Vol. 23 / No. 2 / April 2024

ASBMB TODAY

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

‘Cities under the sea’

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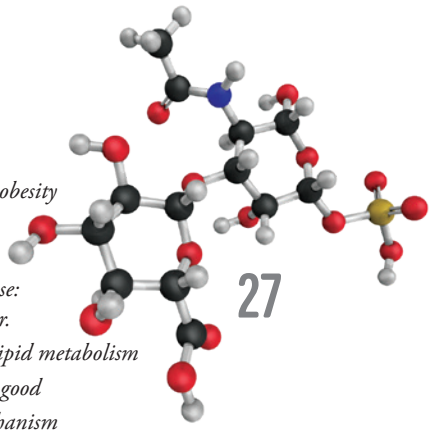


FEATURES

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

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

PERSPECTIVES

Talking about women in biochemistry and molecular biology

By Ann Stock

To increase awareness of the American Society for Biochemistry and Molecular Biology activities, I've been talking to chairs of the committees that steer the society's initiatives.

I recently spoke with Susan Baserga of the Women in Biochemistry and Molecular Biology Committee. Susan holds both M.D. and Ph.D. degrees and is an endowed professor of molecular biophysics and biochemistry and a professor of genetics and therapeutic radiology at the Yale School of Medicine. She has chaired the WIBMB Committee since its founding in 2019.

This conversation has been edited.

ASBMB

Susan Baserga at the podium during the Discover BMB 2023 women's networking event.

AS: When did you become an ASBMB member — and what attracted you to the society?

SB: I've been a member for a very long time, about 20 years. I got more involved in the ASBMB when in 2016 I won the society's William C. Rose Award for biochemistry and mentoring. I figured if an organization was nice enough to give me a prize, I should become more involved. I was a member of the Public Affairs Advisory Committee for six years and then co-founded the Women in Biochemistry and Molecular Biology Committee.

AS: Can you tell me about your research, which was recognized with the Rose Award?

SB: I'm an RNA biologist. We study how ribosomes are made in the cell nucleolus. We study ribosomes both at the basic science level and also the health implications for human diseases resulting from defects in ribosome biogenesis, called ribosomopathies. Also, ribosomes are very important as they drive cancer. We have a separate program that's looking for small molecules that can inhibit ribosome biogenesis in the nucleolus as a new way to treat cancer.

AS: What was the origin of the WIBMB Committee and your role in its founding?

SB: It was started by three of us: me; Kelly Ten Hagen, who's a senior investigator at the National Institutes of Health; and Karen Allen, who's chair and professor of chemistry at Boston University. We decided that the ASBMB would benefit from having a committee that would advocate for women in biochemistry and molecular biology. We presented it to the ASBMB Council over several sessions, and it was officially approved in 2019. We sprung off what was already an active community that had been running the women's networking dinner at the society's annual meeting every year for a number of years. Thus, the committee was relatively easy to launch, because it was a natural extension of what was already going on.

AS: What does the committee provide to women members that they don't find elsewhere in the society?

SB: We've been very organic in the things that we've chosen to work on. We were the first society to show the movie "Picture a Scientist," which is a documentary about barriers faced by women in science. Our society sponsored one of the directors, Sharon Shattuck, to participate in a webinar. The film is fabulous. The webinar was held during the pandemic when we were all stuck at home, and it was a superb event.

We've done a lot of different things of interest to our members. Our theme in 2022 was learning how to say no and the price women pay for what are called "nonpromotable" tasks, particularly in academia. We were very lucky to have Laurie Weingart, one of the authors of a new book called "The No Club," join us for a webinar. She presented a lot of evidence-based analysis of how women say yes too often to tasks that really don't pay off in the long run.

AS: What's on the horizon for future events?

SB: In January, we had a webinar on negotiation strategies for women. One of our new committee members, Mary Jo Ondrechen from Northeastern University, is part of an organization called COACh. It's an organization out of the University of Oregon that teaches women how to be better negotiators.

AS: How do WIBMB committee members contribute to the goals of the committee?

SB: That's a very important question. When I started this committee, I envisioned that it wouldn't just be about me as a leader of the committee. Rather, it would be about having everyone take on the leadership role that they are interested in. So, instead of me running all these webinars and doing all these things, it's our committee members who do it. We have very active participation from all of the different WIBMB members to the extent that they want to be involved, and it really goes a long way toward building and showcasing leadership skills.

