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# ASBMB TODAY

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

## 2019 ASBMB ANNUAL MEETING

at Experimental Biology

SPECIAL SECTION





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American Society for Biochemistry and Molecular Biology

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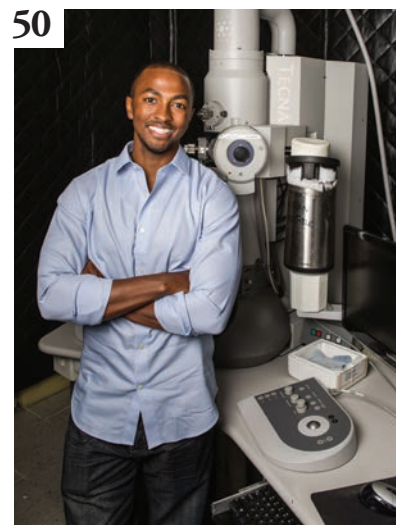
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# ASBMB TODAY

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## EDITOR'S NOTE

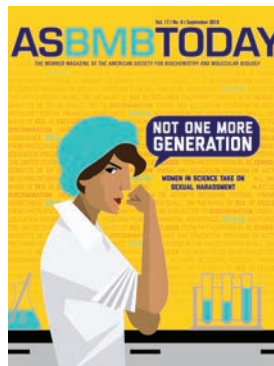
# Look back and listen

By Comfort Dorn

In general, and especially in this space, I like to look ahead. That's my job. This week (about two weeks before you are reading these words), I am making assignments for articles to run in April and editing essays for January. We're deciding on feature stories for the spring and pondering what to include in the 2019 careers issue (scheduled for next August). It's the nature of the beast.

And of course, I'm all about print journalism, one of the breed that used to be called ink-stained wretches. I like to read stories, preferably on paper, interspersed with compelling photos and images. Though I've adapted myself to screen reading, I'd rather turn pages than scroll.

But we all need to jump out of character once in a while, so I'm going to use this space to urge you to go back to the September issue of this magazine, specifically to the online version of Laurel Oldach's powerful article on sexual harassment in science and the women who are working to stop it. And though I want you to read every well-turned phrase, what I'm really juiced about is the audio story that Laurel and our multimedia whiz Allison Frick put together to go with the written words.



My involvement in this work was minimal. Early in the process, when Allison told us she wanted to make an audio article, I dubbed it an "audicle" and won a few laughs. They invited me into the not-quite-soundproof storage room to tape an introduction. Then they asked me to tape it

again. Then two more times. (I have new respect for audio journalists.)

We're all pretty busy around here, so I didn't listen to the piece until it was almost finished. And I was completely blown away. Even though I had read Laurel's story more times than I could count, hearing the voices of the women she interviewed — the anger and resolve and courage — gave it new depths of meaning.

I can't explain it. I can only recommend it.

The audio story was posted late (we're new at this), and we didn't tout it in the September print edition. I'm making up for that now.

Take my word for it: It's totally worth your time.



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

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## Corrections

In the September issue, the article "Not one more generation: Women in science take on sexual harassment" incorrectly stated the American Geophysical Union's chief executive officer's name. She is Chris McEntee.

In the June/July issue, the list of 2018 ASBMB Honor Society members was incomplete. We republish the complete list on page 10 of this issue.

# Weigh in on initiatives across the NIH

By Benjamin Corb

The Public Affairs Advisory Committee represents the members of the American Society for Biochemistry and Molecular Biology not only before elected officials but also at funding agencies to ensure the creation of sound policies that support their research. We do our job best when ASBMB members share their concerns and ideas with us.

Here are some issues we're monitoring. Please consider weighing in.

## Increasing data transparency

The ASBMB PAAC develops policy statements and recommendations. It also responds to requests for comments from funding agencies.

The PAAC supports its arguments using data that are either publicly available or provided by the agency after the PAAC submits a Freedom of Information Act request.

Unfortunately, agency calls for comment sometimes have short submission windows, and materials requested by the PAAC under the FOIA don't always arrive in time for the committee to use them as intended. The PAAC is working with the National Institutes of Health to make more agency data relating to grants publically available.

We often use the NIH's Research Portfolio Online Reporting Tool, called both RePORTer and RePORT, depending on who you talk to.

While RePORT contains lots of data, some are not easy to suss out, particularly when we are trying to analyze historical and demographic information. Making data more eas-

ily accessible will help scientists and scientific societies provide effective and meaningful recommendations to improve the biomedical enterprise.

One final thought on this topic: The blogs of several NIH leaders sometimes offer deep issue analyses and provide information on the NIH's research portfolio that is not publicly available. Deputy Director for Extramural Research Mike Lauer publishes his Open Mike blog, and National Institute for General Medical Sciences Director Jon Lorsch publishes the NIH Feedback Loop. While these blogs include graphs to illustrate data and trends accompanied by useful insight and analyses, the raw data behind these figures are sometimes inaccessible.

## Supporting the next generation of researchers

The PAAC has provided preliminary comments to the NIH working group that is crafting policy recommendations to support the future biomedical research workforce.

Mandated by the U.S. Congress in the 21st Century Cures Act, the Next Generation Researchers Initiative will provide NIH institutes with strategies to better support early-stage and at-risk investigators. The policies that come out of this effort are likely to have an influence on grant funding at all career stages and may result in changes to the research enterprise that are long overdue, including changing the definition of "early-stage investigator" and enacting policies that are aimed at supporting at-risk investigators.

In a recent email, the PAAC asked ASBMB members for comments on how the NIH can support early-stage and at-risk investigators. The PAAC has published several documents on strategies to support young researchers. Because we want our members' voices to be heard, we have created an online tool for you to review these recommendations and share your opinions.

## Diversity of NIH councils

The public affairs staff is analyzing the makeup of the federal advisory councils within the NIH, the groups of scientists who provide guidance to leaders shaping internal NIH policies. Each institute has an advisory council, and several additional advisory councils advise the NIH director.

We are reviewing gender, race and ethnicity, geography, career stage, and other variables. We believe diversity must be considered when filling vacancies on NIH councils. Councils should include a variety of perspectives and professional experiences to advocate for policies that will support all of the research enterprise.

Our analysis is in the early stages, and we look forward to sharing our results with you later this year.

Want to know more about these efforts, or have a topic you'd like us to address? Email us at [publicaffairs@asbmb.org](mailto:publicaffairs@asbmb.org).



Benjamin Corb ([bcorb@asbmb.org](mailto:bcorb@asbmb.org)) is director of public affairs at the ASBMB. Follow him on Twitter @bwcorb.

# Member update

By Erik Chaulk

## Charpentier, Doudna win Kavli Prize

The Norwegian Academy of Science and Letters has announced that Emmanuelle Charpentier and



CHARPENTIER

Jennifer A. Doudna are among the recipients of the 2018 Kavli Prize in nanoscience.

The Kavli Prizes, Norway's highest science honors, are presented every two years in astrophysics, nanoscience and neuroscience. Each recipient receives \$1 million.

Charpentier and Doudna are being honored for their invention of the groundbreaking genetic editing tool CRISPR-Cas9.

Charpentier is scientific director at the Max Planck Institute for Infection Biology and honorary professor at Humbolt University in Berlin.

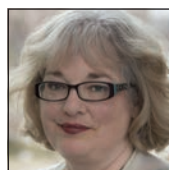
Doudna, a professor of chemistry and of biochemistry and molecular

biology at the University of California, Berkeley, and a Howard Hughes Medical Institute investigator, recently opened a lab at the Gladstone Institute in San Francisco where she was appointed a senior investigator.

Doudna and Charpentier shared the nanoscience prize with Virginijus Šikšnys of Vilnius University in Lithuania. The 2018 Kavli Prizes were awarded in September in Oslo.

## Hanna-Rose receives teaching award

The Pennsylvania State University professor Wendy Hanna-Rose has received the Milton S. Eisenhower Award for Distinguished Teaching.



HANNA-ROSE

Established in 1992, the Eisenhower Award is given to a tenured professor who has demonstrated excellence in both teaching and mentoring students.

Mentoring and developing students has played a crucial role in Hanna-Rose's identity as an educa-

tor. She has written that her teaching philosophy "involves self-identity as a coach who provides motivation, prepares drills, supplies feedback, and reiterates the process, all with the aim of promoting student progression from novice to expert."

Hanna-Rose recently was named head of the department of biochemistry and molecular biology in the Eberly College of Science at Penn State.

## Hochstrasser continues as chair at Yale

Mark Hochstrasser has been reappointed chair of the department of molecular biophysics and biochemistry in the Yale School of Medicine.



HOCHSTRASSER

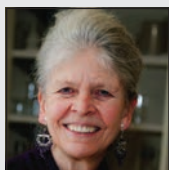
Hochstrasser's appointment is one of four faculty appointments announced in June by the dean of the faculty of arts and

sciences at Yale.

Hochstrasser is the Eugene Higgins professor of molecular biophysics

## ASBMB member wins lifetime achievement Lasker award

The Albert and Mary Lasker Foundation recently announced the recipients of the 2018 Lasker Awards. Among the four recipients was Joan Argetsinger Steitz, a



STEITZ

professor of biophysics and biochemistry at Yale University and member of the American Society for Biochemistry and Molecular Biology.

Steitz received the Lasker-Koshland Special Achievement Award in Medical Science "for four decades of lead-

ership in biomedical science—exemplified by pioneering discoveries in RNA biology, generous mentorship of budding scientists, and vigorous and passionate support of women in science," according to a release from the foundation. Over her pioneering career in RNA biology, for which she won the Herbert Tabor Research Award in 2015, Steitz has been known as a generous mentor to young scientists and an ardent voice for inclusion in the scientific community. She and the other Lasker Award recipients received their awards on Sept. 24.

## Kopchicks give \$23M to Indiana University

John and Char Kopchick will give \$23 million to Indiana University of Pennsylvania, the largest gift in the history of the university.

The alumni couple's gift is part of the university's Imagine Unlimited fundraising campaign, which has increased its initial goal of \$40 million to \$75 million.

The Kopchicks are providing funds to support the university's science and mathematics initiatives, which include a new science building, scholarships and endowed professorships.

John Kopchick is a professor of molecular biology at Ohio University and co-inventor of Somavert, a drug used to treat the growth hormone disorder acromegaly. Char Kopchick serves as the assistant dean of students at Ohio University.



Char and John Kopchick.

and biochemistry and a professor of molecular, cellular and developmental biology.

Research at his lab focuses on the ubiquitin system, one of the fundamental regulatory systems of eukaryotic cells.

## Lüscher wins Penn State faculty scholar medal

Bernhard Lüscher has been awarded the Faculty Scholar Medal in Life Sciences from Penn State.

Faculty Scholar Medals recognize excellence in scholarship and research. Lüscher, professor of biology, biochemistry and molecular biology, is among six faculty members to receive Faculty Scholar Medals.

Lüscher, whose research focuses on gamma-aminobutyric acid, or GABA, the principal inhibitory neurotransmitter in the brain, is being recognized for achievements in the life sciences and his role in building and developing the neurobiology program at Penn State.

He has served as co-director of the neuroscience graduation program and

as interim co-director of the Penn State Neuroscience Institute and currently serves as the founding director of the Center for Molecular Investigation of Neurological Disorders.

## UC Davis honors Callis for teaching, research

Judy Callis has received the University of California, Davis, Prize for Undergraduate Teaching and Scholarly Achievement.



CALLIS

This award recognizes a UC Davis faculty member for excellence in undergraduate teaching and research and carries a \$45,000 prize.

Callis is a professor and vice chair of the department of molecular and cellular biology in the College of Biological Sciences at UC Davis.

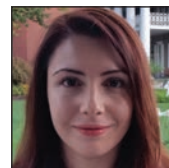
A plant biologist, Callis' research focuses on the ubiquitin protein degradation system in plants.

Callis is highly regarded by students and colleagues. Since joining the UC Davis faculty in 1989, she has taught a number of biochemistry courses, including BIS 103, one in a series of classes taken by most under-

graduates in the College of Biological Sciences.

## Ozber receives teaching award

Penn State graduate student Natali Ozber has won the Harold F. Martin Graduate Assistant Outstanding Teaching Award.



OZBER

Ozber has been teaching at Penn State for about a year and has been praised for her dedication and passion for teaching.

A doctoral candidate in plant biology, Ozber completed her undergraduate and master's degrees in engineering at Koç University in Istanbul.

Her research focuses on plant viruses and how these viruses move inside of plants, causing infection. She received a Penn State College of Agricultural Sciences Graduate Student Competitive Grant for her work.

In addition to her lessons in the classroom, Ozber has been involved with various outreach programs, including the Graduate Women in Science and the Upward Bound programs.

## Bostwick, Mineo and Boettiger win Beckman awards

Alicia Bostwick, Charlotte Mineo and Alistair Boettiger are among the 2018 Beckman award recipients.



**BOSTWICK**

Alicia Bostwick and Charlotte Mineo have been recognized as part of the Beckman Scholars Program, which honors

outstanding undergraduate students in chemistry, biochemistry and the biological sciences at select universities across the United States.

The 2018 Beckman Scholars

awards include more than \$1.5 million in funding for 58 undergraduate students at 12 universities.

A biology major from Hope College in Holland, Michigan, Alicia Bostwick is being honored for her project investigating mechanisms of regulation of mitochondrial DNA transcription.



**MINEO**

Charlotte Mineo, a biochemistry major from Union College in Schenectady, New York, is being honored for her research on changes in the catalytic activity of schizophyllum commune metacaspases in response to impaired

calcium binding.

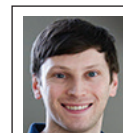
Stanford University researcher Alistair Boettiger has received the



**BOETTIGER**

Beckman Young Investigators Award for his project on highly multiplexed super-resolution imaging of chromatin structure. This

award provides support to early-career faculty members who demonstrate excellence in the chemical and life sciences.



Erik Chaulk (echaulk@asbmb.org) is a peer-review coordinator and digital publications web specialist at the ASBMB.

## Upcoming ASBMB events and deadlines

**OCT**

### National Breast Cancer Awareness Month

**Oct. 1:** Communications Fall Course begins

**Oct. 3–5:** Special Symposium: Science Outreach: Models, Methods and Measures

**Oct. 4–7:** Special Symposium: Transcriptional Regulation by RNA Polymerase II

**Oct. 11–13:** Society for Advancing Chicanos/Hispanics & Native Americans in Science (SACNAS) National Conference

**Oct. 15:** Special Symposium: The Many Faces of Kinases and Pseudokinases poster deadline

**Oct. 15:** ASBMB Accreditation deadline

**NOV**

### American Diabetes Month

**Nov. 1:** Special Symposium: The Many Faces of Kinases and Pseudokinases registration deadline

**Nov. 1:** Special symposia call for proposals for 2020 deadline

**Nov. 14:** Annual meeting abstract deadline

**Nov. 14–17:** Annual Biomedical Research Conference for Minority Students (ABRCMS)

**Nov. 27:** Annual meeting travel award application deadline

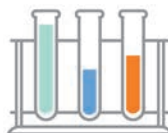
**Nov. 27:** Student chapters renewal deadline

**DEC**

**Dec. 1:** World AIDS Day

**Dec. 4:** ASBMB-Deuel Conference on Lipids early registration deadline

**Dec. 9–12:** Special Symposium The Many Faces of Kinases and Pseudokinases





# Chapter leader finds his niche

By Elizabeth Stivison

From his days poring over “1,000 Facts on Science and Technology,” one of a series of children’s books an uncle sent him, to recently starting a Ph.D. program, Jacob Crosser always has let his interests guide him.

As an undergraduate, Crosser was active in the Purdue University American Society for Biochemistry and Molecular Biology Student Chapter, first as a member and then as outreach chair and eventually as president.

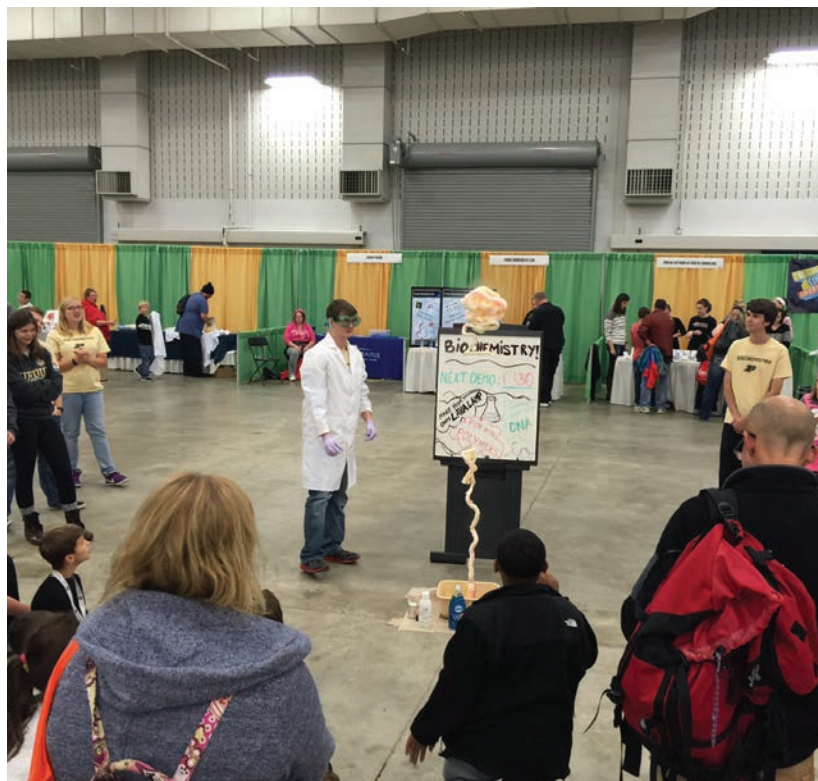


CROSSER

Crosser joined the chapter to get an idea of what working as a biochemistry researcher might be like; he ended up staying active because of its outreach activities. The chapter organized volunteer opportunities, including science demonstrations in local elementary school classrooms, and participated in the Purdue Spring Fest, a day when the university invites people from the surrounding community of West Lafayette, Indiana, to campus to participate in science demonstrations and experiments. Crosser, who grew up in the town, said he was inspired by these events.

“Two years ago, I had done an estimate of how many active participants came by our booth, and it was something on the order of 700 people over two days,” he said.

