplines — everything from highly detailed internal updates to keynote lectures at major conferences. I have tried to learn from each one. What did the speaker do that was great, or not so good? You should do this too; always learn from others and let them learn from you.

I believe that your speaking goal should not be just to get through it but rather to look forward to it and enjoy yourself.

Let public speaking be a satisfying experience.

**Blaise J. Arena** (blaisearena@yahoo.com) is a retired research chemist and project manager with a developer of petrochemical processing technology. He is the author of over 50 patents and publications in the areas of heterogeneous catalysis, carbohydrate chemistry and biotechnology.



### Giving a virtual talk

If you haven't given a virtual presentation already, you will soon enough. This now-common way of communicating comes with some unique challenges. You are right in the face of the viewer, yet you are remote. This makes it much easier to lose your audience. But there is a silver lining in this virtual approach: Stage fright should be greatly decreased.

#### Here are some tips:

- Everything I said about preparation and presentation still stands, and it may take on even greater importance in the virtual world. But two items stand out, and they both relate to how easy it is to lose your audience in a virtual setting:

  1. Give special emphasis to preparation of your slides. Keep them straightforward and easy to grasp. It's better to have more slides with less information on each slide than the other way around.

  2. Start off with an agenda slide and bring it up as you move along. Again, keep the audience with you by referring to this slide before any transition. You may think you're treating the viewers like children, but believe me, it will be appreciated.

- You must find a way to make your presentation stimulating. Don't let it be just your face on the screen. Nor should you only talk over static slides. It's best to alternate between your face and the slides.

- Be animated and upbeat. This will make a good impression, so much better than coming off as uninterested (even if you aren't). I recently attended a virtual talk by a professor who was obviously excited to talk about her work. She really made it enjoyable and memorable.

- Make sure beforehand that your setup is effective, including lighting and camera. Avoid a distracting backdrop. Some people show their book collection, knick-knacks, cats, artwork and stuff you can't even identify. The viewer may want to scrutinize those things instead of paying attention to you. Keep it simple.

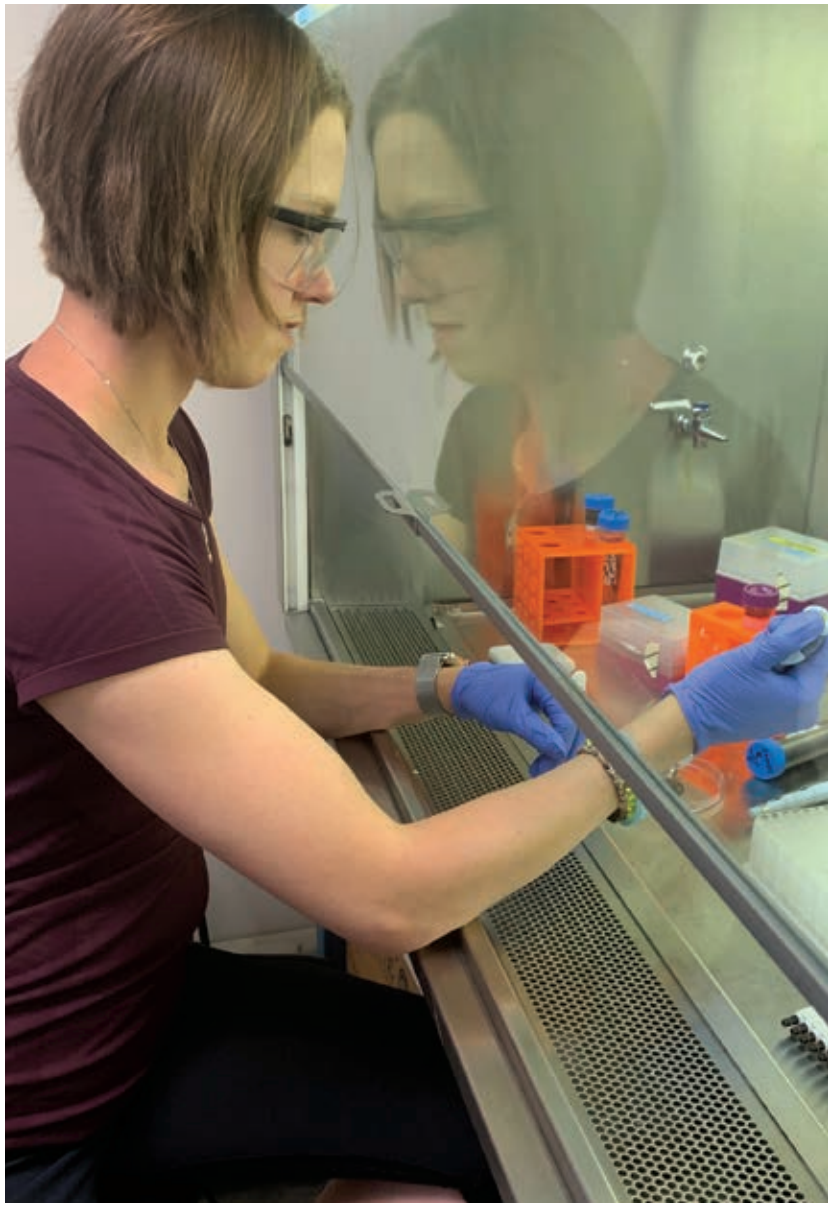
- Some virtual presenters like to have someone in the room with them to serve as a live audience. If this might help you, give it a try. I'm concerned that I might keep looking at the person in the room rather than at the camera. That could be very distracting for viewers, so be careful. Perhaps have the person sit behind or beside the camera.