AS: In what ways can ASBMB members interact with the WIBMB?

SB: Each year, at Discover BMB, the ASBMB's annual meeting, we host the women's networking dinner. It's a fabulous experience. There are usually 250 people at the event, both women and men. The food is usually outstanding. This year, in San Antonio, we had a panel discussion that focused on networking strategies for women. Also, at the 2022 meeting in Philadelphia I started a new wellness walk. The day after the dinner we go for an hourlong walk. It's been a huge success. We're looking forward to seeing everyone in Chicago in 2025.

Ann Stock (stock@cabm.rutgers.edu) is a professor of biochemistry and molecular biology at the Robert Wood Johnson Medical School at Rutgers and resident faculty member at the Center for Advanced Biotechnology and Medicine. She is the ASBMB's president.

Meet the Sewer scholarship winners

By Hailey Reiss

The American Society for Biochemistry and Molecular Biology is pleased to announce the latest recipients of the Marion B. Sewer Distinguished Scholarship for Undergraduates.

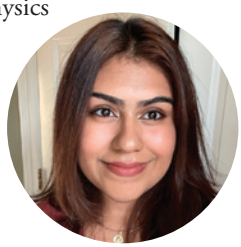
The ASBMB's Maximizing Access Committee, formerly the Minority Affairs Committee, created this award in 2016 to support undergraduate students who demonstrate an interest in the fields of biochemistry and molecular biology and who enhance the diversity of science. Thanks in part to a generous donation from New England Biolabs, the ASBMB is awarding ten $2,000 scholarships that will be applied to undergraduate tuition costs.

The 2023 scholarships went to Rachel Rivera, Michelle Wambui, Omar Afifi, Hannah Barsouk, Kevin Li, Diego Pomales Matos, Antonio Rivera, Dabne Herrera Guerra, Sangita Chakraborty and Sophie Anderson.

The award honors Marion B. Sewer, who died in 2016 at age 43. Sewer was a principal investigator on projects devoted to increasing participation among historically underrepresented groups and furthering student training. Within the ASBMB, she organized the MAC's Interactive Mentoring Activities for Grantsmanship Enhancement, or IMAGE, workshop for postdoctoral fellows and early career scientists, which addresses disparities in scientists' ability to secure federal research grants. She also wrote about issues that historically underrepresented scientists face, such as impostor syndrome.

Here, we share the personal goals of the 2023 Sewer scholarship recipients and describe how they promote diversity.

Rachel Rivera, Yale University



Rivera is a third-year student majoring in biophysics and biochemistry with a concentration in chemical biology. After graduating, she intends to pursue an M.D./Ph.D., specializing in cardiology. She is interested in investigating the relationship between gene regulation and hypertension.

As a physician–scientist, Rivera hopes to ensure that people of color feel supported in navigating the medical system, making medicine and science more accessible.

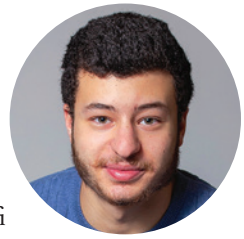
Michelle Wambui, Oregon State University

After gaining experience in both undergraduate research and clinical work, Wambui's career goal is to become a clinician–scientist by pursuing an M.D./Ph.D. After graduating with a degree in biochemistry and molecular biology, she plans to apply to the National Institutes of Health Medical Research Scholars Program.

Wambui's experiences as a Black female student and immigrant have shaped her core values and continue to be a source of inspiration.

Omar Afifi, College of the Holy Cross

A passion for science, art and helping people inspires Afifi to seek a career in health care. He found these interests through involvement in his college where he pursues organic chemistry research, volunteers in the Worcester community and organizes campus events with various clubs.



After graduating with a chemistry degree, Afifi plans to go to dental school with the hope of being able to make people feel more confident in their smiles and improve their overall health.

Hannah Barsouk, Yale University

Barsouk is pursuing a joint bachelor's/master's degree in biophysics and biochemistry with research interests in molecular evolution and the diverse functions of noncoding RNAs. As a first-generation Ukrainian American and public school alum, they aim to give underrepresented students and students with challenging life experiences, including displaced international students, opportunities to fall in love with research and the sciences.

Barsouk has served as a teaching intern and volunteered for a mental health hotline for STEM students with marginalized identities.