He noticed that several children came back to the ASBMB booth year after year, looking forward to making slime out of borax and glue or whatever the science demonstration was for that year. Outreach kept Crosser involved, he said. The chapter helped him figure out what he wanted to do



COURTESY OF JACOB CROSSER

Jacob Crosser does an elephant toothpaste demonstration to introduce chemical reactions and catalysis during Celebrate Science Indiana, an outreach event, in fall 2015 at the Indiana State Fairgrounds.

in his life, so he wanted to help others figure out their potential career paths by exposing them to science while they were young.

“To help someone else figure that out,” he said, “that’s a good feeling.”

The figuring out wasn’t straightforward for Crosser, who started college hoping to study engineering before he realized he wanted to solve the more complex problems that appear in biological systems. After this realization, he discovered biochemistry. That wasn’t quite the answer either, however; Crosser found he really missed doing the math problems he’d enjoyed in school when he was younger. He returned to physics and math and

took an extra year to complete minors in both subjects.

Crosser now has found a niche for himself pursuing a Ph.D. in applied mathematics with a focus in computational biology at the State University of New York at Stony Brook.

“I intend to center my career around the study of the complex biological systems I’ve come to love,” he said, “through the lens of mathematics that I’ve found very natural.”



Elizabeth Stivison (elizabeth.stivison@gmail.com) is a Ph.D. student at Columbia University studying mechanisms of DNA repair.

# Shadow gene gives otters, manatees susceptibility to banned bug-killer

By John Arnst

If you've ever dreamed of being born anew as a sea otter or other marine mammal, you may be in for a neurotoxic surprise.

After the forerunners of modern whales, dolphins and manatees independently turned their backs on terrestrial lives tens of millions of years ago, their descendants soon lost the function of PON1, a gene whose encoded enzyme, paraoxonase, reduces oxidative damage to lipid particles in mammals' bloodstreams. In losing the function of that enzyme, whose gene still lingers, wraithlike, in the animals' genetic code, a vast number of marine mammals also lost its serendipitous secondary ability to break down a neurotoxic metabolite of the pesticide chlorpyrifos.

More than 50 years after Dow Chemical Company introduced chlorpyrifos to the market, it continues to be one of the most widely used insecticides in the United States, although it was banned from residential use in 2000. That ban came on the heels of highly publicized cases of chlorpyrifos poisoning in the '90s that left a West Virginia child paralyzed and a Texas man in a vegetative state.

The 9th Circuit Court of Appeals in Seattle in August ordered the Environmental Protection Agency to a ban the pesticide from agricul-



COURTESY OF ROBERT ENGBERG/ FLICKR

Experts estimate that manatees' mammalian ancestors began adapting to aquatic life around 60 million years ago, whereas the forebears that became both dolphins and whales returned to the ocean nearly 50 million years ago.

tural use within 60 days. The court's decision, a rebuke to the agency after former EPA chief Scott Pruitt denied an environmental group's petition to ban the use of chlorpyrifos on food crops, coincidentally was made public less than an hour after a study on the marine mammals' loss of PON1 function was published in the journal *Science*.

Clement Furlong, a biochemist at the University of Washington and co-author on the paper, applauded the court's action.

"The decision to discontinue the use of chlorpyrifos was based on very solid scientific evidence from many different laboratories, and the (initial)

decision to discontinue the ban was certainly not," Furlong said. "It's to the benefit of sensitive humans, particularly the very young, and animals that have no protection, including the marine mammals, birds, fish, other animals that are missing the paraoxonase function."

In addition to sireni-ans, the taxonomic order containing manatees and the extinct Steller's sea cow, and cetaceans, the order containing dolphins, whales and porpoises, the researchers found that North American beavers as well as pinnipeds such as the Weddell seal, Hawaiian monk seal and elephant seal, lost function of the PON1 gene.

Senior author Nathan Clark believes this may have been an adaptation to the oxidative stresses caused by prolonged diving.

"If we pump up our bodies with tons of oxygen, submerge, deplete all that oxygen and then come back and rapidly reperfuse our bodies with oxygen, proteins and DNA and lipids would just be oxidized like crazy, and that would cause a lot of damage, and we would not survive very long," Clark said.

To deal with the stress, marine mammals have evolved to pump out high amounts of the antioxidants catalase and superoxide dismutase.

"So one thought is that if their



COURTESY OF NEIL HOOTING/FLICKR

Sea otters are among the marine mammals that Nathan Clark and colleagues found to have lost production of an antioxidant enzyme that also breaks down organophosphate pesticides.

upfront defenses for free radical-producing things that would cause oxidative damages are so strong, then maybe PON1 is no longer necessary,” Clark said.

While it is unclear when PON1 evolved, the gene is believed to be ubiquitous among land mammals due to the role it plays in preventing the buildup of arterial plaques. Fish and birds lack PON1, and their populations consequently have been devastated by chlorpyrifos, whose metabolite chlorpyrifos oxon disrupts acetylcholine activity at nerve terminals.

Clark and his colleagues discovered that marine mammals had lost PON1’s functionality by scouring the protein-coding sequences of more than 17,000 genes in 60 species for signs that genes had become non-functional pseudogenes through the addition of early stop codons and frameshift mutations. They tabulated the results in a matrix and used phylogenetic software to score each gene on how quickly it was lost in a species.

“Physiologists and marine biologists have known for decades that dolphins and whales have no sense

of smell, so we thought we’d see a lot of chemosensation genes like olfactory receptors, and we did,” said Clark, a comparative genomicist at the University of Pittsburgh. “Some of our expectations didn’t come out, but then this gene Paraoxonase 1 was sitting right on top of the list.”

Margaret Hunter, a research geneticist at the U.S. Geological Survey’s Wetland and Aquatic Research Center in Gainesville, Florida, who was not an author on the study, is also intrigued at the scope of PON1’s loss of function.

“I thought it was quite surprising, and a pretty interesting find, especially because of the breadth of the mutation in the different species,” she said. “And the evolutionary divergence of all of these animals is extremely broad too, all the way to sirenians, which originated in Africa and are related to elephants and hyraxes.”

Hunter, who specializes in manatee population genetics, said the gene’s loss of function might be less heavily tied to diving, given PON1’s loss in manatees and their preference for coastal waters.

“We’ll see them sometimes at 20 feet, but they really prefer shallower waters,” she said. “They do hold their breath, so that could be related to it, but it is pretty interesting because they’re not diving or holding their breath for a length that we see in some other cetaceans or pinnipeds.”

Clark and his colleagues plan to examine a greater number of marine mammals in their next analysis and begin collaborations with ecologists in Florida to monitor manatees for the presence of chlorpyrifos, which, despite the court-ordered ban, likely will remain in agricultural runoff in the U.S. for the near future.

“Just because you ban a pesticide doesn’t mean it’s removed from the environment very rapidly,” Hunter said. “We still need to monitor populations for these pesticides moving forward.”



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

# 2018 honor society inductees

The American Society for Biochemistry and Molecular Biology Honor Society (Chi Omega Lambda) recognizes exceptional undergraduate juniors and seniors pursuing degrees in the molecular life sciences at colleges or universities with ASBMB Student Chapters. Students are recognized for their scholarly achievement, research accomplishments and outreach activities. Information on nominating a student is at [asbmb.org/education/honorsociety](http://asbmb.org/education/honorsociety).



ASBMB PHOTO

American Society for Biochemistry and Molecular Biology Honor Society inductees pose for a group photo in April during the ASBMB 2018 Annual Meeting in San Diego.

**Benjamin Anderson**, Purdue University  
**Will Barr**, Wesleyan University  
**Shannyn Bird**, University of Nebraska–Lincoln  
**Emily Bliss**, Otterbein University  
**Kyle Boulanger**, Grandview University  
**Kelly Budge**, Goucher College  
**Michael Chen**, University of Massachusetts Amherst  
**Stephanie Choi**, University of Massachusetts Amherst  
**Jacob Crosser**, Purdue University  
**Jocelyn Daubendiek**, University of Nebraska–Lincoln  
**Lauren DeLong**, Salisbury University  
**Amanda Duplan**, Grandview University  
**Grace Ferri**, Boston University  
**Corey Gallen**, Saint Leo University  
**Nina Marie Garcia**, University of San Diego  
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**Thomas Kania**, University of Massachusetts Amherst  
**Emily Kessler**, Wesleyan University  
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**Auston Larratta**, Saint Leo University  
**Cindy Le**, University of Massachusetts Amherst

**Christine Little**, Wesleyan University  
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**Victoria Mak**, Saint Louis University  
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**Alexa Strauss**, Wesleyan University  
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**Danyal Tahseen**, Trinity University  
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**Sirena Tran**, University of San Diego  
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**Derek Wei**, Otterbein University  
**Kathleen Wendover**, Hendrix College  
**Kellie Wong**, Minnesota State University, Mankato

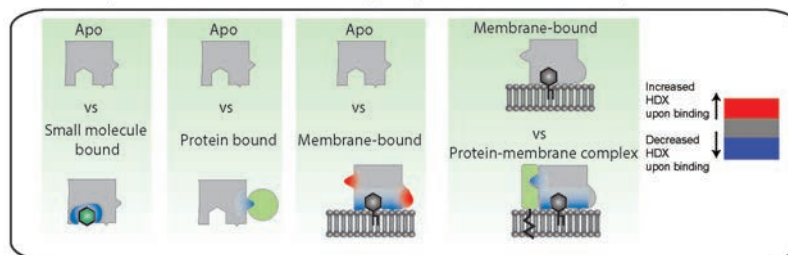
# Studying protein–lipid interactions

By John Burke

**A**lmost every signaling event in cells has a component that includes the recruitment of signaling proteins to lipid membranes. The proper recruitment, assembly and activation of these enzymes is integral to how cells live, divide and move. In recent years, we have seen a sea change in our ability to study lipid signaling systems, primarily through major advancements in cryo-electron microscopy and X-ray crystallography. This allows for molecular analysis of how integral membrane proteins are regulated and provides insight into novel strategies to treat myriad human diseases including cancer and metabolic syndrome.

One remaining challenge in characterizing lipid signaling at the molecular level is the study of peripheral membrane proteins and how they interact with lipids. These proteins (enzymes) reside in a cytosolic location in the absence of signals and, upon activation by various stimuli, are recruited to specific membrane surfaces to carry out their function. Misregulation of how lipid signaling enzymes are recruited to membranes is implicated directly in cancer and immune deficiencies. Researchers have used a variety of techniques to study this problem, including nuclear magnetic resonance, molecular dynamic simulations and other biophysical approaches (surface plasmon resonance, protein-lipid Förster resonance energy transfer, single molecular total internal reflection fluorescence microscopy and so on). All these approaches have distinct advantages and disadvantages, but together they provide unique insight into how proteins interact with and are recruited to specific membrane surfaces.

HDX-MS to probe conformational changes upon small molecules/proteins/membranes



COURTESY OF JOHN BURKE

Hydrogen–deuterium exchange is a useful technique to probe conformational changes that occur upon small molecule, protein, and membrane interactions. Colors in the figure represent regions that undergo conformational changes in the bound state. Experiments require a comparison to an apo unbound state, with all conformational changes representing the sum total of both direct and allosteric conformational changes that occur upon binding.

A new tool used to study how proteins interact with lipid membranes is hydrogen–deuterium exchange mass spectrometry, or HDX-MS. This approach is conceptually simple, as hydrogens, specifically amide hydrogens, within proteins exchange with solvent, and this exchange is dependent primarily on the stability of protein secondary structure. This occurs because amide hydrogens are protected from exchange with solvent by their participation in hydrogen bonds in alpha helices and beta sheets. When a protein is shifted into a different chemical environment, in this case bound to a membrane, any regions with differences in protein conformation will experience a change in amide exchange. The exchange of individual amides is localized through digesting the protein and measuring the mass of fragments using a mass spectrometer. This can be compared across different conditions (apo, membrane bound, bound to specific lipids, disease-linked mutants and so on), revealing unique conformational changes for each.

The technique measures exchange rates throughout the entire protein,

and conformational changes due to either direct membrane interactions or allosteric conformational changes will be observed. This is particularly useful in the study of large, complicated multidomain signaling complexes with experiments on the phosphoinositide 3-kinases revealing how previously undescribed disease-causing mutations mediate altered lipid signaling through unexpected allosteric conformational changes.

Due to great advances in the last decade in the instrumentation and software for HDX-MS experiments, studies examining protein complexes larger than 500 kDa on membrane surfaces are now commonplace. This provides the larger lipid signaling community with novel opportunities to more carefully define how peripheral membrane signaling complexes are regulated.



John Burke (jeburke@uvic.ca) is an assistant professor in the department of biochemistry and microbiology at the University of Victoria and winner of the 2018 ASBMB Shaw Young Investigator Award.

## Scientists sweep cellular neighborhoods where Zika hides out

Interrogating the virus' molecular associates yields clues about where to apply pressure

By Laurel Oldach

Most people infected with Zika never show symptoms. But the virus sometimes causes severe disability — from microcephaly in babies to weakness or partial paralysis in adults — and there is no treatment. In a paper in the journal **Molecular & Cellular Proteomics**, researchers report a comprehensive study of how the virus interacts with host cells. One of their findings gives insight into how Zika escapes immune signaling and proliferates inside the body.

Like most viruses, Zika accomplishes a lot with a few tools. It has just one protein coding gene, which produces a single polypeptide that's cleaved into 10 smaller proteins — a number dwarfed by the estimated 20,000 protein-coding genes in a human cell. Nevertheless, Zika can take over the vastly more complex human cell, repurposing it into a virus factory. Brian Raught, a researcher at the University of Toronto, said he found that process fascinating.

“With just these 10 proteins, this crazy virus turns your cells into zombies that do its bidding,” Raught said. “I always found that mind-blowing.”



COURTESY OF DAVID GOODSSELL/WIKIMEDIA COMMONS

This drawing shows the outside of one Zika virus particle and a cross-section through another as it interacts with a cell. The two main proteins of the viral envelope, the envelope and membrane proteins, are red and purple, respectively. The lipid membrane of the envelope is light lavender. The capsid proteins, in orange, interact with the RNA genome, in yellow, at the center of the virus. The cell-surface receptor proteins are green, the cytoskeleton is blue and blood plasma proteins are gold.

Researchers in Raught's lab, led by postdoctoral fellow Etienne Coyaud, wanted to find out how the handful of Zika proteins were able to hijack the host cell. They knew that the feat must depend on physical interactions between viral proteins and proteins native to the cell — but which ones?

Because of the increasing evidence linking Zika infections in expectant mothers to microcephaly in their children, Raught said, “We thought it better to leave the actual virus work to the experts.”

Instead of using infectious material, the team made 10 strains of human cells, each expressing one of Zika's 10 proteins. By adding a small epitope tag to each viral protein, they were able to retrieve the viral proteins using an antibody that binds to this tag. The host proteins that stuck tightly to each viral protein came along for the ride; the researchers used mass spectrometry to identify those human proteins.

But there was a drawback to using this approach. What if proteins from the human cell were interacting with Zika proteins but separating from them before being extracted? To identify proteins that are close to but not inseparably intertwined with each viral protein, the team used a second technique called proximity labeling. In essence, they rigged each viral protein with an enzyme that would attach a sticky biotin tag onto anything that

CONTINUED ON PAGE 14

# Spectroscopic studies scrutinize links between liver disease and mitochondria

By Laurel Oldach

Nonalcoholic fatty liver disease, or NAFLD, is a metabolic disease that affects up to 40 percent of American adults. Though the condition produces no noticeable symptoms, one out of every five patients will go on to develop a more serious condition called NASH (short for nonalcoholic steatohepatitis).

The inflammation NASH causes can result in scarring, cancer and even organ failure. With those consequences in mind, researchers are working to understand the progression of nonalcoholic fatty liver to NASH.

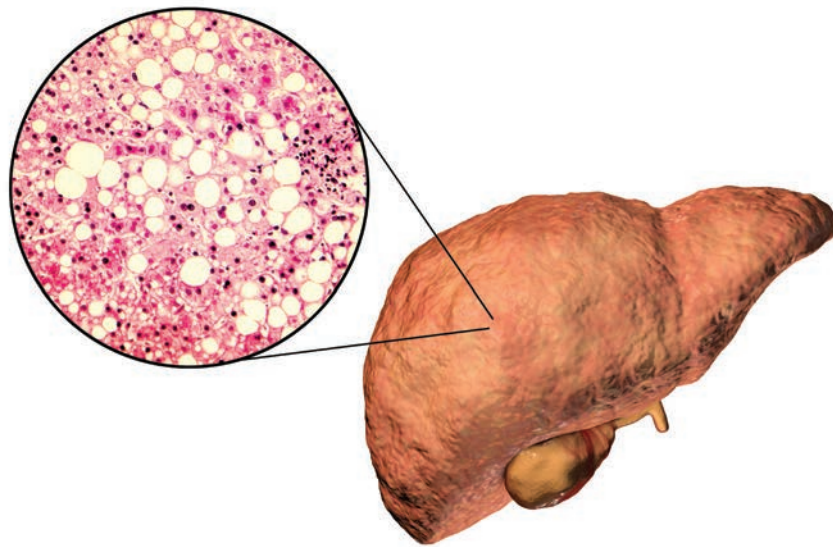
It has been clear for some time that mitochondrial dysfunction has something to do with the onset and progression of nonalcoholic fatty liver. Two recent studies, described below, offer additional information on this front.

The first study illuminates how mitochondrial energy production stutters and fails as fatty liver disease progresses. The second study describes how changes to the liver in the course of disease affect the organ's use of incoming nutrients.

## Overworked cells

Kang-Yu Peng and a team of researchers from Australia and the Netherlands used lipidomics to analyze liver biopsies from obese patients with normal livers, fatty liver disease and full-blown NASH. Their study was published in the **Journal of Lipid Research**.

Some of the changes the research team observed were predictable. For



In fatty liver disease, hepatocytes fill with triglyceride vesicles. At this stage, the condition is reversible, but it can progress to nonalcoholic steatohepatitis, or NASH, which involves irreversible tissue damage.

example, they saw an increase in triglycerides and an increase in acylcarnitine, a molecule that shuttles fatty acids to liver mitochondria so that the organelles can use the lipids in cellular respiration, in the patients with fatty liver disease and NASH. But the team also found significant changes in several lipid types without known connections to fatty liver.

They zeroed in on two lipids that participate in mitochondrial respiration: cardiolipin and ubiquinone. The researchers found that both lipids are elevated in the early stages of fatty liver and stay high as the disease progresses. The researchers think the level of both lipids, which are involved in the electron transport chain, may increase because mitochondria are working harder to deal with the excess energy.