# Summer undergraduate research weathers the pandemic

*By the Streu Summer Research Group*

## What can be learned from these unique experiences?

SARA PALACIOS



Hamline College senior Ash Robinson works on a summer research project in Betsy Martinez–Vaz's biochemistry lab where she studied the microbial degradation of the Type 2 diabetes medication metformin.

The first wave of COVID-19 infections in February and March forced academic labs to decide the fate of their undergraduate research programs, especially summer research. In many cases, that meant canceling research, while in others, students and faculty scrambled to make new plans. As states reopened, grad students and industrial researchers returned to work, but undergraduate research has resumed less consistently.

Undergraduate research programs that were not canceled were reimagined based upon the limitations and guidelines set by their institutions. Some students were able to work in the lab, but even when lab research continued, it was far from normal, according to Joe Provost, professor and chair of chemistry and biochemistry at the University of San Diego.

### Making a plan

Provost and a group of science chairs teamed up with his building manager to develop a plan for the university, following state and county guidelines, that would allow students to return to campus. USD offered both on-campus and remote research, with some students doing a hybrid of both.

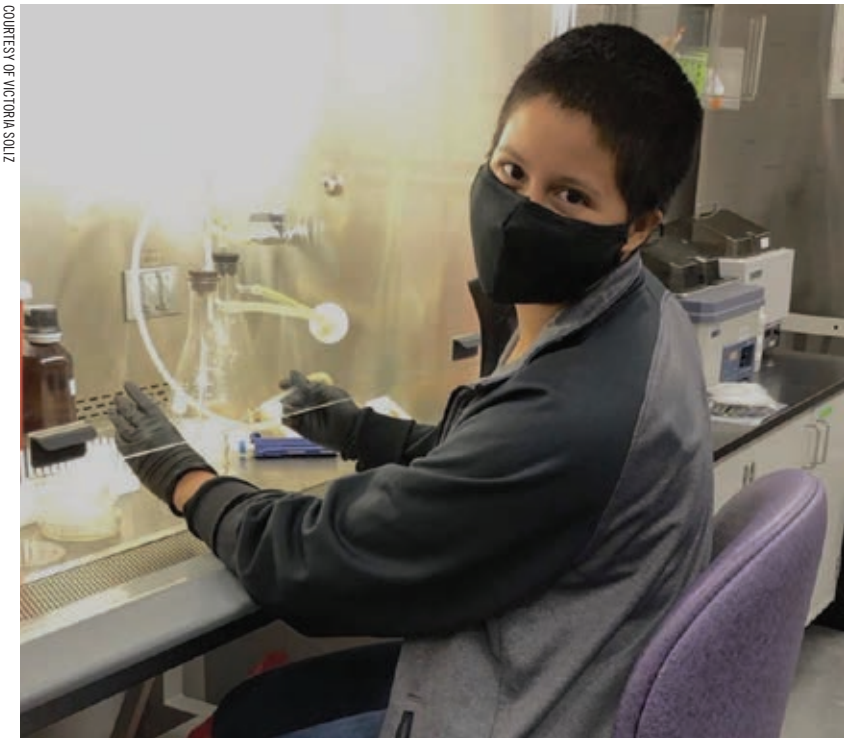
"Part of the issue was waiting to find out what the rules were," Provost said. "Eventually, we decided to research what would be as safe as possible and push our administration to allow research once the state allowed such activities."