Kevin Li, Emory University

Li is a third-year student studying

chemistry and comparative literature. After college, he plans to expand on his current research in breast cancer immunotherapy and tumor immunology by pursuing an M.D./Ph.D. in cancer biology while exploring other areas of passion such as pedagogy and diversity, specifically uprooting the stigmatization of minorities in the hard sciences as a dissuading factor from joining the field.

Li conducts research in Yong Wan's laboratory in the Department of Pharmacology and Chemical Biology.

Diego Pomales Matos, University of Puerto Rico, Río Piedras

After completing a bachelor's degree in cellular and molecular biology, Pomales Matos plans to pursue a Ph.D. in biochemistry and molecular biology and continue exploring mechanisms of disease-associated genetic variation and the role race and ethnicity play in their occurrence and frequency.

Pomales Matos aims to engage in efforts that will result in beneficial translational impacts, especially in minoritized communities.

Antonio Rivera, Wesleyan University

Rivera is a molecular biology and biochemistry and science in society double major. He plans to continue conducting undergraduate research, which will lead to his goal of completing a Ph.D. in biochemistry.

Rivera plans to enter industry and integrate inclusion of underrepresented communities into the private sector of life sciences. He hopes to become a professor after spending time in industry so he can be a mentor to students from underrepresented groups as they navigate higher education and private industry.

Dabne Herrera Guerra, University of Rochester

After completing her undergraduate studies, Herrera Guerra plans to pursue an M.D./Ph.D. with a Ph.D. concentration in biochemistry and biophysics. She hopes to simultaneously pursue a medical residency in neurosurgery and complete her postdoctoral training. Her research interests are focused on RNA-guided gene regulation, and she hopes to develop a device using microfluidics for early detection of diseases and other medical conditions.

She was awarded an NIH Undergraduate Scholarship and plans to devote her life to bringing solutions to complex science problems.

Sangita Chakraborty, City University of New York – Hunter College

After graduating with a double major in biological sciences and interdisciplinary studies, Chakraborty intends to pursue an M.D./Ph.D. degree in hopes of leading her own research group and helping empower future generations of scientists. By studying the molecular and cellular principles governing stem cell biology, she hopes to develop therapies targeting difficult-to-treat cancers.

Chakraborty aspires to make a difference in the lives of patients, especially in marginalized communities.

Sophie Anderson, Vassar College

Anderson aims to become a physician–scientist and pursue a career in pediatric oncology research. After witnessing the life-saving value of timely medical treatment and intervention after her father's late-stage cancer diagnosis and her volunteer work with pediatric patients through Project Sunshine, she wants to contribute to scientific advancements with the goal of discovering improved methods of disease treatment and prevention.

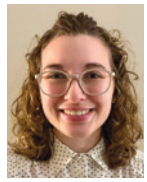
After graduation, she will complete an accelerated master's in public health at Columbia University during her gap year before applying to M.D./Ph.D. programs.

HOW TO APPLY

Applications for the 2024 Marion B. Sewer Distinguished Scholarship for Undergraduates are now being accepted. The deadline is May 31.

To apply, you must be an ASBMB member at the time of your application and submit an application using the online portal. More information about the scholarship and eligibility requirements is available at asbmb.org.

Hailey Reiss (hreiss@asbmb.org) is the ASBMB's undergraduate education coordinator. She holds a B.S. with honors in immunology and infectious disease from Pennsylvania State University's Schreyer Honors College.



JLR announces new junior associate editors

By Marissa Locke Rottinghaus

The Journal of Lipid Research, a gold open-access, peer-reviewed journal published by the American Society for Biochemistry and Molecular Biology, has named six junior faculty members to its editorial leadership team.

The journal's editors created the junior associate editor program in 2019 to demystify the peer-review process and train the next generation of journal leaders. Each junior associate editor will be partnered with a JLR associate editor and will serve a two-year term.

Michele Alves–Bezerra
University of Cádiz

Michele Alves–Bezerra is a principal investigator and the head of the Lipid Metabolism and Metabolic Disease Group at the University of Cádiz, Spain. Her lab uses cell and mouse models to determine the metabolic alterations that lead to nonalcoholic fatty liver disease, or NAFLD, progression. Alves–Bezerra is also developing liver-targeted gene therapies to treat NAFLD and related comorbidities, such as dyslipidemia and cardiovascular diseases. She earned her Ph.D. at the Federal University of Rio de Janeiro and conducted postdoctoral research at Harvard Medical School and Weill Cornell Medical College. Before moving to Spain, she was a junior group leader at Baylor College of Medicine. During her term, she will work with Nada Abumrad, a professor of medicine and obesity research at Washington University School of Medicine in St. Louis.