This finding seems to support the notion that higher mitochondrial respiration compensates for having more

triglycerides early in fatty liver disease. However, because of the increase in reactive oxygen byproducts, raising mitochondrial respiration also can be risky. For example, cardiolipin is highly susceptible to a chemical reaction called peroxidation, which can cause mitochondrial dysfunction.

The study also reported that the fatty liver biopsies had higher than normal accumulation of phosphatidylcholine and several types of ceramide. The significance of these changes isn't yet clear.

More detailed study will be needed to determine whether, as the authors hypothesize, mitochondrial overwork contributes causally to mitochondrial failure and liver disease progression.

## Building lipids, not glucose

One of the liver's most important roles is to regulate the level of glucose

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## CONTINUED FROM PAGE 12

came close enough.

Proximity labeling is especially useful for detecting interactions with proteins embedded in cell membranes; those molecules are notoriously difficult to isolate.

“This is a really big asset of a proximity-labeling approach compared to traditional approaches,” Coyaud said.

Because Zika, like many viruses, enters the cell in a membrane-bound envelope and reorganizes many of its host’s membrane-bound organelles in the course of infection, its interactions with membrane proteins might be key to understanding the viral life cycle.

When the researchers combined the results of the two approaches, they could piece together a detailed picture of what Raught calls the “neighborhood” within the cell where each Zika protein takes up residence.

For example, the researchers found that one Zika protein, called NS2A, interacted with many human neigh-

bors in a host organelle called the peroxisome. Peroxisomes are involved in innate immune signaling, a type of early-warning alarm that goes off when viruses are present. Proteins from dengue and West Nile viruses, which are in the same family as Zika, have been shown to associate with peroxisomes and disrupt antiviral signaling.

Using fluorescence microscopy, Raught said, “we could see that this one protein (NS2A) only localized to peroxisomes.”

Because NS2A is thought to be involved in replication of the virus’ genome and construction of its protein shell, its preference for the peroxisome led the team to investigate whether the peroxisome might be involved in replication. The team recruited some virologists with access to a biocontainment facility who could test whether infectious Zika virus can proliferate in cells without peroxisomes. Turns out, in those cells, the virus proliferates more slowly.

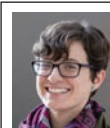
“There really does appear to be an

important link between having a peroxisome and being able to efficiently make Zika virus,” Raught said. “We don’t know exactly why that is.” But the host-virus protein interaction data showed them where to look.

The data set Raught’s lab has collected is full of such clues. Slightly more than half of the human proteins the researchers found interacting with viral proteins are known to be involved in other viral infections, while the rest had not yet been described.

According to Raught, “A better understanding of these processes will allow us to identify specific vulnerabilities in the virus life cycle, where antiviral drugs can be targeted.”

DOI: 10.1074/mcp.TIR118.000800



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## CONTINUED FROM PAGE 13

in the blood, supplying energy to other tissues. When glucose is low, liver cells make more available by breaking down glycogen or converting other molecules to glucose. When glucose is plentiful, cells in the liver convert the sugar to other types of molecules or break it down and store the energy as ATP.

In a paper in the **Journal of Lipid Research**, Eunsook Jin and colleagues at the University of Texas Southwestern Medical Center studied hepatocyte metabolism in obese individuals with normal or fatty livers.

The researchers used isotopically labeled glycerol, a versatile precursor of many organic molecules that can be made by breaking down glucose, to track metabolism. After a per-

son absorbs a quantity of glycerol while fasting, their liver cells have a choice to make about the resource. Do they convert the molecule into a quick hit of glucose for energy; use it for longer-term energy storage as a triglyceride, which can be broken back down into glycerol later; or build nucleotides and amino acids? By analyzing patients’ plasma over time, the researchers could track how cells used the labeled molecules.

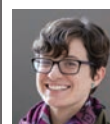
Patients with fatty livers tended to use glycerol to generate triglycerides more quickly than patients with normal livers and were slower to use it for making new glucose. There was no difference between groups in the pentose phosphate pathway that contributes to building other types of molecules.

The authors compared the liver

cells’ preference for making more triglycerides, rather than using a new energy source right away, to a phenomenon observed in diabetic patients called metabolic inflexibility. That is, the fatty liver cells were slower to change from using stored carbohydrates to making new carbohydrates than the healthy liver cells. How the changes in metabolism of an incoming energy source may affect the progression of the disease remains to be seen.

DOI: 10.1194/jlr.M085613 (Peng)

DOI: 10.1194/jlr.M086405 (Jin)



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# Scientists fill in a piece of the copper transport puzzle

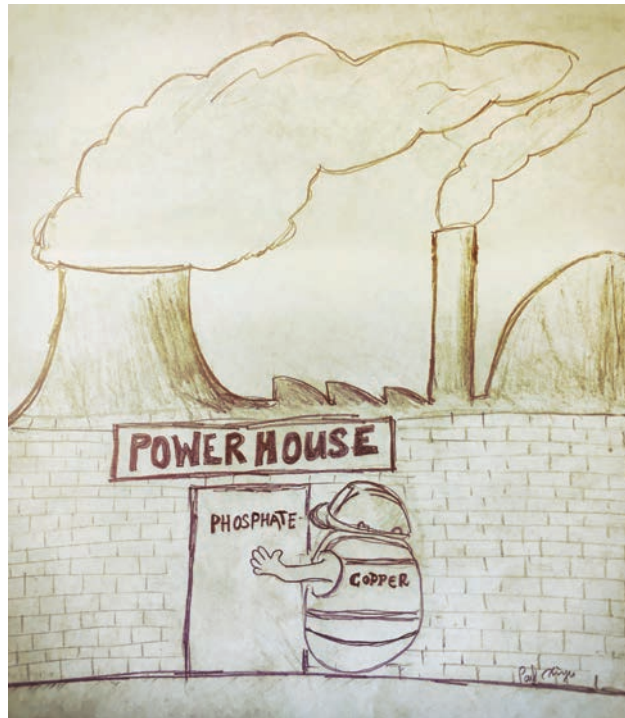
By Sasha Mushegian

Researchers have identified the protein that carries copper into mitochondria, where copper is required for the functioning of the cell's energy conversion machinery. The discovery, published in the **Journal of Biological Chemistry**, fills in a piece of the puzzle of how copper is distributed and used in the cell.

Humans acquire copper in trace amounts from food. Despite its low levels, copper is essential for the functioning of numerous important enzymes, such as some of those involved in synthesizing collagen and neurotransmitters. Notably, copper is required for building cytochrome c oxidase, known as COX, a large protein complex in mitochondria that forms the last step of the electron transport chain, which harvests energy for the production of ATP, the energy currency of the cell.

Paul Cobine of Auburn University and his collaborator Scot Leary at the University of Saskatchewan have been working for more than 10 years on understanding how copper is used to assemble COX. One basic question was, how does copper get across the membranes in mitochondria?

"To get (copper) to the correct address (in the cell) without interfering with other proteins, or disrupting other targets that have a high chance of binding copper, is a herculean delivery effort," Cobine said. "This is akin to finding your way to an exit in



COURTESY OF PAUL COBINE AND XINYU ZHU/AUBURN UNIVERSITY

Mitochondria, the powerhouses of the cell, need copper to produce energy. Copper enters the mitochondria through a previously identified phosphate transporter.

a crowded bar without touching the other people or getting redirected. Then after finding the exit, you must make sure you go through the right door."

The researchers used multiple lines of evidence to arrive at an answer: Copper is transported within mitochondria by a protein called SLC25A3. This discovery was surprising because SLC25A3 was already known to transport phosphate, a negatively charged ion, whereas copper ions carry a positive charge. The researchers speculate that the copper ions may need to bind to another partner, forming a negatively charged complex, for SLC25A3 to be able to transport it. The next question they

want to address is how the transporter distinguishes between its different types of cargo.

Previously known mutations in the gene encoding SLC25A3 are responsible for poorly understood genetic disorders involving dysfunctional heart and muscle fibers, leading to enlarged hearts and low muscle tone. As these tissues require large amounts of energy, it seems plausible that these patients' symptoms could be related to insufficient copper transport in mitochondria.

These symptoms "all sound like they could be related to both ATP production and cytochrome c oxidase," Cobine said.

With the discovery of the copper transport pathway within mitochondria, the health effects of copper can be studied in more detail because researchers will be able to distinguish the effects of copper on COX from the other pathways it's involved in.

"If we don't deal with copper properly throughout our life, what are the metabolic diseases that come up?" Cobine asks. "Now we have the ability to look at what happens when you lose mitochondrial copper at different (developmental) stages."

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# What bacteria can teach us about combating atrazine contamination

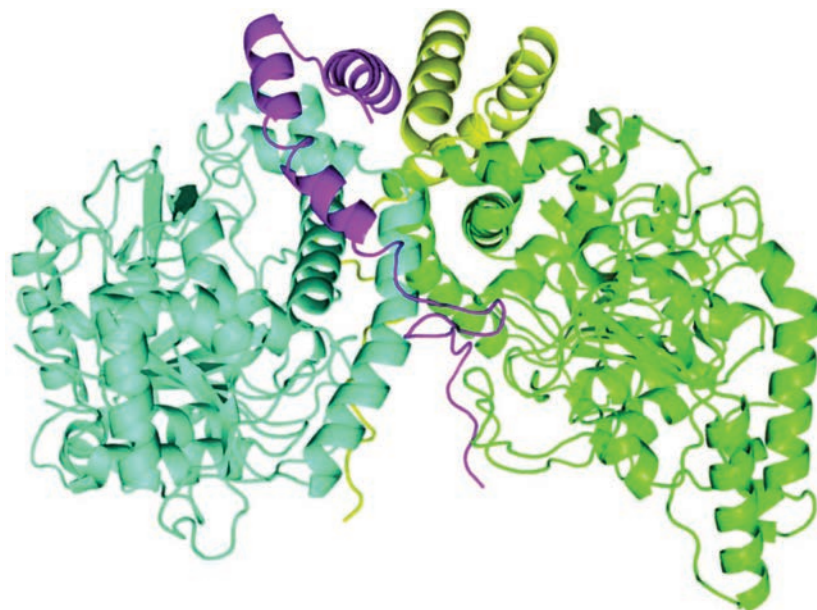
By *Sasha Mushegian*

Atrazine, a controversial herbicide introduced to agriculture in the 1950s, has been banned in the European Union but is used widely in the United States and Australia. In the decades that atrazine has been accumulating in agricultural fields, some bacteria in those soils have evolved the ability to take advantage of this nitrogen-rich compound, metabolizing it and using it to grow.

Researchers at the Commonwealth Scientific and Industrial Research Organization of Australia, or CSIRO, are interested in harnessing bacterial ability to degrade atrazine in order to remediate atrazine-polluted environments. In a research paper published in the **Journal of Biological Chemistry**, a team from CSIRO and the Australian National University describe previously unknown proteins involved in atrazine degradation — and the insights these can give us into how bacteria evolve new abilities in response to chemicals synthesized by humans.

“Bacteria are really good at evolving to be able to exploit new nutrient sources, and they do this by adapting existing cellular machinery for novel functions,” said Colin Scott, leader of the Biocatalysis and Synthetic Biology Team at CSIRO, who oversaw the work.

Turning atrazine into a usable nitrogen source is a multistep process for bacteria, involving multiple enzymes. Before widespread atrazine pollution, each of these enzymes served different functions in bacterial cells. In atrazine-degrading bacteria, the genes encoding these enzymes are grouped on a section of DNA called a plasmid, which can be passed easily between bacteria, giving them a



COURTESY OF COLIN SCOTT/CSIRO

A newly described protein complex carries out a step in bacterial breakdown of the herbicide atrazine. The two AtzE molecules are in blue and green, and the two AtzG molecules are in yellow and magenta.

ready-made adaptation.

“Within 10 years from its original discovery (in the 1990s), genes from this pathway were found (in bacteria) on pretty much every continent except Antarctica,” Scott said.

In other words, as atrazine use spread across the globe, so did the bacterial ability to metabolize it.

Whereas the enzymes involved in several of these steps have been described thoroughly, the structure of one of them, called AztE, was still unknown. AztE is crucial for converting cyanuric acid — an intermediate step in the atrazine degradation process — into ammonia.

Lygie Esquirol, a Ph.D. student in Scott’s lab, led the effort to purify this protein. When the team examined the protein, it found something surprising: another very small protein,

the existence of which had not been predicted from the bacterium’s genome sequence, forming a complex with AztE. This new protein, which the team named AztG, seemed to be necessary to stabilize the structure of AztE.

Together, the structure of AztE and AztG resembled a different bacterial protein complex — the transamidosome, which helps make bacterial transfer RNA. Thus, it appeared that proteins involved in the basic functions of the bacterial cell were retooled for the new atrazine pathway.

The transamidosome “is absolutely essential for bacteria in the way that they make their tRNAs,” Scott said. “It was somewhat surprising that our protein, which is involved in pesticide catabolism, was (similar) to this protein complex that’s used in central

metabolism.”

The promise of synthetic biology is that humans can combine genes encoding different functions in an organism in creative ways. However, although it’s relatively simple to insert genes into new contexts, a newly constructed pathway is not guaranteed to work as intended. It’s therefore instructive to examine pathways like the atrazine degradation pathway, in which bacteria have successfully repurposed a series of unrelated genes to do something new.

“This (pathway) has come from other places and been cobbled together, but there must be some underlying rules and constraints

about how to do that,” Scott said. “We don’t know at the moment what the design rules are for complex pathways in terms of their genetic architecture. What we want to do is to use the cyanuric acid pathway as a model to understand some of those design principles.”

Atrazine-degrading bacteria convert atrazine into nitrogenous compounds that plants potentially could use as fertilizer, but this poses its own problems: Nitrogen runoff into water causes algal blooms and animal die-offs. Thus, a key problem that CSIRO researchers are trying to solve is how to contain the reaction so that it occurs only where and how

humans need it. One approach is to use targeted application of enzymes purified from these bacteria rather than the bacteria themselves.

“As a technology, we’ve gone out to the field and proven that (the enzymes) can work,” Scott said. “The next step is working with industry to try to implement some of these solutions.”

DOI: 10.1074/jbc.RA118.001996



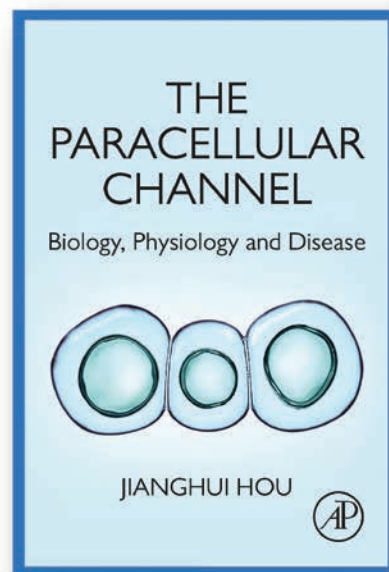
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## BOOKS BY ASBMB MEMBERS

### **The Paracellular Channel: Biology, Physiology and Disease**

By Jianghui Hou, associate professor of medicine, Washington University

The Paracellular Channel: Biology, Physiology and Disease offers a cohesive and unifying picture of the critical functions of paracellular channels (tight junctions) in different tissues. This new class of ion channel utilizes a completely different mechanism to create ion passage pathways across the cell membrane. This volume outlines common principles that govern the organization and regulation of these diverse cellular structures, describes the methodology of study and highlights the pathophysiologic consequence of abnormal structures and functions of the paracellular channels in human diseases.



#### **Are you an ASBMB member who has published a book in 2018?**

If so, we’d like to feature your work in an upcoming issue of ASBMB Today. Please email a synopsis (<100 words), an image of the book’s cover and your headshot to [asbmbtoday@asbmb.org](mailto:asbmbtoday@asbmb.org).

# Award winners pen essays for JBC

The American Society for Biochemistry and Molecular Biology's annual awards honor scientific contributions across multiple dimensions: teaching, research in several sub-disciplines, groundbreaking discoveries and whole lifetimes of work. To celebrate the multifaceted careers of the 2018 ASBMB award winners, the editors of the Journal of Biological Chemistry invited them to submit articles on topics of their choosing, from reflecting on their paths through science to taking the bird's-eye view of research in their fields.

Here we share excerpts for these articles. To explore these topics in more depth, go to "ASBMB award winners in the spotlight" on the Virtual Issues page at [jbc.org](http://jbc.org).

## What I got wrong about shelterin

By Titia de Lange

### Bert and Natalie Vallee Award in Biomedical Science



DE LANGE

The ASBMB award honors our work on shelterin, a protein complex that helps cells distinguish the chromosome ends from sites of DNA damage. Shelterin protects telomeres from all aspects of the DNA damage response, including ATM and ATR serine/threonine kinase signaling and several forms of double-strand break repair. Today, this six-subunit protein complex could easily be identified in one single proteomics step. But it took us more than 15 years to piece together the entire shelterin complex, one protein at a time. Although we did a lot of things right, here I tell the story of shelterin's discovery with an emphasis on the things that I got wrong along the way.

## Lessons from my undergraduate research students

By Paul A. Craig

### ASBMB Award for Exemplary Contributions to Education



CRAIG

From very early on, my personal/professional life has been shaped by teachers in many different settings. Teaching and learning form a two-way street. In the process of teaching undergraduate students, particularly in the research lab, I have learned some profound lessons about the importance of listening to them, challenging them, giving them autonomy, and allowing them to enjoy success and to risk failure. I am now working with a team of faculty members to implement these lessons in a course-based undergraduate research experience in the biochemistry teaching laboratory. Our goal is to seek answers to the question "How do students become scientists?" and to implement those answers with our future students.

## Mechanism of premature translation termination on a sense codon

By Andrei Korostelev

### Earl and Thressa Stadtman Young Scholar Award



KOROSTELEV

Accurate translation termination by release factors is critical for the integrity of cellular proteomes. Premature termination on sense codons, for example, results in truncated proteins, whose accumulation could be detrimental to the cell. Nevertheless, some sense codons are prone to triggering premature termination, but the structural basis for this is unclear. To investigate premature termination, we determined a cryo-EM structure of the Escherichia coli 70S ribosome bound with RF1 in response to a UAU sense codon. The structure reveals that RF1 recognizes a UAU codon similarly to a UAG stop codon, suggesting that sense codons induce premature termination because they structurally mimic a stop codon.