Getting students and faculty back into the lab was critical not just for the summer but also as remote teaching in the fall became more likely, Provost said. "The students still need this important event in their experiences of college. Getting into a lab to be creative and learn to be a scientist is important, and having the ability to continue in this mode in the fall makes all the work to get research going even more important."

Some undergraduates' time in the lab was limited to essential experiments while they performed other functions remotely. Victoria Soliz, a student at the University of Illinois at Chicago, said, "My lab mentor would recommend me papers to read and ask me questions I should work on answering … In-lab research is only when an experiment needs to be done."

About 400 miles from Chicago, at Hamline University in Minnesota, Ash Robinson said she performed remote work and also drove to campus to complete key experiments in the lab.

COURTESY OF VICTORIA SOLIZ



**With lab access limited, Victoria Soliz, a student at the University of Illinois at Chicago, and her lab mates read many academic papers this summer.**

## Switching gears

This approach worked for students who could get into their research labs, but some labs were shut down completely for the summer. Many students changed their research methods so they could work remotely. The modified projects included anything from crystallographic structure refinement to computational modeling.

Prior to COVID-19 restrictions, Caleb Rosenthal at Hamline University planned to spend the summer in the lab doing hands-on work, but he ended up involved in bioinformatics, using programs such as Qiime and DNA Subway. He found the transition to be fruitful.

"Now that I am completing bioinformatic research, I am invested in it and find it to be very crucial to the field of science," Rosenthal said.

Dean Young, also from Hamline, said he realized that "there is more to do with bioinformatics than one could ever hope to accomplish in a single summer."

Like Rosenthal and Young, Elizabeth Nelson of Boston University found some unanticipated benefits in her new projects. "Since things are remote, I feel the experience has been improved in the sense of responsibility and ownership," she said.

Nelson's PI was flexible and enthusiastic about developing a new research plan that involved freedom to explore new topics at her own pace. In a remote format, students could take initiative in their projects and develop a sense of independence.

With the quick change to remote work, some researchers spent significant time reading about their new or modified projects. Several students said that reading articles and learning more about their projects before working on them in the lab provided a deeper understanding, especially for those who were new to their subject matter. Some proposed that an additional period of background research might help students considering starting in the lab even in nonpandemic times.

## The challenges

Working remotely did present unique challenges. "Zoom exhaust is a newly discussed and very valid topic," Nelson said. "It's challenging to sit in the same seat for three or four hours at a time with back-to-back-to-back (-to-back, sometimes) calls. In the pre-pandemic world, there would be walking in between meeting locations, breaks for lunch, and probably just fewer meetings than now."

Students noted that internet and computer issues caused problems in

processing large data sets. And the adjustment from campus to a new environment did not always support learning new techniques. For example, a remote setup meant students no longer could walk to their advisers' offices to ask quick questions.