Robert Helsley
University of Kentucky

Robert "Nate" Helsley is an assistant professor of medicine at the University of Kentucky College of Medicine. His lab studies the mechanisms linking dietary nutrient metabolism to obesity and associated metabolic disorders. Specifically, the Helsley lab investigates how fructose consumption and long-chain fatty acid oxidation disorders contribute to cardiometabolic disease. He received his Ph.D. and completed a postdoctoral fellowship at the Cleveland Clinic. In addition, Helsley is a part-time clinical trial consultant. He will partner with Jean Schaffer, a senior investigator and associate research director at Harvard University.

Matthew Mitsche
University of Texas Southwestern

Matthew Mitsche is an assistant professor of human nutrition and molecular genetics at the University of Texas Southwestern. His lab works to understand the progression of fatty liver disease by focusing on dysfunction in fatty acid sorting between lipid classes. Mitsche is particularly interested in developing high-sensitivity deuterium tracing technology and characterizing genes causing fatty liver. Mitsche earned his Ph.D. in biophysics from Boston University and completed postdoctoral training at UT Southwestern before becoming faculty. During his term, he will work with Sean Davidson, a professor and vice chair of research at the University of Cincinnati.

Shannon Reilly
Weill Cornell Medicine

Shannon Reilly is an assistant professor of metabolic health in medicine at Weill Cornell Medicine. Her lab investigates the molecular pathways regulating lipolysis-driven respiration and their role in adipocyte energy balance and obesity. Reilly is particularly interested in identifying new therapeutics for obesity. She received her Ph.D. in metabolic disease from Harvard University and conducted postdoctoral training at the University of Michigan. Before joining the Weill Cornell Medicine faculty, she was an assistant

adjunct professor at the University of California, San Diego. She will partner with Alan Attie, a professor of biochemistry at the University of Wisconsin–Madison, during her term.

Marcus Seldin
University of California, Irvine

Marcus Seldin is an associate professor of biological chemistry at the University of California, Irvine. The Seldin lab studies natural variation in mice and humans to dissect interorgan communication. Specifically, they examine large population data sets to look for patterns in genetic architecture, clinical traits, transcriptomics, proteomics and metabolomics. Seldin received his Ph.D. from Johns Hopkins University and pursued a postdoctoral fellowship at UCLA. During his JLR term, he will work with Silvia Sookoian, head of clinical and molecular hepatology at the National Scientific and Technical Research Council in Argentina.

Ze Zheng
Medical College of Wisconsin

Ze Zheng is an assistant professor of endocrinology and molecular medicine and an associate investigator at the Versiti Blood Research Institute at the Medical College of Wisconsin. Her lab studies the role of hepatocyte-derived fibrinolytic enzymes in dyslipidemia-associated atherosclerosis, thrombosis and hemostasis. One of the lab's goals is to develop diagnostic, preventative and therapeutic strategies to combat atherosclerosis, thrombosis and bleeding disorders. Zheng earned her Ph.D. from Wayne State University and completed postdoctoral work at Columbia University Medical Center. During her term, she will partner with Karin Bornfeldt, a professor and director of the Diabetes Complications Program at the University of Washington.

Marissa Locke Rottinghaus (mlocke@asbmb.org) is the science writer for the ASBMB.

A series of happy accidents guided this MOSAIC scholar

By Elisabeth Adkins Marnik

Timothy Hines' entry into science wasn't planned. An undergraduate research placement sparked an interest in studying the brain, a fortuitous hallway meeting steered his choice for grad school and well-timed attendance at a conference pointed him to his postdoc.

All this, plus hard work, set Hines up to become one of this year's American Society for Biochemistry and Molecular Biology Maximizing Opportunities for Scientific and Academic Independent Careers, or MOSAIC, scholars. The MOSAIC award provides Hines with two years of postdoctoral funding, followed by three years of R01-level funding to launch his independent faculty career.

As an undergraduate studying psychology at Appalachian State University, he worked in the laboratory of Mark Zrull where he was introduced to the field of neuroscience.

"I really enjoyed doing the research a lot more than sitting in class," Hines said. "I spent a lot of time in the lab looking at slides under the microscope and doing brain sectioning."

Hines was inspired by this experience. After earning a B.A. and B.S. in psychology with a minor in chemistry and German, he decided to pursue a Ph.D.