## My winding trail while fulfilling my love for science and family

By Kim Orth

### ASBMB-Merck Award



ORTH

My winding path toward a career in science was awkward, like an adolescent finding an identity. It did not follow a classic course; it had many interruptions, complications and challenges. It also involved a bit of luck and extremely supportive colleagues, mentors and family, including my husband, children and in-laws. I was inspired to tell my story here because I met a young woman interviewing in 2018 for graduate school who is growing up with the same complicated family expectations, social challenges, love for science and desire to be a scientist as I had four decades ago. Her future is uncertain, because her chosen academic path is not encouraged by those around her. We, as a society, must find ways to

encourage, promote, enable, and give strength to those who want to follow their dreams, despite facing many challenges in their lives. Here are some things I learned on my career path that I hope might be helpful for others.

## Visual cycle proteins: structure, function and roles in human retinal disease

By Andrew Tsin

### Ruth Kirschstein Diversity in Science Award



TSIN

Genetic retinal disorders such as retinitis pigmentosa, Leber's congenital amaurosis, and Stargardt's disease are linked to structural changes in visual cycle proteins. Moreover, recent reports suggest that visual cycle proteins may also play a role in the development of diabetic retinopathy.

Basic science has laid the groundwork

for finding a cure for many of these blindness-causing afflictions, but much work remains. Some translational research projects have advanced to the clinical trial stage, while many others are still in progress, and more are at the ideas stage and remain yet to be tested. Progress in our understanding of the visual cycle will inform intervention strategies to preserve human vision and prevent blindness.

## The ribosome: a hot spot for the identification of new types of protein methyltransferases

By Steven G. Clarke

### William C. Rose Award



CLARKE

There are presently few systems where the full physiological role of protein methylation is understood. The question then arises of how useful is it to discover new types of protein methylation reactions when we do not fully understand the systems already described. Do such discovery efforts represent mere cataloging of modification enzymes and their substrates? The fact that the proteins are methylated by the products of genes that have often been conserved throughout the evolutionary development of organisms suggests that a full understanding of the biology of an organism needs to include an appreciation of these modifications and their functions. As we learn more from each new protein methylation system described, the range of functional roles also increases, and we are provided new targets for therapeutic intervention into human diseases.



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## From the journals

By *Nathalie Gerassimov, Dawn Hayward & Sasha Mushegian*

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

### Restoring balance in cystic fibrosis

Cystic fibrosis sometimes is characterized as a disease of protease-anti-protease imbalance. Apparao Kummerapuruguru and colleagues at Virginia Commonwealth University examined whether using heparin to inhibit the protease neutrophil elastase, or NE, could restore this balance. They found that heparins inhibited NE in the presence of dornase, a drug used in cystic fibrosis patients to reduce sputum viscosity. Further studies suggested that heparin bound NE more potently than other NE ligands, suggesting that it can be developed further as an antiprotease therapy. The results were published in the **Journal of Biological Chemistry**.  
DOI: 10.1074/jbc.RA118.002644

### Adventures in influenza

Perhaps inspired by the annual 3 million to 5 million cases of severe influenza worldwide, the Guinness World Record organization is advertising for individuals or organizations to attempt a record for the most people getting a flu awareness lesson at once. Meanwhile, a smaller group of people is making a more focused attempt to learn about lots of flu proteins. Andrea C. Becker at the University of Freiburg and her colleagues in Germany and Switzerland investigated the effect of the flu-causing virus influenza A on three lung-derived cell lines and published their results in the journal **Molecular**

### & Cellular Proteomics.

The study quantified virus-induced changes in protein levels and found that a majority of the changes are cell-line specific. More specifically, they quantified the protein levels of 70 percent of the roughly 7,000 proteins they could detect using a mass spectrometry-based isotope labeling approach known as SILAC. Influenza infection of lung cells changed the overall abundance of only a few proteins, mostly related to immunity, but SILAC comparisons showed that the virus changes the cellular location of many proteins. In particular, the authors detected an increase in viral and ribosomal proteins in the autophagosome, which they linked to a reduction in successful autophagy, suggesting that the virus may hijack autophagosomes, perhaps using the compartments for viral protein translation.

DOI: 10.1074/mcp.RA117.000364

### Stinginess with zinc aids resistance

Beta-lactam antibiotics like penicillin are among the first-line drugs for infections, but many bacteria express beta-lactamase enzymes that enable bacteria to resist beta-lactam antibiotics. A special class of these enzymes called metallo-beta-lactamases additionally are resistant to beta-lactamase inhibitors used in combination therapies. In a paper in the **Journal of Biological Chemistry**, Zishuo Cheng and colleagues at Miami University describe how they examined the structure and function of clinical variants of metallo-beta-lactamases. They found that structure, stability and function of these enzymes were critically affected by zinc availability

and that some variants have evolved to function with one, rather than two, zinc ions.

DOI: 10.1074/jbc.RA118.003835

### Rods, cones and fatty acids

Photoreceptors in the eye come in two main flavors, rods and cones. Rods are used for vision at low light and cones for color and bright light. Certain animals can be cone or rod dominant. For example, the tree squirrel and tree shrew have higher levels of cone receptors and are better adapted to bright light. All these photoreceptors use molecules called polyunsaturated fatty acids, or PUFAs, during retinal development, and PUFA synthesis is dysregulated in the cone receptors during diseases such as Startgardt-like macular dystrophy. To study the PUFAs' role in cone receptors, Martin-Paul G. Agbaba and colleagues of the University of Oklahoma Health Sciences Center examined PUFA levels using animals with a majority of cone receptors either naturally occurring or through genetic manipulation. Under normal circumstances, researchers found that cone-dominant animals have surprisingly low levels of PUFA precursors and products. This suggests that different lipids are important for cone receptors, as healthy rod receptors have higher PUFA levels yet are unaffected in the Startgardt-like macular dystrophy. While rods and cone photoreceptors work together to achieve vision, they are fine-tuned differently to allow this to occur. This study was published in the **Journal of Lipid Research**.

DOI: 10.1194/jlr.M082495

## Risks on risks: how genes interact to influence Type 2 diabetes

Researchers at Imperial College London, publishing in the **Journal of Biological Chemistry**, have found that the same gene can have opposite effects on Type 2 diabetes risk depending on what's going on elsewhere in the genome.

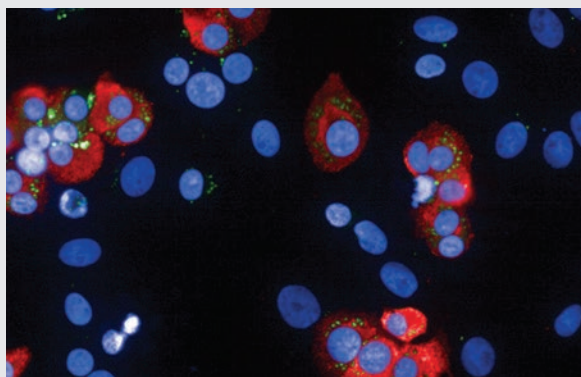
Massive genomewide association studies have shown that individuals carrying a particular variant of the gene transcription factor 7-like 2, or TCF7L2, have a greater risk of developing Type 2 diabetes.

Guy Rutter's team at Imperial College previously had shown that knocking out the TCF7L2 gene in the pancreatic beta cells in mice caused the cells to secrete less insulin. But the team suspected that this was an oversimplification compared to how Type 2 diabetes works outside the laboratory.

"There are subtypes of Type 2 diabetes, four different types, which are distinguished by the severity of the disease, when it happens in life, whether you are overweight or lean, and so forth," Rutter said. "And it turns out that the impact of the genetic variant in (TCF7L2) differs when you're in different subgroups."

The team decided to investigate whether there were other genes that modified how much of an effect TCF7L2 would have. They produced knockout mice characterized by overproliferating beta cells. Then they further knocked out TCF7L2 in these mice.

To their surprise, knocking out TCF7L2 in this mouse model had the opposite effect on insulin secretion compared to its effect in standard mice. That is,



COURTESY OF WIKIMANUI/WIKIMEDIA COMMONS

Human beta cells and insulin granules.

when mice had an overproliferation of beta cells, the absence of TCF7L2 caused those beta cells to produce more insulin, not less.

There are many conditions in humans that can lead to a similar proliferation of beta cells, such as pregnancy, pre-diabetic conditions or the presence of certain genetic variants. This means that knowing what variant of TCF7L2 an individual has isn't the whole story; how TCF7L2 affects diabetes risk also depends on other factors.

"This is important information if we are to use risk genes as clinically useful predictors of who will develop the disease and who won't," Rutter said.

DOI: 10.1074/jbc.RA118.003613

— *Sasha Mushegian*

## When synonymous substitutions aren't

The nucleic acid code has some redundancies built in: Multiple trinucleotides, called synonymous codons, can code for the same amino acid. However, it's increasingly recognized that even if two codons encode the same amino acid, there can be subtly different consequences for using one or the other. Alexander Bertalovitz and colleagues at the University of South Florida examined synonymous nucleotide substitutions in the gene that encodes the hERG ion channel, which contributes to regulating heartbeats. They found that, depending on the codons used, the levels of hERG mRNA and protein expressed

differed. Thus the search for hERG mutations that affect heart disease should be expanded to include seemingly synonymous substitutions. The research was published in the **Journal of Biological Chemistry**.

DOI: 10.1074/jbc.RA118.001805

## New tool to study protein–protein interaction

Science demands evidence to support truth, and science is often limited by technology. Therefore technical innovation is a major driving force for discovery. Payman Samavarchi-Tehrani of the Lunenfeld-Tanenbaum Research Institute, Canada, and her colleagues in Anne-Claude Gingras'

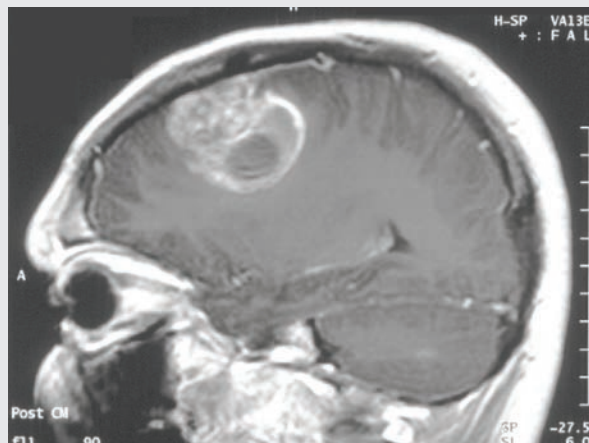
lab describe an improvement to a tool used to study protein-protein interactions in a sub-cellular context. Specifically, they adapt methods for enzymatic biotinylation — addition of a chemical group called biotin — to be more useful in disease-relevant cell types. They write about this work in **Molecular & Cellular Proteomics**. Existing methods rely on cell lines into which the enzyme used for labeling attached to a protein of interest can be introduced (transfected) easily. These cells tend to be immortalized or cancer-derived cells, which may have other proteomic changes. Now researchers can use primary cells — or cells recently derived from an organism with a limited life span — to perform the same types of experi-

## Deadly cooperation in glioblastoma

U.S. Sens. John McCain of Arizona and Ted Kennedy of Massachusetts died exactly nine years apart, both after battling glioblastoma multiforme, or GBM. GBM is a rare and highly aggressive brain cancer that occurs mainly in older adults. Between 40 percent and 70 percent of patients with this disease have altered signaling through the epidermal growth factor receptor, or EGFR.

In a study published in **Molecular & Cellular Proteomics**, Dongsic Choi of McGill University in Canada and colleagues describe the effects of one frequently observed tumor-causing variant, called EGFRvIII, on the protein composition of extracellular vesicles, or EVs, secreted by GBM cells. These small bilayer vesicles containing lipids, proteins and nucleic acids are secreted from cells and can stimulate physiologic processes in the surrounding environment, such as cell migration and blood vessel formation. Cancer cells use EVs in many diverse processes. For example, EGFRvIII mRNA and protein can be a cargo in GBM-derived EVs that are taken up by surrounding cells. The presence of EGFRvIII makes tumor cells more migratory and aggressive, which contributes to cancer metastasis.

Using quantitative proteomics, the researchers found that expression of EGFRvIII in tumor cells significantly increases the levels of invasion-promoting proteins in



COURTESY OF CHRISTARAS A/WIKIMEDIA COMMONS

This MRI sagittal view shows a grade IV glioblastoma in a 15-year-old boy.

the cargo of the EVs and that the presence of EGFRvIII in cells promotes uptake of EV from other cells. This study refines current understanding of glioblastoma mechanisms and may offer new opportunities for biomarker development and future therapies.

DOI: 10.1074/mcp.RA118.000644

— Nathalie Gerassimov

ments. The researchers developed a set of lentiviral vectors that harbor the biotinylation enzyme, and these can be requested by other researchers.

DOI: 10.1074/mcp.TIR118.000902

## Flood alarms in plants

In response to flooding, plants upregulate genes involved in tolerance of low-oxygen conditions. This response is mediated by transcriptional activators called group VII ethylene response factors, which are degraded once oxygen conditions return to normal. How these factors sense oxygen conditions is poorly understood. Mark D. White and colleagues at the University of Oxford showed that plant cysteine oxidases, which oxidize ethylene response factors and lead to their degradation, might act as these crucial oxygen sensors, because their activity was rate-limited by oxygen availability in

a physiologically relevant range. The study was published in the **Journal of Biological Chemistry**.

DOI: 10.1074/jbc.RA118.003496

## When HDL is lowered, the brain suffers

Inflammation in key areas of the brain is seen as an early step before weight gain occurs in people who consume excess calories. To probe this connection, Anna Götz and colleagues at the German Research Center for Environmental Health lowered the levels of high-density lipoprotein, or HDL, known as “good cholesterol,” in a mouse model by knocking out apolipoprotein A1, which is critical for HDL formation. They then examined whether this change caused neuronal inflammation and other metabolic dysfunctions. In a paper published in

the **Journal of Lipid Research**, the researchers report that astrogliosis, the pro-inflammatory process in which neuronal astrocytes abnormally increase, was higher in the mice with lowered HDL levels. In addition, mitochondrial function was compromised in these mice, even when they were fed a low-fat diet. Treatment with HDL to restore normal levels reduced fat accumulation and alleviated the inflammation. Researchers hope that use of HDL could reverse the early brain damage that follows increased caloric intake before weight gain occurs.

DOI: 10.1194/jlr.M085456

## CRISPR/Cas9 is right on target

Developing CRISPR/Cas9-based gene editing for clinical applications requires a thorough understanding



## Stopping cardiovascular disease with citrus

Obesity and its associated diseases, such as Type 2 diabetes, atherosclerosis and metabolic dysfunction, are a worldwide health issue. Many therapies have harmful side effects, result in weight regain or, in the case of gastric bypass surgery, are limited to patients with a high body mass index. Amy C. Burke and colleagues at the University of Western Ontario recently published a study in the **Journal of Lipid Research** using a mouse model of obesity to test how citrus flavonoids, plant compounds found in grapefruit and oranges, could intervene.

While previous studies looked at preventing obesity in mice with flavonoids, Burke and colleagues aimed to reverse obesity. They compared mice on a high-fat, high-cholesterol diet with a high-cholesterol genetic background in two sets, one with normal chow meal replacement and a second with the addition of a flavonoid, after 12 weeks. While complete diet replacement reversed much of the metabolic dysfunction, flavonoid intervention with the high-fat diet had a similar effect. The mice given flavonoids lost weight and had lowered inflammation, enhanced insulin sensitivity and aortic plaque composition changes while still on the



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Citrus flavonoids, which are found in grapefruit and oranges, were used in mice to reverse obesity induced by a high-fat diet.

HFHC diet.

The authors point out that such treatment in humans has mixed results due to variations in metabolism and low bioavailability, but this study demonstrates how intervention, even while eating an unhealthy diet, can reverse symptoms associated with cardiovascular disease.

DOI: 10.1194/jlr.M087387

— Dawn Hayward

of off-target mutations. In a paper in the **Journal of Biological Chemistry**, Shuang Wang and colleagues at the Kunming University of Science and Technology describe how they studied a rhesus monkey model of Duchenne muscular dystrophy, or DMD, produced using CRISPR/Cas9. Whole-genome sequencing of DMD monkeys and wild-type controls showed that, besides the one- or two-base-pair deletions that caused the DMD phenotype, there were no other mutations in functional genes, suggesting that there are no off-target effects of CRISPR/Cas9 editing in this system.

DOI: 10.1074/jbc.AC118.004404

## Immune role of choline metabolism

Phospholipid metabolism in the cells of the innate immune system is not well understood. Shayne Snider and colleagues at the University of

Ottawa examined the role of choline, an essential nutrient for the synthesis of phosphatidylcholine, in macrophage function. They found that choline uptake and phosphatidylcholine synthesis increased when macrophages were stimulated with pro-inflammatory signals, and that choline uptake inhibition changed the makeup of secreted cytokines. Thus choline metabolism may have an unappreciated importance in immune responses. The study was published in the **Journal of Biological Chemistry**.

DOI: 10.1074/jbc.RA118.003180

## Mitochondrial protein stress responses

In addition to having their own genome, mitochondria have their own protein quality control system for maintaining the function of mitochondrially encoded proteins under stress. Anne Wilkening and colleagues at the University of Bonn investigated

the effect of physiological heat stress on mitochondrial proteins from HeLa cells. They found that a mitochondrial translation elongation factor aggregated and lost solubility under even mild heat stress. In a paper published in the **Journal of Biological Chemistry**, the authors propose that inactivation of the elongation factor may prevent accumulation of misfolded proteins in mitochondria under stressful conditions.

DOI: 10.1074/jbc.RA118.002122



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# Meet Mona Nemer, Canada's top science adviser

*By Angela Hopp & André Porter*

**M**ona Nemer was appointed Canada's chief science adviser by Prime Minister Justin Trudeau in the fall of 2017. For the past year, she has been responsible for counseling Trudeau and his cabinet, in particular the science minister, Kirsty Duncan, on pressing scientific matters. She also is tasked with fostering collaboration among scientists in academia and government and serving as a champion of science in the public sphere.

Like many members of the American Society for Biochemistry and Molecular Biology, Nemer, a heart researcher, spent most of her career in academic science. She earned her Ph.D. in bio-organic chemistry at McGill University, worked in industry, became a faculty member and later administrator at the University of Montreal, and then moved to the University of Ottawa, where she was a professor, director of the university's Molecular Genetics and Cardiac Regeneration Laboratory, and, for 11 years, vice president for research.