When they had overcome these problems, however, the undergrads said the ends did justify the difficult means. "Another benefit to spending hours on a database or computational tool is gaining fluency with that tool," Young said. "I am picking up tricks I would have missed from a more casual use and finding ways to extract more relevant information from database searches. This produces skills that can be used in future research and listed on a resume or CV."

Students generally were grateful that they could complete summer research in any capacity, although they had difficulty recapturing the human connection that comes from working closely with others in a research lab. Marissa Lopez at the University of California, Davis, said, "As human beings we have a dependence on other humans."

## The benefits

Students and their advisers worked to stay connected. Zhela Sabir from Arizona State University said video conferencing actually developed a "sense of togetherness" that otherwise wouldn't have existed. Video communication helped her realize that "there is a deep value in working as a team," she said, especially during a global crisis.

Several undergraduate researchers said they built close relationships with their mentors and lab mates as everyone struggled to navigate the pandemic. At Albion College, Jeremy Hogaboom said joint and individual meetings were a valuable part of the summer experience. Students also participated with others across campus in meetings and fitness activities. "(Our research program) has done a wonderful job of cultivating a learning community among Albion students, even when we can't be together," he said. "Fun (fitness) challenges ... have been a great way to keep working out and stay healthy during a time where it is way too easy to let your health and well-being slip."

Other benefits of working remotely weren't lost on the researchers. With video conferencing, participants could stay up to date on their projects from any location that had adequate internet. Some were able to multitask during meetings, while others spent more time with relatives. Although she might have been more productive working in the lab, Lopez said she valued spending her summer doing remote research while enjoying a cup of cafecito con leche with her family.

Many students said they learned a lot from their experiences this summer and changes that improved efficiency or contributed positively to their understanding of their projects, such as remote video conferencing and additional literature review, should be implemented long term. Victoria Soliz said her lab group hopes to use their additional literature research to write a review paper.

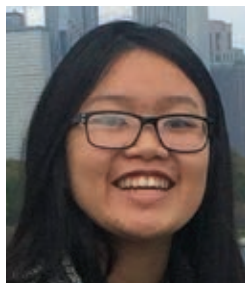
As Elizabeth Nelson pointed out, "It would simply be unfair to go back to normal without retaining any adaptations."

## About the project — and the writers

Undergraduates who aspire to careers in biomolecular science need to show prospective employers and graduate schools that they have research experience. With this in mind, we wondered what types of research experiences students and faculty had managed this summer.

In addition to researching this article, we all worked remotely on computational projects at Albion College in Michigan over the summer. Pictured below, left to right: Anna Crysler is a junior biochemistry major. Peter Filbrandt is a sophomore biochemistry major. Kaitlyn Piontkowsky is a sophomore biochemistry major. San Pham is a senior biochemistry and music double major. Craig Streu is an associate professor of biochemistry in the department of chemistry at Albion and a member of the Student Chapters Subcommittee of the ASBMB's Education and Professional Development Committee.




# ASBMB Today call for submissions

**ASBMB Today is accepting submissions for two upcoming special issues.**

## The wellness issue

January 2021
Deadline: November 2, 2020

With our lives upended by a worldwide pandemic, how have you kept yourself well? If you are a professor, investigator or supervisor, how have you looked after your students' and workers' wellness? Write about the physical and mental challenges you faced and overcame in 2020.

## The reimagining issue

June/July 2021
Deadline: March 15, 2021

When the world reopens after COVID-19, it will be a different place. It's a good time to reimagine ways the scientific enterprise could be more sensible and just. We want your ideas for how to do that. Think about the systems around you. Can they be improved? Should they be replaced? Tell us what you would do to make them better.