While visiting graduate schools, he ran into Deanna Smith in a hallway at the University of South Carolina. Smith was on her way to teach a class, but they had a conversation that ended with Smith inviting Hines to rotate in her laboratory. He ultimately decided to attend USC and ended up joining Smith's lab. Hines studied axonal transport with a specific focus on the role of dynein and how it is regulated through protein–protein interactions. He received the Sloan Minority Ph.D. Fellowship from the Alfred P. Sloan Foundation to support this work.

COURTESY OF TIM HINES

Tim Hines is a postdoc studying neurodegeneration at the Jackson Laboratory in Bar Harbor, Maine.

In 2016, Hines attended a conference at the Jackson Laboratory, or JAX, in Bar Harbor, Maine.

"As soon as we were driving onto the island, I was like, 'Man, this place is awesome.'" Hines said. "Then we were walking about town the next day and I had the thought that I should try to find a postdoc here."

A few years later, as he was preparing to defend his Ph.D., a mentor sent him a job posting for a postdoc at JAX in the lab of Robert Burgess, whom he'd met during his 2016 visit.

Hines applied and was accepted; he now studies the mechanisms underlying the neurodegeneration that occurs in Charcot–Marie–Tooth disease using both mouse models and induced pluripotent stem cells. He also mentors students from a variety of backgrounds and plans to continue to pay forward all the guidance he's received.

"I've gotten pretty lucky with mentors throughout my career," Hines said. "One thing I definitely want to be is a good mentor. None of this is being done by myself; it is always a team effort. Being a good mentor involves helping people get to where they want to be. Doing that in a way that is inclusive and promotes diversity is always the goal."

August 2023 was a monumental month for Hines. He married the love of his life, Ann Wells, a fellow scientist he met at JAX, and the National Institutes of Health notified him of his MOSAIC award, which involves mentoring from both Burgess and another scientist at JAX — Martin Pera.

He is excited about the opportunity to use this award to launch his career. He plans to become a faculty member so he can continue to study neurodegeneration and help mentor the next generation of scientists.

Elisabeth Adkins Marnik (marnike@husson.edu) is an assistant professor of molecular biochemistry at Husson University. She studies the mechanisms that help maintain germline stem cells and how these can be co-opted in cancer. She is an ASBMB Today volunteer contributor.

Decoding the genetic recipe book

How an aspiring lawyer in Puerto Rico became a passionate protein scientist

By Farah Aziz Annesha

Inspired by movies and TV, young José A. Rodríguez–Martínez envisioned himself as a lawyer. He viewed the law as an infinitely exciting profession in which he could defend his views using concrete evidence.

Born and raised in Puerto Rico, the son of a chemical engineer, Rodríguez–Martínez decided to major in environmental science as an undergraduate, with hopes of continuing on to law school. He wanted to practice environmental law and go into politics as a member of what he called a "green" party.

However, by his sophomore year, Rodríguez–Martínez had concluded that law was not as fascinating as he expected. His organic chemistry professor at the University of Puerto Rico suggested he try scientific research. After switching his major to chemistry, his vision of science changed overnight.

"Stepping into a lab was transformative," Rodríguez–Martínez said, "even if all I did was listen in to discussions about research problems while cleaning the glassware."

It only took a few weeks in a chemistry lab to fortify his desire for a career in science.

In hindsight, Rodríguez–Martínez mused that his fascinations with science and law were not all that different. "To some degree, science is similar to law," he said. "Once we have our data sets, we put a story together that best explains our results. Then we try our best to defend and communicate our science."

Rodríguez–Martínez continued as a graduate student in chemistry at the University of Puerto Rico. He switched from an analytical chemistry lab to a protein chemistry lab, not knowing that proteins would fascinate him for decades to come.

In a special topics course on nucleic acids, Rodríguez–Martínez learned about Peter Dervan's discovery of what he described as "molecules that bind to specific sequences of DNA" — and he was hooked. He wondered how the molecules recognized these DNA sequences and through what mechanism they were bound.

These questions hovered in the back of his mind, waiting to be explored.

A year and a half before he defended his thesis, Rodríguez–Martínez began attending scientific conferences. At one meeting, he met Aseem Ansari, a researcher working with transcription-targeted therapeutics, who gave a talk on using chemical compounds to design artificial transcription factors that could bind specific sequences in DNA. This topic piqued Rodríguez–Martínez's dormant curiosity about these proteins. Impressed with Ansari's presentation, he went home to Puerto Rico and began thinking of ways to reconnect with the speaker.