The last time Canada had a national science adviser was about a decade ago.

Prime Minister Paul Martin of the Liberal Party appointed the first in 2004. His electoral successor, Stephen Harper of the Conservative Party, eliminated the position, along with the top technology adviser spot, in

2008 shortly after his government established the Science, Technology and Innovation Council.

Given that the newly formed council had less public visibility, critics saw the office closures as part of the Harper government's broader effort to sideline science and muzzle scientists.

When Trudeau ran as the Liberal Party candidate in 2015, he made the appointment of a chief science adviser part of his platform. He and his party won, and Nemer's appointment fulfilled that campaign promise.

Nemer grew up in Lebanon, the eldest of three children born to a schoolteacher and a mechanic for Beirut newspapers. She attended an all-girls high school. At that time, the mid-1970s, the school didn't have a science track, so Nemer and her peers began a campaign to get one. "We had a sort of mini-revolt," she told the *Toronto Star* last year. The effort was successful, and Nemer was one of 17 students admitted to the new program.

Already fluent in Arabic and French, Nemer worked on her English while at a Beirut university for more than a year. She then transferred to Wichita State University in Kansas, where she had relatives.

The move was a culture shock. Beirut had been a bustling, multilingual and multicultural metropolitan. Wichita was not. Nevertheless, she



ALL PHOTOS COURTESY OF MONA NEMER'S OFFICE

Canadian Prime Minister Justin Trudeau (left) made appointing a chief science adviser part of his campaign platform in 2015. When he and the Liberal Party won election, Mona Nemer applied for the job. She was appointed in 2017.

persisted.

Come graduation time, Nemer had a scholarship offer from a Ph.D. program at the University of Michigan. But a quick trip with friends to Montreal scuttled those plans.

Attracted by the offerings of city life, Nemer decided to pass on Michigan and instead go to McGill, where she later did postdoctoral work as well.

ASBMB Today's executive editor, Angela Hopp, and the ASBMB's policy analyst, André Porter, talked to Nemer about her experiences on the job over the past year, what students and researchers should know about doing science in Canada, the role of scientists in policy-making, and how to make science more inclusive for women and underrepresented minorities. The interview has been edited for

length and clarity.

### **Could you talk a bit about what is expected of you on a day-to-day basis?**

It's very varied, and that's what makes this job exciting. It goes from meetings with the senior bureaucrats or ministers to discuss specific programs or scientific activities within their department and ministries, to meeting various stakeholders from the Association of Physicists, to having conversations both within government and with outside people on the best way forward on certain major themes or initiatives — say like artificial intelligence and its applications to various fields — to how we would go about having a national strategy for personalized medicine or Arctic research. It's different activities



Before becoming Canada's chief science adviser, Mona Nemer served as the University of Ottawa's vice president for research and as a professor of biochemistry. Her lab focused on the molecular pathways underlying cardiac cell growth and differentiation.

— from science literacy and science promotion to visiting major infrastructure, both nationally and internationally, to representing Canada on different panels.

**Do you think that there are any misconceptions about the purpose of your role or what you do?**

I think, by and large, the (Canadian) public understands the importance of evidence-based decision-making. The reception of my appointment was way beyond expectations.

In terms of the scientific community, their expectation is that I'll serve as a bridge between the extramural science community and government, perhaps enhance understanding of what the research activity and the science are about — how the enterprise

functions — clearly with the expectation that there will be enhanced recognition and support for research.

**You've been in it for almost a year now. How is the reality different from your expectations?**

The reality is that the position that I have — and that exists in many places around the world — is really much needed. It's not just political posturing. It's interesting to have someone who's not in a ministry or a specific department taking a look and trying to convene people from all these stakeholder sectors and disciplines.

The reality is that government actually moves really slowly. This may not be the discovery of the century, but it's sort of even slower than I thought. I thought universities were

slow and you needed to do multiple consultations and so on. Some days, I think, “Well, maybe it’s, in a way, a safeguard. It may take the ship a long time to turn, but it will also take it a long time to sink.” Maybe it’s a sort of guarantee of some stability for our democracy. But I just wish that we could do things a bit faster.

**Prime Minister Harper was known for having cut funding for certain types of research. Trudeau appears to be trying to reverse that seemingly negative view or skepticism of science. What impediments are there to improving perceptions?**

If I compare Canada with countries with a longer history, for example in Europe, I would say that the scientist in Canada has been generally less involved in public policy and interactions with politicians and with the public in general. I think it’s fair to say that most of the interactions between scientists and elected officials have been around asking for more funding, so then they’re viewed (by elected officials) as just basically another interest group.

But the bigger picture is that, because of this dynamic, science literacy and the appreciation of science and of research more generally in Canada lag behind countries like France and Germany and the U.K. It used to be that the public cared about typical scientific issues around health. But increasingly in the past several years, the public has shown greater interest in environmental issues, about food safety, about water safety, in addition to health of course, and then things like data security.

We have had here a sort of conundrum. On the one hand, the population wants to learn more; on the other, we haven’t had intense or even appropriate engagement by scientists,

whether they are within or outside government.

I guess the tipping point came when the public started hearing that, basically, scientists were being muzzled and started to worry whether legislation was being conducted with evidence or simply based on ideology.

The ground there is very fertile for scientists to engage with the public and for the public to be receptive.

**One of the things that we’re concerned with in the U.S. is rhetoric deterring international talent.**

The U.S. is the perfect example of how a nation has prospered because they were able to attract the best scientists and engineers from across the globe. U.S. dominance in terms of science started after World War II. I think there is a pretty interesting link with all the folks who fled Europe and other places in the world since then and came over to the United States. The U.S. is the perfect example of what science internationalization and openness to the world has actually done in terms of positive impact on the country itself. It’s a little bit surprising when governments talk about restricting international collaboration, because, historically, researchers have collaborated across borders.

**People in the U.S. often say that they will move to Canada if some sort of terrible political thing happens. But in all seriousness, can you talk about what Canada has to offer students and researchers?**

First of all, we have the same North American educational system. If you’re in Europe or the Far East or the Middle East and you want a North American-type education and networking and exposure, Canada certainly can offer as good an environ-

ment as the U.S.

Canada generally is viewed as a more welcoming society. Canada is viewed as perhaps more multicultural than other countries and also has less tension between the different cultures.

In the past year, Canada has taken some serious steps in terms of immigration. There are, for example, much shortened or accelerated visa programs and other immigration changes for students, for researchers being hired at Canadian universities or in the private sector. In fact, some of the tech companies from the States have opened branches in Canada — both on the west coast, in Vancouver, and in Toronto — because they find it easier actually to recruit talent from across the globe to Canada, where there are more simplified immigration procedures than for the U.S.

Canada has also put in place many programs to attract disgruntled researchers or researchers who are feeling destabilized by geopolitical conditions. Of course, it's not only in the Americas, but it's also in Europe with Brexit and some other European countries where the economic situation is not as good.

You have, for example, the Canada 150 Research Chairs program that was announced and actually all filled up last year. (Author's note: The Canadian government established the research chair program in 2017 “in celebration of Canada's 150th anniversary” with an initial investment of \$117.6 million. Each awardee gets a seven-year appointment and up to \$1 million for research annually.) There were only 25 of these chairs, and I think that we got over 10 times that number of applications. These were from very, very highly qualified researchers. There was an initial screen at the university level because they knew that it was a very high level, so you can imagine how many more researchers actually applied.

## **Canada's 2018 budget included specific language for support for early-career researchers. What was the reasoning for carving out those funds, and will they be in future budgets?**

Maybe I should just step a bit back and say that the present government believes that the way we're going to prosper in the coming years — with what I guess everybody's referring to as the fourth Industrial Revolution — is through science, research and innovation. For this, the skills training and capacity building are extremely important. The government wanted to make sure that we have funding and support for graduate students and postdocs to acquire the skills and to contribute in their best innovative and creative years.

The fact that we don't have mandatory retirement has meant that the average age of researchers and professors in academic institutions is increasing. Of course, many of them, thankfully, are still very productive researchers. But then it just becomes a little bit of an uneven field for the young ones to compete with established investigators within the same pot of money.

To be consistent with the fact that we're saying, “Hey. We're opening up the country to the best researchers and scientists from around the globe,” we better make sure that they have funding to get their start. This was the thinking behind it. I think the government has made it clear that this is not a one-off.

## **One of the things that the U.S. has been grappling with is the lack of diversity in science, technology, engineering and mathematics. Could you talk about diversity in STEM in Canada?**

Diversity in STEM is a priority for the government, a priority for the



Women with STEM backgrounds are front and center in the Canadian government. Kirsty Duncan (left), a medical geographer, is the country's science minister. Mona Nemer (right), an expert in the molecular mechanisms of the heart, is the chief science adviser. Julie Payette, who served as the chief astronaut for the Canadian Space Agency, is the governor general.

minister of science and for the prime minister. We call these equity, diversity and inclusion policies. They're targeted at increasing the number of women and the number from under-represented groups — so groups, for example, with disabilities, people who identify as indigenous, visible minorities.

(Author's note: About three-fourths of Canadians self-identify as having European roots, but the number of those who identify as indigenous is on the rise. Also, the country has one of the highest immigration rates in the world, and its immigrant diversity score, according to the Pew Institute, is greater than that of the United States.)

A year and a half ago, the government was unhappy that most universities had not achieved the

aspirational targets that they had set. They actually demanded action plans from all institutions, and the institutions have until the end of 2019 to meet their targets. If they don't, any application that does not contribute to these targets will not be reviewed and funded. This is one very clear and direct sort of policy or intervention.

One has to appreciate that higher education in Canada is under provincial jurisdiction. The federal government has to be careful about too much policy direction in that context. But nonetheless, because of the federal government raising the issue and its importance, the universities have voluntarily decided that they're going to have targets for diversity and inclusion not only for the chair program but within the entire professorate and the staff within the universities.



Though Mona Nemer's expertise is cardiac biology, as Canada's chief science adviser, she keeps up with all manner of scientific topics. In late August, she went to the Arctic. Here she's seen on Petermann ice island, an iceberg cleaved from the Petermann Glacier off the northeastern tip of Newfoundland, with glaciologists from Laval University and the University of Ottawa.

**The academic science community in the U.S. is dealing right now with gender bias and sexual harassment on campus.**

I am always struck by the number of women — and they're students, they're young faculty, sometimes people involved with the research enterprise such as communications people, research assistants, and those who are part of the research landscape but not necessarily scientists — who just walk up to me and say how great it is to see that there are women scientists who occupy leadership positions.

I think that we will rest on the day when it's so normal that nobody walks up to any woman in a leadership position and says how great it is, because I don't think any guy walks up to a prime minister or a president

and says, "Oh, isn't it wonderful that we have a white man who's a leader?"

In terms of the harassment on campuses, a year or a year and a half ago, the provincial government actually mandated that all universities have a sexual harassment policy. All universities had to develop and post them. That's to say it's a problem on all campuses, not just in the U.S. They're tough issues to handle, but they're also issues that need to be faced and managed, because for too long certain behaviors have been acceptable that should not be acceptable. I think that our universities are microcosms of our society, and it's really important that we bring up the new generation in a climate of respect for each other and respect for diversity, for all humans.

**We hear often from young scientists that they feel like their principal investigators are disappointed in them when they don't want to become PIs. What are your feelings on that?**

This is a very important point.

The whole idea that most Ph.D.s need to go to work at universities came when we started expanding higher education — probably in the 1960s and '70s. But, I can tell you, all of us in university right now, if we reflect on who we trained with who has ended up in the academic sector, it's never been more than 20 percent or 30 percent max.

My first job was not in a university. It was actually in a biotech company in Washington, D.C. The best people graduating in molecular biology at the time were not going to universities; they were going to the booming biotech sector. In chemistry, if all the Ph.D.s in the 1960s and '70s had gone to academic positions, you would never have had any of the great chemical companies in the U.S. that not only sell products but do great research, like DuPont, not to mention the pharmaceutical industry.

The idea that Ph.D.s have to go to a university and if they don't go it's a





Mona Nemer, right, served as director of the Molecular Genetics and Cardiac Regeneration Laboratory at the University of Ottawa from 2006 until she was tapped by the Canadian prime minister to advise him and the nation's science minister on scientific matters.

waste for them and society is terrible and actually goes against what we're trying to do with the Googles of this world that will need to have these Ph.D.s to innovate. Not to mention the government scientists. How are we going to have government scientists doing proper science if all the good scientists are at universities?

**It's a shame these young people feeling like they're major disappointments when in fact they're going to go off and do wonderful things.**

It's terrible. It may reflect the fact that all of us in academia need to

open up our eyes to the reality of this world. Perhaps if we were a bit more engaged with colleagues outside of our institutions, we would stop having these kinds of attitudes and approaches that are totally counter-productive for society.



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# The photosynthesis fix

As world food needs rise, so does the need for faster, more efficient plant growth. Bypassing an error-prone enzyme is one way to do it.

*By Rachel Ehrenberg, Knowable Magazine*

In a dimly lit basement at the University of Illinois at Urbana-Champaign, not far from a nurtured, sunlit plot of corn at the center of campus, there's a torture chamber for plants. It looks pretty innocuous: a plywood box the size of a small coffee table, with air sifting in through a tube and out from a fist-size hole in the lid. The box has two tiers. The top holds tiny, nine-day-old tobacco seed-

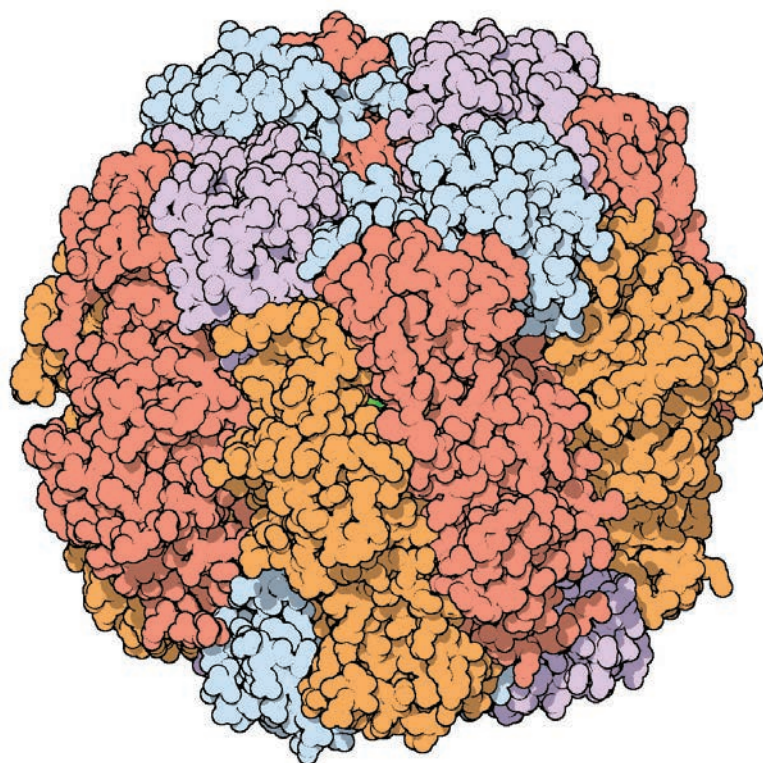
lings, no bigger than your thumbnail. The bottom is layered with soda lime, a granular, Kitty-Litter-like material. It's the same stuff they use in submarines to scrub carbon dioxide from the air.

For someone in a submarine, getting rid of carbon dioxide is life-saving. For the little plants in the box, it is a death sentence — unless, that is, they've inherited a protective



HALEY AHLERS/UNIVERSITY OF ILLINOIS

University of Illinois researchers Paul South (left) and Caroline Keller (right) bag tobacco plants that have set seed in the greenhouse. They are in the process of sifting through 1,500 plants to identify those with the genetically engineered changes that the scientists seek.



LAGUNA DESIGN/SCIENCE SOURCE

Molecular structure of rubisco, a pivotal enzyme in photosynthesis. It captures carbon dioxide that enters the leaf — but sometimes captures oxygen by mistake. Rubisco's sloppiness wastes a lot of energy.

genetic tweak. If a seedling can sweat it out for 24 hours and emerge with its chloroplasts unruffled, the UI scientists know they've got something special.

Plants need just three basic ingredients — sun, water and carbon dioxide in the air — to create the sugars that ultimately sustain most of life on Earth. Photosynthesis makes the world go round: It provides the oxygen we breathe, the food we eat and the fuel we burn. But though it is a marvel, it is also stupefyingly inefficient. From a given amount of sunshine, most plants convert less than five percent of that light energy into biomass, and under some environmental conditions, as little as one percent.

And yet that very inefficiency is giving scientists hope, because it offers room for improvement and a way to provide for humankind's future. If plants could photosynthe-

size better, the extra growth might help feed the nearly 10 billion people that the United Nations estimates will populate the planet by 2050. And it could help offset other anticipated challenges: global dietary shifts toward meat and dairy, an uptick in demand for biofuels that leaves less land available to grow food, and a hotter landscape that will meddle with many crops' photosynthesizing skills.

"There is much uncertainty about how we will get to the yield increases we need in the future," says agricultural scientist Tony Fischer of the Commonwealth Scientific and Industrial Research Organization in Australia. "We need to be trying every tool in the toolbox."

Part of the solution may lie with a little seedling gasping for air, right now, in the box in that Illinois basement.



CLAIRE BENJAMIN/UNIVERSITY OF ILLINOIS

Scientists plant tobacco in SoyFACE (Soybean Free Air Concentration Enrichment), an outdoor laboratory that allows them to manipulate temperature and carbon dioxide levels and see how the plants fare under different environmental conditions.

## The limits of good breeding

Traditional crop-improvement tools have already led to extraordinary leaps in yield. Starting as far back as the 1920s, plant breeders created plants that not only grew faster, allowing for more plantings per season, but also produced more calories for eating. Those gains, part of a larger agricultural initiative known as the Green Revolution, were partly achieved by selecting for two traits: plants with leaves that would intercept as much light as possible and plants that would funnel as much biomass as possible into the edible seeds. Today's premier varieties of soybeans capture nearly 90 percent of available sunshine and pack as much as 60 percent of their biomass into the bean; wheat and rice also saw hefty boosts in yield.