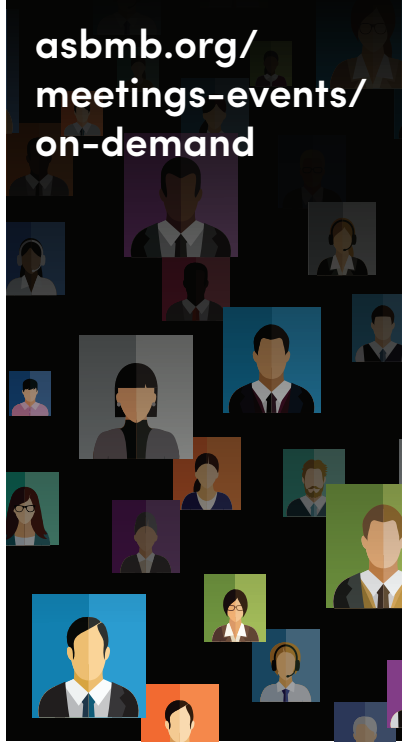
**For information, email asbmbtoday@asbmb.org or go to asbmb.org/asbmbtoday and click SUBMIT.**

ASBMB

# Learn something new.

Watch on-demand webinars and events including scientific presentations and discussions on topics related to career development, education, funding and more.

**asbmb.org/meetings-events/on-demand**



# On managing and mentoring

## 5 QUESTIONS FOR JENNA HENDERSHOT

*By Laurel Oldach*

Jenna Hendershot, a longtime member of the American Society for biochemistry and Molecular Biology Education and Professional Development Committee, recently started as a senior scientist at the diagnostic testing company Progenity. She works with a team that's developing a proteomic test for preeclampsia, a dangerous complication of pregnancy.

ASBMB Today caught up with Hendershot in July. This conversation has been condensed and edited.

### 1 How did you come to pursue a career in biotechnology?

In grad school, I received a grant that required a three-month internship in industry. I ended up in a summer research program designed for undergrads at Dow Agrosciences in Indianapolis. It completely changed my whole perspective on my career. I fell in love with the pace of the projects and working for something that will go out and change people's lives.

### 2 What does a day in your life look like?

Most of my day is meetings. I have one-on-ones with my group members, and I lead a lot of cross-disciplinary meetings. I make sure scheduling is on track, help plan experiments, and do analysis and protocol documentation. There's a lot to fit into limited time. I'm trying to adjust and figure out the new normal for work–life balance: in this position and in the time of COVID.

### 3 What skills do you need in your current role that you didn't learn in graduate school?

Dealing with people. As a student, you're used to looking at data and being at the bench for hours; if you don't want to, you don't have to interact with very many people. I'm learning on the job, which is working OK, but I would love to have some sort of course in my back pocket.

### 4 Tell me a little about the role of networking and mentoring in your career.

I think it happens that people come into your life at the perfect moment, and sometimes they vanish from your life naturally. I've had incredibly helpful people come and go, but have not had a whole-career mentor. Maybe that doesn't exist. I don't know.

### 5 Any advice for students interested in following a similar path?

I didn't realize how critical that one three-month internship was going to be. It completely changed my career path. I know it's really hard, because advisers don't want you leaving the lab — but if you're interested in anything other than academia, my No. 1 recommendation would be to apply for an internship. If you're not allowed to, then do informational interviews.

**Jenna Hendershot**

**CURRENT POSITION**
Senior scientist, protein biomarkers, Progenity Inc.

**EDUCATION**
Ph.D., University of Michigan Medical School, 2014

**FIRST JOB OUTSIDE OF ACADEMIA**
Scientist I, product development, Cayman Chemical

**FAVORITE MOLECULE OR PROTEIN**
Adenine DNA glycosylase. "It flips a damaged DNA base 180 degrees out of the DNA, into the enzyme's active site. In graduate school, I studied that on a millisecond timescale."

*Read an extended version of this interview at asbmb.org/asbmbtoday.*

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

# CLASSIFIEDS

## Postdoctoral Position — Scaraffia Research Group

Tulane University School of Public Health and Tropical Medicine

Dr. Patricia Scaraffia´s lab performs metabolic studies on mosquitoes. Her laboratory is particularly interested in unraveling the physiological, biochemical, and molecular basis underlying the regulation of nitrogen and carbon metabolism in mosquitoes, as well as in discovering new metabolic targets that can be used for the design of better mosquito–control strategies. The successful candidate will apply traditional and modern biochemical approaches to investigate the mechanistic regulation of ammonia metabolism in Aedes aegypti mosquitoes.