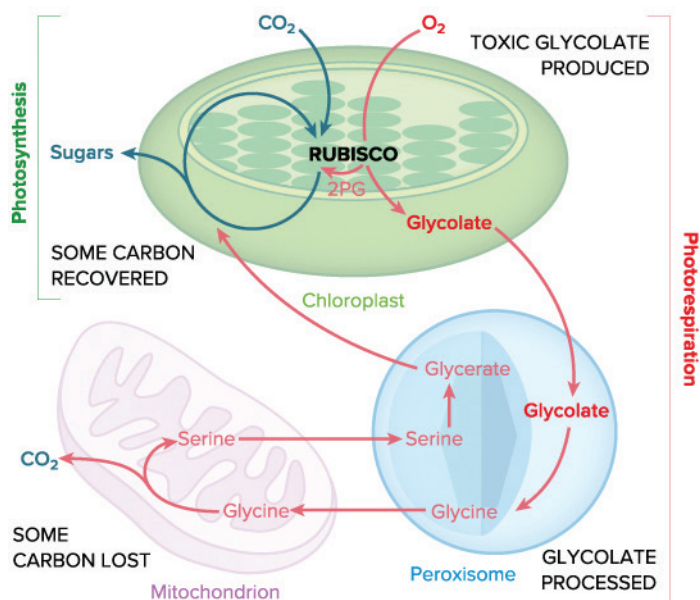
But the gains are approaching a ceiling — a plant can't be nothing

but seed, after all. Where might crop scientists turn? The inefficiencies of photosynthesis are an obvious choice, says Don Ort, a plant biologist at the Urbana-Champaign campus. The Green Revolution didn't tackle this feature. Conventional plant breeding harnesses natural variation, seeking out individual plants with traits of interest: slightly larger seeds than their neighbors, for example, or significantly shorter stems. But that strategy doesn't work for photosynthesis, Ort says. Most plants' photosynthetic machinery chugs along at pretty much the same rate — there isn't a spectrum of lousy to superstar to select from.

Still, research that would lay the groundwork for confronting those inefficiencies was underway at the University of Illinois many decades back. In 1965, the U. S. Department of Agriculture hired William Ogren

## A costly mistake

In photosynthesis, plants make sugars using CO<sub>2</sub> (left) from air. But the enzyme rubisco, which adds CO<sub>2</sub> to the photosynthesis assembly line, is sloppy and sometimes adds oxygen (right). This generates a toxic compound, glycolate, and kicks off a process called photorespiration. Glycolate is dismantled and some carbon is recovered to build sugars. But the process uses energy and some carbon is lost.



SOURCE: REPORTING BY R. EHRENBERG

ERIN HUNTER / KNOWABLE

to work at the campus and look into improving soybean photosynthesis. The mild-mannered chemist would end up doing groundbreaking research that set off some fiery years in plant biology and saw more than one academic meeting devolve into shouting matches.

Ogren — and much of the plant physiology community — was intrigued by what appeared to be a major glitch in photosynthesis. Under certain circumstances, plants produced a toxic compound called glycolate. Plants make it, but because it's toxic they then have to dismantle it. Making and then cleaning up glycolate — a process called photorespiration — is a major waste; it leads to chemical reactions that release valuable carbon back into the air. So what caused the plants to make the glycolate in the first place? Ogren and

his postdoctoral researcher George Bowes discovered the culprit: the enzyme in charge of one of the first steps of photosynthesis. Known today as rubisco (shorthand for ribulose-1,5-bisphosphate carboxylase/oxygenase), this enzyme's job is to grab carbon dioxide that enters the leaf and tack it onto another molecule in the assembly line. It turned out that the inept enzyme will happily grab oxygen instead, sending it along in carbon dioxide's place. And when rubisco passes oxygen into the photosynthesis assembly line, glycolate results, gumming up the works.

Rubisco's mistake is costly. Estimates suggest that photorespiration can reduce the efficiency of photosynthesis by more than 40 percent. "If you designed that, it would be considered an engineering failure," says biochemist Sabeeha Merchant



CLAIRE BENJAMIN/UNIVERSITY OF ILLINOIS

An unmodified tobacco plant (left) is dwarfed by one the same age that has been genetically modified to bypass the inefficiencies of photorespiration (right).

of the University of California, Los Angeles.

Yet rubisco's sloppiness today is rooted in its ancient origins and stunning past success. It is ubiquitous — possibly the most abundant protein on Earth. Plants, algae and light-harvesting bacteria all depend on it for turning inorganic carbon into usable organic matter. It is responsible for more than 99 percent of global

primary production, that remarkable process whereby biomass emerges from thin air.

Billions of years ago, when rubisco began doing its job, there was barely any oxygen in the air. It didn't matter if the enzyme picked up the occasional oxygen molecule — there wasn't much of the stuff around. Rubisco's life work, photosynthesis, changed that. Over the eons, it



BEAU BARBER/UNIVERSITY OF ILLINOIS

Aerial drone shot of tobacco during a 2017 experiment to test plants that were engineered to bypass photorespiration.

pumped more and more oxygen into the atmosphere. Today, atmospheric oxygen is roughly 500 times more abundant than  $\text{CO}_2$ . That oxygen is rubisco's Achilles's heel: Though precise numbers vary depending on environment, broad-brush calculations suggest that for every five carbon dioxides, rubisco grabs two oxygen molecules. And rubisco could not evolve later on to fix its biochemical promiscuity: Scientists surmise that its evolutionary journey had boxed it in, such that minor mutations would knock out its function altogether.

"When we think about plants, we forget that they've been around for so long," says Amanda Cavanagh, a University of Illinois postdoc, as we descend in an elevator toward an underground tunnel that serves double duty as a campus tornado shelter and a quick shortcut between buildings. "Their machinery can't cope with the current high-oxygen environment, the environment they shaped. It's a problem for the plant, and it's a problem for the food system."

## A genetic bypass

I'm in the tunnel with Cavanagh and Paul South, a molecular biologist with the U.S. Department of Agriculture, headed to the tobacco seedling torture chamber. The tunnel is well-lit and clean, though South gleefully points out a budding stalagmite on the floor, the result of a slow drip through a ceiling crack. Somewhere above us, a few hundred yards of dirt away, is the greenhouse where Ogren grew his soybeans decades earlier.

Six-day-old seedlings sprout perkily in a tray next to the torture chamber, unaware of their future. The box is a crucial first test after months of genetic tinkering by South. If his efforts are successful, some of those baby tobacco plants won't mind the dangerously low levels of carbon dioxide they're being subjected to. They contain a genetic workaround, a bypass that will compensate for rubisco's cursed affinity for oxygen. Their photosynthesis machinery will keep humming even as neighbor seedlings without the bypass ultimately wilt

## Is more CO<sub>2</sub> good for plants?

Plants need carbon dioxide to grow, and CO<sub>2</sub> levels are rising. Still, a CO<sub>2</sub>-rich world won't necessarily bode well for plants. The uptick in temperature that comes with the uptick in atmospheric CO<sub>2</sub> poses several problems:

- Rubisco, an already sloppy photosynthesis enzyme, gets sloppier at higher temperatures. That suggests it will make more errors, mistakenly grabbing oxygen instead of CO<sub>2</sub>, as the climate warms.
- Many plants close their pores in hotter weather to prevent water loss. This means oxygen builds up inside the leaves, which translates into lower photosynthesis rates.
- While some experiments find that crops grow bigger when exposed to higher CO<sub>2</sub> concentrations, those plants typically don't pack as hefty a nutritive punch. They are lower in essentials such as iron and zinc.

— R. Ehrenberg

and die, their chlorophyll ravaged by the toxic product of rubisco's mistake.

Photorespiration is a convoluted process, akin to trekking through three different buildings to get waste to the curb. The glycolate is modified piecemeal. It is made in the chloroplast, then transits through two other cellular compartments, the peroxisome and the mitochondrion. Some of its carbon is recycled along the way and sent back to the chloroplast to make sugars, but the effort still adds up to loss. The idea behind the scientists' bypass is to modify the plant's genetic material and so recycle glycolate immediately — right in the chloroplast — recovering all the carbon and saving energy. "Photorespiration takes the country roads," says South. "The bypass is like installing a freeway."

The idea has a proven track record. A decade ago, for example, researchers led by plant biologist Christoph Peterhänsel, then at RWTH Aachen University in Germany, successfully created a photorespiration bypass in the weedy mustard *Arabidopsis*, the plant-biology equivalent of the lab rat. Their approach, reported in *Nature Biotechnology* in 2007, borrowed genes from the bacterium *Escherichia coli* to streamline the glycolate cleanup. The plants responded, growing faster and producing more shoots and roots than their ordinary counterparts.

Another approach, led by plant biochemist Veronica Maurino of Heinrich Heine University in Germany, used genes from both plants and *E. coli*. Published in 2012 in *Frontiers in Plant Science*, that work also led to enthusiastic growth. But these past efforts didn't use the tools available to today's genetic engineers, which make it possible to insert several desirable genes in a row, and to include bits of DNA that can dial up or down the activity of the inserted genes.

Also in the years since, researchers have discovered two more proteins to play with. Their job is to ferry glycolate out of the chloroplast, allowing the by-product to escape. The Illinois scientists have tools to inactivate these, in what's now a full-court anti-photorespiration press.

The Illinois work also adds a grand computational twist. Rather than deciding which precise genes to modify and how, South has used computer programming to generate 24 potential designs that mix and match the bypass machinery. They cover an array of alterations: new arrangements of already-tested bypass genes; genes snipped from different sources such as algae; and sundry DNA switches to turn various genes on and off (or dial photorespiration back up if it turns out to be more important than scientists assume).

The end result of all this shuffling is 140 genetically distinct tobacco plant lines with distinct bypass designs. Each will undergo a battery of tests, including greenhouse and field trials. Maurino, whose early bypass research helped fuel the current work, is confident in the approach. "Their results seem very promising," she says. "I'm very excited to hear more."

The researchers may not end up with one "best" solution — in fact, they don't want to, because real-world environments vary greatly. Working with several bypass designs will allow them to identify versions that would excel in, say, drought conditions, nitrogen-poor soils or very hot temperatures. That would be the mark of success: ramped up photosynthesis in a true crop plant, grown the way a farmer might grow it. The current work modifies a cigar variety of tobacco called Petit Havana, but soybean, potato, and cowpea — a staple in sub-Saharan Africa — are all on the horizon.





CLAIRE BENJAMIN/UNIVERSITY OF ILLINOIS

In a 2016 field experiment, an infrared gas analyzer measures carbon dioxide intake — and thus photosynthesis rate — of plants genetically engineered to bypass photorespiration.

## Green machines?

Early results are encouraging. I'm taken to one of the lab greenhouses and the bypass plants are easy to pick out, with flowering shoots that stretch above the fledgling greenery of their ordinary neighbors. In field trials conducted in 2016, tobacco plants with a bypass had 18 to 20 percent more biomass — the added heft in leaves and stems — than ones that hadn't been tinkered with (the results will be published early in 2018). They also flowered earlier, which could enable two plantings a year, Cavanagh explains. She is testing the plants to see how different versions of the bypass handle different environmental conditions, taking advantage of a unique university field station where

you can manipulate temperature and gas concentrations in plants grown outdoors. She notes that people often assume that the higher carbon dioxide levels of the future will be better for plants, but this isn't necessarily the case (see sidebar).

Researchers aren't putting all their seeds in one basket, though. The bypass project is just one prong in a larger international initiative called RIPE (Realizing Improved Photosynthetic Efficiency), headquartered at the Illinois campus and with collaborators at the University of California, Berkeley; Louisiana State University; and institutions in Australia, the United Kingdom and China. RIPE is targeting weak links and bottlenecks all along the roughly 160 steps of

photosynthesis, supported by \$25 million from the Bill and Melinda Gates Foundation and \$20 million more from the Foundation for Food and Agricultural Research and the UK's Department for International Development. The ultimate goal is to increase the output of staple food crops.

There's an urgent need to push this work along, says University of Illinois crop physiologist Steve Long, director of RIPE. Revving up the various sluggish spots in the photosynthesis pathway and bringing them all together through a mix of genetic engineering, computer modeling and conventional plant breeding will be a long, slow process. And though it might be hard for Americans to conceive of a world short of calories, the forecasted population increases, combined with global warming and their heavy toll on the environment may mean more expensive food in many parts of the world. "Whatever we invent today is not going to be available for 20 years or more, so we need to be looking now at what are the best technologies we can put on the shelf," Long says.

Dealing with rubisco's shortcomings is one major focus. In addition to the bypass project, researchers at RIPE and elsewhere are working on ways to swathe rubisco with CO<sub>2</sub> so it doesn't encounter oxygen to begin with, and scouring algae and wild plants for versions of rubisco that stay on task, ignoring oxygen.

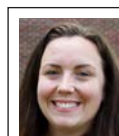
The team is also tackling aspects of photosynthesis that aren't the fault of rubisco but of inefficient use of light. When sunlight gets too strong, plants shed the extra energy as heat, to avoid damage. This light-quenching mode can take minutes to hours to turn off, even after clouds have moved in — a major waste. To fix the problem, Long and his RIPE colleagues added genes to tobacco plants to speed the bounce-back. The strategy, reported

in *Science* in 2016, upped the amount of biomass in plants by 14 to 20 percent.

Other scientists outside of RIPE are tackling the photosynthesis problem by trying to mimic a strategy that has evolved numerous times in the natural world. Roughly three percent of land plants use a different enzyme, one that ignores oxygen, to snatch up CO<sub>2</sub>. These "C4" plants, which include crabgrass, sugarcane and corn, have a very different anatomical structure that keeps rubisco away from oxygen. (Rubisco still has jobs later on in the photosynthesis assembly line.) Such plants have very low levels of photorespiration. Inspired by this, a team led by plant developmental geneticist Jane Langdale at the University of Oxford in England are trying to engineer a C4 version of rice. The project, funded by the Gates foundation, is complex, but in a solid step toward that goal, the scientists reported this November in *Current Biology* that they'd engineered anatomical tweaks to bring rice closer to C4 anatomy.

Of course, science won't be enough to feed the world of the future, says Fischer of the Commonwealth research organization. It's also going to take policy changes and basic infrastructure improvements, such as roads and electricity, in developing parts of the world. "All of these have to be fixed as farmers embrace new technologies, and that means huge changes in public and private investment and in governance," Fischer says.

Those are gargantuan challenges. But in the hopes they will be met, researchers are doggedly torturing one generation of plants at a time and seeing what bears fruit.



Rachel Ehrenberg covers the intersection of plants, food and policy from Boston. Reach her at [rehrenbe@nasw.org](mailto:rehrenbe@nasw.org) or on Twitter at [@Rachelwrit](https://twitter.com/Rachelwrit).

# Scientific session snapshots

**B**elow are brief descriptions of the scientific sessions slated for the 2019 American Society of Biochemistry and Molecular Biology Annual meeting scheduled for April 6–9 in Orlando. We asked session organizers for their pithiest pitches of the science they will share.

## Lipid metabolism

**Brian Finck, Washington University**

This session hits on several major themes, including the regulation of lipolysis, metabolites as signaling molecules and integrated control of metabolism. Attendees will learn about the latest from speakers who approach metabolism from different angles and use a variety of experimental systems to test hypotheses.

**Keywords:** lipolysis, lipogenesis, intermediary metabolism

**Who should attend:** anyone who has grown tired of the lines at Disney

**Theme song:** “Lipid la Vida Loca”

*This session is powered by caffeine.*

## Microbiome and disease

**Julie Segre, National Human Genome Research Institute**

Ever wondered about the bacteria, fungi and viruses that live in and on you? What do they do? How do we begin to understand their biochemical potential and how this is mediated by interactions with the host?

**Keywords:** bacteria, bioreactor, bioinformatics

**Who should attend:** the full range from organic chemistry to microbiology, molecular biology, bioinformatics, sequencing, genomics and microbiome

**Theme song:** “We are Family” by Sister Sledge

*This session is powered by ORF function unknown.*

## Plant biochemistry

**Natalia Dudareva, Purdue University**

This session is devoted to biochemistry and evolution of plant primary and secondary metabolites and will cover recent innovations in multidisciplinary analysis of plant metabolic networks from transcriptional regulation to synthetic evolution and biotechnological applications.

**Keywords:** plant metabolic networks

**Who should attend:** undergraduate, graduate, and postgraduate-level students and professional scientists of plant evolutionary biology, plant physiology and botany, as well as researchers working in the fields of secondary metabolites, metabolic biochemistry, genetic engineering, molecular biology and horticulture

**Theme song:** “The Eggplant That Ate Chicago” by Dr. West’s Medicine Show and Junk Band

*This session is powered by innovations.*

## Catalysis and enzyme action

**Pablo Sobrado, Virginia Tech**

The session will focus on macromolecular structure and function, enzymatic reactions, identification of new enzymes in novel metabolic pathways and the evolution of new chemistry.

**Keywords:** enzymes, spliceosome, protein evolution, enzyme engineering, flavin-dependent reactions

**Who should attend:** biochemists,

enzymologists, chemical biologists, structural biochemists and anyone interested in biological chemistry.

**Theme song:** “The Future’s So Bright I Gotta Wear Shades” by Timbuk3, because it is a great time to be an enzymologist.

*This session is powered by high-affinity interactions.*

## Inflammation and disease

**Judy Lieberman, Boston Children’s Hospital, Harvard Medical School**

Inflammation contributes to almost every disease. This session will highlight new mechanistic insights into how pathogens and danger signals are recognized in cells and trigger the formation of large multicomponent complexes (inflammasomes) that cause inflammatory cell death (pyroptosis) and release of inflammatory cytokines. It will also discuss how these insights could be translated to treat disease.

**Keywords:** inflammation, inflammasome, pyroptosis, gasdermin, caspase, sepsis

**Who should attend:** everyone

**Theme song:** “It’s Too Darn Hot”

*This session is powered by feverish energy.*

## DNA repair, recombination and replication

**Anja Katrin Bielinsky, University of Minnesota**

This session will feature cutting-edge research at the interface of DNA repair, recombination and replication.

Defects in these processes are known to cause human diseases, such as cancer and developmental and neurological pathologies. Our discussion will span a wide array of experimental applications, including single cell/molecule technologies, genomics and proteomics.

**Keywords:** Genome stability, recombinational repair, replication stress

**Theme song:** “Extreme Ways” by Moby, because the science in this field is as fast-paced as the soundtrack to the Bourne trilogy.