**Requirements**

- PhD degree in biochemistry or related discipline with a strong background in protein biochemistry, and metabolic signaling
- Research experience in metabolic studies in insects strongly preferred
- Documented experience in biochemical techniques including western blotting, immunoprecipitation and immunofluorescence microscopy
- Excellent communication skills and ability to work independently as well as part of a team

**Application**

Submit a single PDF file to mmobilliot@tulane.edu with the subject Postdoc Application and include:

(1) a cover letter describing research interests, (no more than 1 page);
(2) your curriculum vitae; and
(3) contact information for three references.

## Postdoctoral Position

University of Connecticut

A postdoctoral position in molecular biology is available in the group of Prof. Andrew Wiemer (wiemer.lab.uconn.edu). The lab is focused on drug discovery related to cancer and immunology. The applicant would apply molecular biology techniques to research immune system proteins and to develop novel antibody-based drugs. The ideal applicant will have a background in molecular cloning and interests in drug discovery, cancer, immunology, pharmacology, and/or biochemistry.

This is an exciting opportunity to engage in a multi-disciplinary environment that employs state-of-art techniques in molecular medicine. The successful candidate can grow toward research independence in their chosen area of specialization. Professional development activities are available, supported and encouraged. The position is funded by extramural research grants and will receive an NIH-level stipend.

Primary responsibilities:

- Molecular cloning and evaluation of novel protein constructs.
- Disseminate research results through publications in peer-reviewed journals.
- Participate in grant writing and fellowship applications.
- Attend lab meetings and journal clubs.

**https://careers.asbmb.org/job/postdoctoral-position/54543453/**

## Metabolism Lead Investigator

Morgridge Institute for Research

The Morgridge Institute for Research, part of the dynamic research community at the University of Wisconsin-Madison, seeks an accomplished investigator to spearhead a campus-wide Metabolism research initiative. We are particularly interested in attracting an energetic and talented researcher with an innovative and collaborative research team addressing key questions in fundamental metabolic processes. The successful candidate will lead the Morgridge metabolism program, which has nucleated a thriving campus-wide network of metabolism researchers, and will have the opportunity to recruit both wet lab and computational scientists to our active interdisciplinary research community.

This is an extraordinary opportunity for an individual with a proven track record of high-quality research related to metabolism. We seek someone who is enthusiastic about mentoring young scientists and engaging the public about the importance of research. We also encourage applications from individuals who are committed to strengthening a collaborative environment that advances the Institute's mission and to building a more equitable and diverse scholarly environment. The successful candidate will also be appointed to a tenure-track or tenured position in an appropriate University of Wisconsin-Madison department, and receive an attractive salary and benefits package plus generous start-up support.

**https://careers.asbmb.org/job/metabolism-lead-investigator/54585807/**

## Senior Scientist, Mathematical Modeler

Applied BioMath, LLC

At Applied BioMath, our passion for science, technology and helping patients is what drives our desire to revolutionize drug invention. Our team members are innovators and entrepreneurs at heart, and enjoy pioneering this paradigm shift of how drug invention is done. We love to learn, challenge ourselves and others, and create new science.

We are currently seeking a talented and innovative Senior Scientist, Mathematical Modeler to join our team in Concord, MA (the Boston/Cambridge area) or Pleasanton, CA (the Bay Area). The ideal candidate will work closely with Pharmaceutical and Biotech teams to build fit-for-purpose mathematical models that help drive decisions in drug development. Models may describe drug's mechanism of action, signaling pathways (intra- and cell-cell signaling), disease mechanisms (description and mechanistic), and drug toxicities. Modeling approaches include quantitative systems pharmacology (QSP), mechanistic pharmacokinetic/pharmacodynamic (PKPD), and traditional PKPD modeling of small and large molecules and novel therapeutics.

**careers.asbmb.org/job/senior-scientist-mathematical-modeler/54471785**

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