*This session is powered by 3R.*

## Glycobiology

*Anne Imberty, French National Centre for Scientific Research*

Glycobiology is the study of glycans (sugar chains in oligosaccharides, polysaccharides and glycoconjugates), biomolecules that are involved in a large range of biological processes. We will focus on glycans and receptors in infection and immunity, since viruses, bacteria, fungi and parasites use protein–glycan interaction to attach to human tissue or to fool our immune system.

**Keywords:** Innate immunity, microbiome, polysaccharide

**Who should attend:** everyone in chemistry, biology, or biochemistry who wants to know how “Create-Read-Update-Delete” coding rules are applied by nature in the complex world of glycosciences

**Theme song:** “50 Ways to Leave Your Lover,” because there are “50 ways to bind your sugar”

*This session is powered by our sweet tooth.*

## Epigenomics and chromatin dynamics

*Yang Shi, Boston Children’s Hospital, Harvard Medical School*

This session will discuss dynamic regulation of epigenomes, including covalent modifications of chromatin

as well as non-covalent, ATP-driven chromatin remodeling, and the roles and mechanisms of action of these modifications in cancer.

**Keywords:** epigenome, chromatin modifications, cancer

**Who should attend:** graduate students, postdoctoral fellows, professors, scientists from pharmaceutical and biotech industries

*This session is powered by infinite creativity.*

## Mitochondrial biology

*P. Darrell Neuffer, East Carolina University*

This session explores the role mitochondria play in creating the continuous flow of energy and electricity that is essential to generating and sustaining cellular life. The session will focus on providing new data on how mitochondrial function is specialized in different cell types, how it is regulated in health and disease, and how it may be targeted therapeutically.

**Keywords:** bioenergetics, metabolism, disease

**Who should attend:** those interested in the driving forces central to life and, by implication, disease

**Theme song:** “Into The Mystic” by Van Morrison — even though “non-equilibrium thermodynamics” is not in the lyrics, that’s what it’s about!

*This session is powered by oxygen.*

## Circadian rhythms

*Amita Sehgal, Perelman School of Medicine, University of Pennsylvania*

The session will cover mechanisms of the circadian (~24-hour) clock across species, from the simple cyanobacteria model to humans, and demonstrate how circadian rhythms pervade virtually all aspects of physiology and behavior. Health consequences of disrupted circadian rhythms will also be discussed.

**Keywords:** clock genes, protein phos-

phorylation, transcriptional control, sleep, disease

**Who should attend:** all who are interested in our daily rhythms (and in sleep)

**Theme song:** “Day After Day” because it emphasizes the rhythmic nature of life

*This session is powered by light and life.*

## Aging and longevity

*Laura Niedernhofer, University of Minnesota, Minneapolis*

We are facing an unprecedented number of elderly in our world population, most of whom have multiple chronic diseases. This has stimulated tremendous interest and progress in discovering fundamental mechanisms that drive aging and its concomitant spectrum of diseases. In model organisms, tweaking these mechanisms affords greater health and longevity.

**Keywords:** aging, lifespan, frailty, mitochondria, metabolism, oxidative stress, muscle, microbiome, senescence

**Who should attend:** everyone; we are all afflicted by aging multiple times during our lifetimes as our grandparents, then parents, then ourselves age

**Theme song:** “Hope I Die Before I Get Old” (“My Generation”) by Roger Daltry and the Who

*This session is powered by confidence — that aging is modifiable.*

## Synthetic biology

*Michelle Chang, University of California, Berkeley*

Please join us in discussing the development of new tools and approaches for the design, study and engineering of macromolecular and cell function.

**Keywords:** synthetic biology, metabolic engineering, bioengineering, directed evolution, genome-scale engineering, protein engineering,

biosynthesis

**Who should attend:** biochemists, enzymologists, protein engineers, molecular biologists, systems biologists, computational biologists, students, postdocs and faculty

**Theme song:** “Computer Love” by Zapp & Roger

The session may be a little different from traditional areas of biochemistry and molecular biology, but we hope attendees “can share that special love” with us, “thanks to modern technology.”

*This session is powered by evolution.*

## Inequities in precision medicine

*Sonia C. Flores, University of Colorado Anschutz Medical Campus*

The future of American medicine depends on the integration of complex data and will require extensive expertise in the utilization of -omics technologies and precision medicine, and the relevant interpretation of data generated using these technologies. However, disparities in the application and interpretation of genomic data to populations with African or other ancestries have been identified. These issues present challenges with implementation, interpretation and cost-effectiveness of precision medicine initiatives when treating minority populations. Our session will focus on strategies to address these issues.

**Keywords:** ancestry, precision, genomics

**Who should attend:** anybody interested in using big data analytics (genomics, proteomics, pharmacogenomics) to make inferences about susceptibility to diseases or responses to pharmacological agents in populations of different ancestries

**Theme song:** “Bridge Over Troubled Water.” This clearly betrays my age, but is perfect to describe how the power of big data has built bridges

to understanding complex human diseases. The challenge is to make sure the data are interpreted in the context of the troubled waters of marginalized populations.

*This session is powered by the need for inclusion and justice.*

## Autophagy and proteostasis

*Beth Levine, University of Texas Southwestern Medical Center and Howard Hughes Medical Institute*

The turnover of proteins and organelles is essential for cellular differentiation and homeostasis. This session will highlight recent advances related to molecular mechanisms of selective degradation of organelles by autophagy, cross-talk between autophagy and other metabolic pathways, and the role of ubiquitinating factors in remodeling proteomes during cellular differentiation.

**Keywords:** autophagy, mitophagy, ER-phagy, proteostasis, ubiquitin

**Who should attend:** all people interested in understanding how cellular degradation and recycling pathways keep our cells healthy

**Theme song:** “Circle of Life” by Elton John

## Cryo-EM

*Yifan Cheng, University of California, San Francisco*

With recent technological breakthroughs, single-particle cryo-EM has become a major tool and a game-changer for structural biology. Speakers in this session will highlight both recent technological advances in single-particle cryo-EM and its applications in various biological systems, such as membrane proteins.

**Keywords:** single-particle cryo-EM, structural biology

**Who should attend:** anyone interested in how protein or protein machinery works

**Theme song:** “All I Want is You” by U2

All anyone and everyone doing structural work wants is cryo-EM because it’s so cool and so hot.

*This session is powered by a technology breakthrough.*

## Single-molecule and single-cell studies

*Xiaoliang Sunney Xie, Peking University*

Advances in single-molecule and single-cell studies, with new technology and new knowledge continuing to emerge, have changed the way life processes are investigated, making an impact in biology.

**Keywords:** single-molecule enzymology, single-cell genomics, single-cell transcriptomics, single-cell imaging

**Who should attend:** enzymologists, biochemists, molecular biologists, cell biologists, systems biologists, genome biologists

**Theme song:** “When Stochasticity Meets Precision”

## RNA structural dynamics

*Hashim Al-Hashimi, Duke University*

RNA is increasingly recognized as a key player in biology. RNA dynamics play essential roles in the assembly and function of machines such as the ribosome. RNAs exchange between the nucleus and cytoplasm, and their functions are modified by post-transcriptional modifications. This session will examine the dynamic complexity of RNAs.

**Keywords:** RNA biology, ribonucleoprotein complexes, RNA post-transcriptional modifications

**Who should attend:** everyone

**Theme song:** “Dancing Queen”  
You’ll have the dance of your life!  
*This session is powered by dynamics.*

# Abstract advice

It's abstract season at the American Society for Biochemistry and Molecular Biology. We want you to share your exciting science at our 2019 annual meeting, and the first step to doing that is submitting your abstract.

Abstract writing is hard. To get you motivated, seven members of the ASBMB Meetings Committee offer some advice on how to get your abstract noticed — and also what NOT to do when writing an abstract.

The deadline for abstract submissions is Nov. 14.

For details on submitting your abstract (and more advice), go to the Meetings page at [asbmb.org](http://asbmb.org).

## Daniel M. Raben, Johns Hopkins University School of Medicine

### How to get your abstract noticed (in a good way):

Things that help are: (a) a “catchy” title that gives the reader a reason to want to read more — what is this abstract about and why is it exciting? (b) making sure the abstract is clear to a uninitiated reader; (c) clearly stating what was being tested/examined and the experimental approach focusing on KEY points; (d) explaining conclusions clearly, and finally (e) implications of the study in two to three sentences. Remember, there are a lot of abstracts, attracting attention, and making the abstract easy to understand will go a long way.

**What to AVOID when writing your abstract:** Avoid jargon that only those in the field would know. Avoid overly complicated/detailed explanations/descriptions. Avoid parenthetical comments that detract from your point.

## Sonia Flores, University of Colorado Anschutz Medical Campus

### How to get your abstract noticed (in a good way):

You want to have a title that tells the story and a compelling conclusion.

### What to AVOID when writing your abstract:

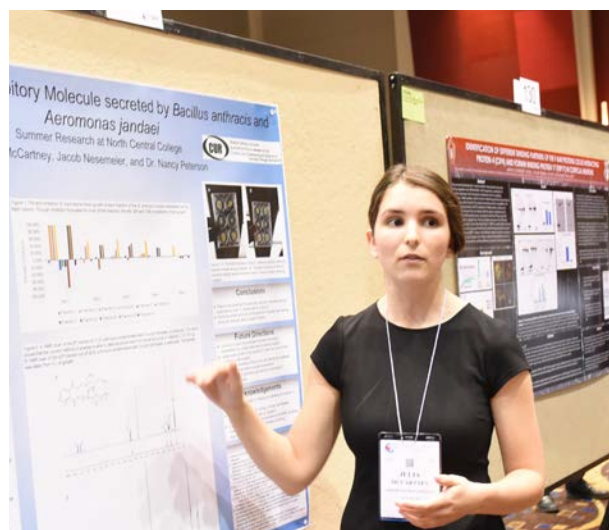
Avoid repetition and descriptive sentences.

## Patrick Grant, University of Virginia

### How to get your abstract noticed (in a good way):

Clearly demonstrate the scientific problem, providing a hypothesis or objective up front. Finish with the impact that your work has on your field. Provide an overview of the approach and key results in a summary form, but also highlight what is distinctive about your methods and/or results.

### What to AVOID when writing your abstract:



PHOTOS COURTESY OF ASBMB

At the undergraduate poster competition at the 2017 ASBMB Annual Meeting in Chicago, Julia McCartney of North Central College presents her research on bacterial species that can be found on frog egg masses and inhibit pathogenic water molds.

Avoid being over technical in the description of your work, as you would like your abstract to be understood by a broad audience. Also check for grammatical and typographical errors.

## Y. Jessie Zhang, University of Texas, Austin

### How to your abstract noticed (in a good way):

You want your audience to understand the significance right away. In the first two sentences, set the stage for the field and the key question in the field you are trying to address. Also, summarize in the last sentence how your research impacts the field.

### What to AVOID when writing your abstract:

Use a minimalist strategy to describe the results of your research. This is only supposed to be a movie preview, so no experimental details.



Young scientists present their research at the undergraduate poster competition at the 2017 ASBMB Annual Meeting in Chicago.

## **Evette Radisky, Mayo Clinic**

### **How to get your abstract noticed (in a good way):**

Lay the foundation: start with a clear, concise sentence or two that lays out background (only the most essential) and conveys your problem/question and its significance to a broad audience. Then include some specifics about general methodology/approach and your results so far. Conclude with a summary sentence that may extrapolate to the broader implications or future directions of your main finding.

### **What to AVOID when writing your abstract:**

Avoid undefined acronyms. Avoid too many numbers; even if your study is very quantitative in nature, your abstract may appeal to a broader audience by describing your key findings in a more qualitative fashion.

## **Enrique M. De La Cruz, Yale University**

### **How to get your abstract noticed (in a good way):**

Try to have a title with a conclusion (e.g. "Membrane Protein X is a voltage-gated water channel" rather than "Characterization of..."). Readers will walk away learning something, even if they read only the title.

### **What to AVOID when writing your abstract:**

Avoid too much detail. This can be found on the poster

and/or paper, so communicate general behaviors, observations, etc.

## **Kelly G. Ten Hagen, National Institutes of Health**

### **How to get your abstract noticed (in a good way):**

Clearly convey why your study is relevant/noteworthy by tailoring background information to your audience (more general for more diverse groups and a bit more detailed for specialized groups). Clearly state the question being asked/problem being investigated. After stating the results and conclusions, circle back to a bigger picture perspective.

### **What to AVOID when writing your abstract:**

Avoid jargon and unnecessary details.

## **Lan Huang, University of California, Irvine**

### **How to get your abstract noticed (in a good way):**

1. Make a concise and eye-catching title. 2. Emphasize the significance and novelty of the work. 3. Describe main discovery clearly that is important to the field.

### **What to AVOID when writing your abstract:**

Try not to just have research background in the abstract.

# Abstract topics

## 2000 ASBMB Genome Dynamics: DNA Replication, Repair and Recombination

2001 ASBMB DNA Recombination, Structure and Topology

2002 ASBMB CRISPR/genome engineering

2003 ASBMB DNA Polymerases, Telomerase, Replicases and Replisomes

2004 ASBMB DNA Damage and Repair

## 2010 ASBMB Chromatin Structure, Remodeling and Gene Expression

2011 ASBMB Chromosomes Structure/Dynamics

2012 ASBMB Epigenetic Modifications of DNA and RNA

2013 ASBMB Histone Modifications

2014 ASBMB Transcriptional Mechanisms, Regulation and RNA Polymerases

2015 ASBMB Transcriptomics

## 2020 ASBMB RNA: Processing, Transport, and Regulatory Mechanisms

2021 ASBMB RNA Polymerases

2022 ASBMB RNA Binding Proteins

2023 ASBMB RNA Structure, Folding and Dynamics

2024 ASBMB Non-coding RNAs

2025 ASBMB CRISPR: Methods and Applications

2026 ASBMB RNA Processing and Editing

## 2030 ASBMB Protein Synthesis, Structure, Modifications and Interactions

2031 ASBMB Ribosomes

2032 ASBMB Mechanisms and Regulation of Protein Synthesis and Dynamics

2033 ASBMB tRNA and tRNA Synthetases

2034 ASBMB Protein Interactions and Binding

2035 ASBMB Protein Modifications

2036 ASBMB Protein Structure and Biophysics

2037 ASBMB Protein Folding and Chaperones

2038 ASBMB Protein Dynamics and Fluctuations, Turnover and Quality Control

2039 ASBMB Protein Turnover, Misfolding, Aggregation and Degradation

2040 ASBMB Intrinsically Disordered Proteins, Prions and Amyloids

2041 ASBMB Ubiquitin Pathway and Targeting

2042 ASBMB Proteasomes: Structure and Regulation

2043 ASBMB Proteolytic Enzymes and Inhibitors

## 2050 ASBMB Enzyme Chemistry and Catalysis

2051 ASBMB Biomolecular Catalysis

2052 ASBMB Enzyme Mechanisms, Kinetics and Energetics

2053 ASBMB Structural Dynamics of Enzymes and Multienzyme Complexes

2054 ASBMB Enzyme Regulation and Allostereism

2055 ASBMB Cytochromes P450

2056 ASBMB Enzyme Inhibitors and Drug Design

## 2060 ASBMB Chemical Biology, Drug Discovery and Bioanalytical Methods

2061 ASBMB Drug Screening and Development

2062 ASBMB Chemical Biology of Natural Products, Nucleic Acids and Small Molecules

2063 ASBMB Chemical Probes, Biosensors and Biomarkers

2064 ASBMB Protein and Peptide Chemistry

2065 ASBMB Protein Engineering and Design

2066 ASBMB Protein–Small Molecule Interactions

2067 ASBMB Bioanalytical and Biophysical Methods

2068 ASBMB Nanotechnology

## 2070 ASBMB Genomics, Proteomics and Metabolomics

2071 ASBMB Next-generation sequencing

2072 ASBMB Genomics

2073 ASBMB Lipidomics, Pharmacogenomics and Toxicogenomics

2074 ASBMB Proteomics

2075 ASBMB Metabolomics

2076 ASBMB Glycomics

2077 ASBMB Systems Biology and Regulatory Networks

2078 ASBMB Computational Biology and Bioinformatics

## 2080 ASBMB Signal Transduction and Cellular Regulation

2081 ASBMB Hormone Signaling in Animals and Plants

2082 ASBMB Extracellular Matrix and Cell Signaling

2083 ASBMB G proteins and Small GTPases

2084 ASBMB Protein Kinases

2085 ASBMB Phosphatases

2086 ASBMB Ion Channels

2087 ASBMB Cyclic Nucleotides

2088 ASBMB Inositol Phosphates

2089 ASBMB Calcium, Nitric Oxide and other Chemical Regulators

2090 ASBMB Redox Signaling

2091 ASBMB Apoptosis and Cell Death

2092 ASBMB Cell Stress and Xenobiotics

2093 ASBMB Allosteric Control of Signaling Pathways

2094 ASBMB Spatiotemporal Control of Signaling

2095 ASBMB Cell Motility and Migration

2096 ASBMB Tumor Suppressors and Tumor Drivers

2097 ASBMB Cancer Signaling and Therapeutics

2098 ASBMB Neurobiology and Neuronal Signaling

2099 ASBMB Immune Signaling

2100 ASBMB Targeted Therapies and New Targets for Drug Discovery

## 2110 ASBMB Bacteria and Parasites: From Microbiome to Antibiotics

2111 ASBMB Microbe/Parasite-Host Interactions

2112 ASBMB Antibiotic Resistance

2113 ASBMB Antibacterial Targets and Drug Discovery

2114 ASBMB Microbiomes

## 2120 ASBMB Metabolism and Bioenergetics

2121 ASBMB Plant Metabolism and Biosynthetic Pathways

2122 ASBMB Energy Metabolism, Oxidative Phosphorylation

2123 ASBMB Oxidative Stress and Reactive Oxygen

2124 ASBMB Mechanisms and Metabolism of Aging

2125 ASBMB Metabolism and Cancer

2126 ASBMB Metabolism and Nutrition

2127 ASBMB Diabetes, Obesity and Metabolic Syndrome

## 2130 ASBMB Lipids and Membranes

2131 ASBMB Biofuels and Lipid Metabolizing Enzymes

2132 ASBMB Regulation of Lipid Metabolism

2133 ASBMB Lipid Signaling and Eicosanoids

2134 ASBMB Lipids and Inflammation

2135 ASBMB Lipid Storage and Trafficking

2136 ASBMB Membrane Proteins and Lipid Interactions

2137 ASBMB Lipid Domains and Lipid Rafts

2138 ASBMB Membrane Transport and Channels

## 2140 ASBMB Biochemistry of Organelles and Organelle Trafficking

2141 ASBMB Organelle Structure and Biogenesis and Disease Association

2142 ASBMB Vesicle Trafficking and Cargo

2143 ASBMB Mitochondria in Health and Disease

2144 ASBMB Organelle Dynamics and Dysfunctions

## 2150 ASBMB Glycans and Glycobiology

2151 ASBMB Glycosyltransferases and Hydrolases

2152 ASBMB Protein-Glycan Interactions

2153 ASBMB Glycan Biotechnology and Drug Development

## 2160 ASBMB Interdisciplinary/Translational Science (SEBM)

2161 ASBMB Mitochondria Dysfunction & Disease (SEBM)

2162 ASBMB Free Radical Biology (SEBM)

2163 ASBMB Structural Biology (SEBM)

2164 ASBMB Sirtuins in Cancer Biology (SEBM)

2165 ASBMB Biotherapies & Immunotherapies (SEBM)

2166 ASBMB Molecular Medicine (SEBM)

## 2170 ASBMB BMB Education and Professional Development

2171 ASBMB Active Learning in the Molecular Life Sciences

2172 ASBMB Big data in Molecular Life Sciences, student projects, labs and the classroom

2173 ASBMB Institutional change and faculty perspectives about teaching in the life sciences

2174 ASBMB Service learning initiatives, community involvement and context dependent Biochemistry instruction



# CALL FOR SUBMISSIONS

## ASBMB Today will launch two essay series in 2019:

### What I wish people understood about \_\_\_\_

Is there an aspect of your life, personal or professional, that others just don't get? Fill in the blank in this sentence, and then set the record straight.

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Life does not end when the sun goes down, and our experiences are often heightened at night. Tell us a story about what you do while others sleep.

## We are also looking for submissions for:

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We seek prose and art about contributions by black scientists to the biosciences, including essays, nonfiction, photographs and illustrations. Deadline: Dec. 1

For information, email [asmbtoday@asbmb.org](mailto:asmbtoday@asbmb.org) or go to [asbmb.org/asmbtoday](http://asbmb.org/asmbtoday) and click **SUBMIT**.

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### Evolution and Core Processes in Gene Expression

May 9–12, 2019, East Lansing, Mich.

### Transforming Undergraduate education in the Molecular Life Sciences

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Reminder: ASBMB members save on meeting registration.

[www.asbmb.org/specialsymposia](http://www.asbmb.org/specialsymposia)

The ASBMB logo features a stylized white DNA double helix on the left, followed by the letters "ASBMB" in a bold, white, sans-serif font on a red background.

# Policy is your BFF

Navigating difficult situations as an early-career faculty member

By Cheryl Bailey & Marvin Payne

**Y**ou have finally landed that first faculty appointment. You start to build a lab, take on student researchers, build your classes and find out where you fit in your institution's cultural landscape. But suddenly, all the things you haven't been trained for start happening. Part and parcel of your career as a faculty member who assigns grades, manages a laboratory and works with colleagues is navigating contentious situations that can consume your time and energy and cause considerable stress.

In this article we provide some advice to reduce the stress of everyone involved. This is where policy is your friend. From our experiences as faculty and administrators, we have learned, sometimes the hard way, that following a policy and corresponding structured process can minimize stress and contribute to a better outcome.

## The scenario

You have just taught Introduction to Biochemistry for the first time, and you made several adjustments to grading schemes during the semester. To compensate for your inexperience, you were extra generous with your grading.

Now that the course is over, a student emails a request for a meeting during which they tell you that the failing grade you assigned them is not fair. They assert that if you had followed your syllabus grading scheme — and taught better, by the way — they would have a much better grade; you have now negatively affected their career.

You feel some anxiety. You know this wasn't your best effort, but you really tried to foster learning and compensate with generous grading. You make a couple of attempts to re-explain how you graded their work, but this student seems unable to accept any personal responsibility for not passing.

Here are four possible responses:

(1) "Look, you are the only one who didn't pass, and if you had spent any reasonable amount of time studying, you would have made it."

(2) "OK, I'm going to raise your grade, but promise not to tell anyone."

(3) "I'm sorry. We are unable to resolve your grade issue. We have an appeal process, and you should contact (the appropriate person) for further discussion. I'll send you the appeal process by email."

(4) "All the students in this class were graded with the same metric. Please submit a written argument for the change in grade you are requesting."

Scenarios like this are quite common. Sometimes we just want to make the problem go away.

## The response

The problem with (1) is that you are personally judging the student and escalating the problem that will ensue if they push the matter further. If you're not careful, this could go beyond a grade discussion into charges of microaggression. We have found that it is better to listen sympathetically to a student; there are a thousand reasons they might not have

performed well. It is easy to jump to conclusions that may be biased and should not be asserted, even if you have evidence for them. We are not here to judge the student but to evaluate their academic performance fairly.

At first glance, (2) seems like a simple way to make the problem go away and help the student move on. However, giving selective advantage to one student over others is problematic, because it degrades the integrity of the academic process associated with grades and is not equitable. It's legitimate to re-evaluate how you graded and act accordingly. If this student deserves some adjustment, so does everyone else. One of the authors actually turned in a large stack of grade change forms for a whole class once after a student pointed out an error.

Another big problem with (2) is thinking the student will keep your confidence; it is inappropriate to ask that of them. Anything you say, even casually in the hallway, may be repeated. One of the authors once was hurrying down a hall to go somewhere and said, "I've got to get out of here." Within days, the rumor was all over campus that they were angry and leaving the institution. This required a lot of damage control.

The best response is either (3) or (4), depending on your institution's policies. Many universities prefer that a faculty member attempt to resolve a problem with a student before it goes to the appeal stage. Even then, a conversation with your chair is a good idea, especially the first time.

If the appeal process is needed,

it should preserve your academic and personal integrity and honor the student's desire for closure. Let the system work for both of you. Document your interactions with the student and your rationale for the grade. An appeal process will evaluate whether you followed your syllabus. You likely will do a better job next time you teach Introduction to Biochemistry, and you will see why it's important to have a stable grading scheme.

## Practical advice

**Take a deep breath.** Control your emotions. Remain professional no matter what horrible characteristics are attributed to you or another person. Staying calm always will promote a better outcome. Be purposeful at stress control, using techniques such as exercise or meditation.

**Educate yourself.** Become familiar with governing documents, such as faculty and student handbooks, and look for guidance. Ideally, you will be familiar with these policies before you need them. You may have to search a bit, since different policies apply to different situations: academic integrity, integrity in research, grievance, etc. Most internal policies are derivatives of larger mandates. Two important examples for academics are the Federal Right to Privacy Act and Title IX of the Educational Amendments of 1972. Both are complex, but more knowledge is better.

Whether you realize it or not, when someone brings a concern to you, a policy and corresponding procedure has been set in motion, even if you are not yet familiar with that policy and procedure. The concern may end with an informal conversation, but it also may progress to formal steps.

**Get good advice.** As a faculty



member, start by asking your department chair what policy covers the issue you are facing. Different policies are housed in different university departments for different concerns. For example, grade appeals commonly are housed in academics, while harassment concerns may be housed in student affairs. You need a clear understanding of both the policy and where it is housed in the university structure.

**Keep a record.** Make sure you have an easily accessible written record of all interactions. Choose both spoken and written words very carefully. Follow up on in-person and phone conversations with an email summarizing the conversation so that both you and the other person in the conversation can view and respond to the summary. Even if a concern is resolved amicably early in a process, it might be revisited later.

**Know your deadlines.** Make sure your responses and formal actions are completed in a timely fashion and include everyone who needs to be included. Be aware that many issues should be shared only with individuals who have a need to know. Avoid sharing with large groups, such as your department faculty, unless there is a clear reason to include them.

**Be thoughtful.** Many decisions involve making a judgement call about a complex issue without a clear right or wrong. Most policies have

appeals and administrative reviews built in. It is OK to be overruled if you have a rational explanation of your decision. Throughout the process, ask yourself what a reasonable person would do in this situation. Acting reasonably should minimize any long-term consequences.

**Let it go.** Learn from your experience, reflect on best practices moving forward and let it go. Every concern is unique. Emotions from one concern can create

bias in future concerns, and you want to avoid this. Even with the best intentions, everyone is likely to be involved in a formal process at some point. This does not mean you are a bad person. The process allows all perspectives to be heard. With reflection, the process can lead to positive changes in everyone involved. The next time you are involved in a formal process will be easier, and the value of the process will become apparent.

**Make it better.** Sometimes, after being involved in a process, you will want to suggest changes to improve the policy. All the previous advice also applies if you decide to go on a quest to change institutional policy. Institutions have a lot of inertia, and working through a legislative process can be frustrating and time consuming, so be prepared. You may want to run your ideas by some of your senior colleagues and let someone else be the standard bearer while you put more time into your research and moving toward rank and tenure.



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# Managing underrepresentation

*By Suzanne E. Barbour*

In the first article in this series, five African-American men in the molecular biosciences discussed mentoring and other factors that led to their career decisions and contributed to their persistence in the science, technology, engineering and math career pipeline. This article will focus on challenges and impediments that may be unique to this demographic group and the strategies these five men have developed to overcome those challenges.

African-American men are highly underrepresented in the sciences. According to the Survey of Earned Doctorates, African-American men earned only 214 of the 12,520 doctorates awarded in the life sciences in 2015. Although this represents a nearly 1.5-fold increase over the 2006 number, it is still only 1.7 percent of earned doctorates in our field (and far below the percentage of African-American men in the U.S. population, approximately 6.5 percent).

## Politics, science and race

The men surveyed for this article (see box) provide insights from the era before Barack Obama was elected president (when Carleton Barbour and Craig Cameron trained) versus the years after the first Obama election (when Nisan Hubbard and Christopher Barnes have been in training). Though none perceived a change in his experience as an African-American man related to Obama's election, each commented on the impact of politics on science.

"My status quo has been remarkably steady over the past 21 years," Cameron said. "The doubling of the NIH budget during the Clinton

administration contributed to this stability early."

The Obama administration's focus on STEM increased awareness, Barnes said, and programs such as the National Cancer Institute's Cancer Moonshot and the National Institutes of Health's Brain Initiative provided more funds to the scientific community.

Hubbard wondered if certain priorities would continue. "With Obama, there was an increasing initiative for diversity in STEM with a focus on progressing science in society," he said. "We are about halfway through Trump's term, so we will have to see if he is going to quell that or keep the needle where it is in terms of the diversity initiatives."

Chaney summarized the sentiments of all five participants. "While the Obama presidency solidified for me and my colleagues that nothing was impossible for a person of color, I cannot say that there were any concrete changes in my experience as an African-American biochemist," he said. "The truth is that there are still real obstacles out there, particularly for underrepresented persons, and we all must do our part to help the next generation of scientists realize their dreams."

Hubbard, the youngest participant, described his challenges. "There are not many people who look like me in this field, so it feels sometimes that there is a certain stigma that I am fighting against while trying to excel and achieve within my work and in the community," he said. "There is also the 'imposter syndrome' that is prevalent among people of color within higher education at these

## Imposter syndrome

Originally defined in a 1978 paper, imposter syndrome is the self-perceived notion that one is not worthy, a fraud or an imposter. Although many high-achieving people suffer from imposter syndrome, studies show the incidence is particularly high in women and minorities in STEM disciplines.

stages (or any stage, for that matter)."

Barbour, the oldest in the group, had similar concerns. "The most challenging part of (my) career has been managing my perceptions of the stereotypes applied to African-American men," he said. "It was reinforced early in my career that some supervisors and colleagues would judge my performance based on my race and not my productivity."

The men were generally optimistic, however, and emphasized the importance of supportive relationships and programs.

Joseph Chaney explained, "My ethnicity has never been a hindrance in my career because I have been fortunate to be surrounded by people who challenged me to aim for high goals and to not be afraid to have unique interests. I have had to get used to being the only minority in the room often at dinners, meetings and conferences."

Cameron expressed similar sentiments: "Without positive people and positive environments, my minority status could have easily disincentivized my pursuit of science and being a scientist."

## AFRICAN-AMERICAN MEN IN THE MOLECULAR BIOSCIENCES — A THREE-PART SERIES

This is the second of three articles exploring the experiences of African-American men in the molecular biosciences through interviews with five African-American men at various stages in their careers, including two students, two faculty members and a researcher in the biotechnology industry.

The careers of these five men span nearly four decades when taken together and include experiences in academia, industry and consulting. Although each has had unique experiences, the commonalities in their stories provide insight into the challenges and opportunities facing African-American men in the molecular biosciences. This series is an exploration of their lived experiences, hopes for the future and advice to the next generation of African-American men who aspire to careers in the molecular biosciences.



HUBBARD

**NISAN HUBBARD**, a doctoral candidate at Northwestern University, is completing a Ph.D. in reproductive biology.



CAMERON

**CRAIG CAMERON** holds the Eberly family endowed chair in biochemistry and molecular biology at the Pennsylvania State University, and his laboratory focuses on genetic replication in positive-strand RNA viruses.



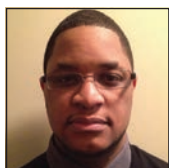
BARNES

**CHRISTOPHER BARNES** is a Howard Hughes Medical Institute Hannah Gray postdoctoral fellow in Pamela Bjorkman's laboratory at the California Institute of Technology.



BARBOUR

**CARLETON BARBOUR** is lead scientist in process and analytical development at Emergent BioSolutions, a biotechnology company focused on developing medical countermeasures for biological and chemical threats. He is also the author's brother.



CHANEY

**JOSEPH CHANEY** is an assistant professor of biochemistry at Xavier University of Louisiana, where he studies molecular nanomotors.

### Managing the impact

Each man said that support was instrumental in his persistence and success. Sources of support included the federal Minority Access to Research Careers and Alliances for Graduate Education and the Professoriate programs; institutional fellowships and assistantships; and private sources including the Burroughs Wellcome Fund.

Barnes said his ethnicity has provided opportunities that benefited his career. "While some may view programs to increase diversity as an

unnecessary helping hand that gives women and minorities an unfair advantage, I believe that if the playing field was fair, such programs wouldn't need to exist," he said. "By embracing these programs throughout my career as a scientist, I have provided myself opportunities to discuss my work at numerous scientific meetings, obtained my own funding and expanded my scientific network in ways that I could not have done."

The participants also commented on the unique opportunities to "give back" that were afforded to them as

African-American men.

Hubbard was an assistant coordinator for Northwestern University's Summer Research Opportunities Program, helping to develop programming to train summer scholars. "This role provided a way to help refine and prepare the next generation of researchers and peers to help advance knowledge and foundations of learning," he said, "while encouraging students of a wide variety of backgrounds to pursue a Ph.D. in their fields."

Opportunities to give back were

not limited to academics. Through his work with chemical manufacturer Rohm and Haas, Barbour became a campus recruiter and participated in the National Organization of Black Chemists and Chemical Engineers. “I believe Rohm and Haas encouraged me to take on the recruiter role to increase the diversity of their campus recruiters,” he said. “It showed my employer trusted my judgement to find and attract future generations of company employers. My involvement provided opportunities to demonstrate job skills my science job did not require.”

Although they emphasized the importance of seizing opportunities, the participants also recognized the challenge of doing so — especially when one is the only African-American man in the room.

To this day, Cameron is often the only black male scientist, or one of a few, at meetings or serving on boards, he said. “For an adult, this can be an intimidating situation. So, as a trainee, this circumstance was absolutely terrifying. I was blessed to have welcoming and nurturing people around me in most of these situations.”

These challenges offer potential for personal growth, Hubbard said. “I have had a lot of advice and opportunities that don’t necessarily get offered normally, and I had to learn to place myself in these situations even if it made me uncomfortable.”

## Love of science

Another convergent theme was the participants’ love of science and its impact on their persistence in their career paths.

“I am passionate about applying scientific principles to solve practical problems,” Barbour said. “I love it when a plan comes together. The most rewarding part of my career has been sharing knowledge with col-

leagues and using the shared experience to solve problems. While only a few of my projects have reached approval and commercialization, the product development journey continues to fan my passion for science.”

Barnes, a generation younger, expressed similar sentiments. “I think the most challenging part about this career is that you will inevitably fail more times than you will succeed, no matter how hard you work or try to solve a problem,” he said. “Working on a project for months to years at a time and not seeing progress is very challenging and will oftentimes make you question your own abilities. So, learning to persevere despite these challenges and setbacks is a skill that is essential to becoming a good scientist.”

In a comment that will likely resonate with most molecular bioscientists no matter their race, ethnicity, age or subfield specialty, Barnes said, “The most rewarding part of this career is the realization of data that help support your hypotheses. Knowing that science is mostly failures, those moments are truly exhilarating, especially when the data leads to scientific breakthroughs or opens up a new path in your field.”

## Career–life balance

Most researchers appreciate that breakthrough moments can be few and far between. While it is challenging for any molecular bioscientist to remain optimistic and focused between breakthroughs, this can be particularly true for African-American men, who sometimes lack the nurturing support systems that others take for granted. Our participants emphasized the importance of keeping things in perspective and maintaining appropriate career-life balance.

“The most challenging part of my job is time management,” Chaney said. “As a new professor, I have

learned that there are many responsibilities, and all of them are important, but not all of them are important at the same time. So, finding that balance is what I am constantly working on improving.”

Cameron echoed this theme, “Science is indeed my hobby, so it is easy to be completely consumed by science and being a scientist,” he said. “My greatest challenge therefore is managing my time to give equal time to the many other activities and people that I enjoy.”

Barbour took this topic a step further, reflecting on the direct relationship between self-care and career success. “Throughout my early career, I focused on avoiding failure at work, not achieving success,” he said. “This perspective resulted in stress and little time away from the job to rest, recharge and enjoy family life.”

These comments illustrate some of the challenges that African-American men face and provide insight into the strategies these five individuals have used to face those challenges and succeed in their careers. In next month’s article, they will offer advice for aspiring scientists in hopes that the next generation of molecular bioscientists will be more diverse and closely aligned with the demographics of the U.S. population.

### About part one

The first article in this three-part series focused on the importance of mentoring, particularly for African-American men in the biosciences. Read the first article at [asbmb.org/asbmbtoday](http://asbmb.org/asbmbtoday).



Suzanne E. Barbour (sbarbour@uga.edu) is the dean of the University of Georgia Graduate School.

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The University of Vermont  
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