In his Ph.D. program, grad students could invite guest lecturers and organize special events, so Rodríguez–Martínez invited Ansari to Puerto Rico the following spring. After the event, they talked about the younger researcher's deep interest in understanding how transcription factor proteins recognize DNA sequences. Impressed by his interest, Ansari offered Rodríguez–Martínez a postdoctoral position in his lab at the University of Wisconsin–Madison and became his adviser.

COURTESY OF JOSÉ A. RODRÍGUEZ–MARTÍNEZ

José A. Rodríguez–Martínez is a research scientist in Puerto Rico and a member of the ASBMB Maximizing Access Committee.

Following his postdoc, Rodríguez–Martínez returned to Puerto Rico and was appointed an assistant professor at his alma mater in 2016. He started his research lab at the university, studying the same proteins that drive his curiosity to this day.

How to make a protein feast

Rodríguez–Martínez uses a kitchen metaphor to describe his research.

The genome is a book of recipes for making different types of cells in the body, he said. The proteins called

transcription factors select recipes to form each cell.

If, for example, a cell is to become a Christmas feast, the transcription factors will choose the recipes of the right entree, main course and dessert — maybe smoked salmon starters, roast turkey and Christmas pudding. They will recognize the right recipes, select them and prepare the ingredients.

Out of the million recipes in the book, how do these proteins recognize the correct ones? What happens if there's a change in the proteins? Will they recognize the same recipes, or will the Christmas feast become something different?

Rodríguez–Martínez strives to answer these questions in his lab, which is now working on three main projects.

The first is understanding what he calls the "grammar rules" of cardiac transcription factor proteins. These proteins bind to specific places on the genome known as DNA binding sites, and, once bound, they read the genetic information in the DNA sequence. Understanding how these proteins bind to the DNA, including the orientation of the proteins, the composition of the binding site and spaces between each binding site, is crucial to determining how the genome is decoded and gene expression is regulated.

This project also studies how mutations in the transcription factor proteins and in noncoding regions of the genome affect how well these proteins bind to the DNA. Many disorders, such as cardiovascular diseases, have been associated with mutations in transcription factors.

The second project aims to decipher how transcription factors have evolved and how changes over generations affect their DNA-binding properties.

COURTESY OF JOSÉ A. RODRÍGUEZ–MARTÍNEZ

The first doctoral students to graduate from the Rodríguez–Martínez lab are Anthony R. Rivera–Barreto (left) and Emmanuel A. Carrasquilo–Dones (right).

A research collaboration related to this project started after a conversation with Riccardo Papa, a university colleague. Papa studies the genetics of butterfly wing patterns, and his lab had discovered proteins that, when concentrated on a certain area of the wing, cause that area to turn red. Rodríguez–Martínez told them he'd be happy to run tests on these transcription factor proteins at his lab. He was surprised to find they were a class that is involved in human eye development.

After finding that the same proteins can cause such varying effects on phenotype in different species, the researchers wondered how they evolved to do so.

The Rodríguez–Martínez lab's third major project cropped up during the COVID-19 pandemic. Using their protein–DNA binding expertise, the researchers developed a high-affinity and high-specificity diagnostic reagent for detecting viruses. The reagent is a DNA aptamer, a short, single-stranded DNA molecule that selectively binds to specific viral proteins.

Between all these research projects and teaching classes, Rodríguez–Martínez spends a considerable amount of time with his students. He feels joy and pride when they succeed in their research tasks.

"Purifying proteins is an integral part of my research, and it's quite an art to do so successfully," he said. "I am elated every time one of my students successfully purifies a protein. It's enough cause for a celebration."

Doing science in Puerto Rico

"The challenges of being a research scientist here are many and diverse," Rodríguez–Martínez said of working in Puerto Rico.

Aspiring scientists are challenged by scarce funding for scientific research and by geographical isolation. His university's budget has been cut heavily in recent decades, so resources and support have decreased. Local

COURTESY OF JOSÉ A. RODRÍGUEZ-MARTÍNEZ

José A. Rodríguez–Martínez and his current lab team.

government funding for scientific research is often insufficient, which compels aspiring scientists to apply for funds from the National Institutes of Health, the National Science Foundation and other private institutions — as they do on the mainland. Because Puerto Rico is an island, attending conferences, training programs or science symposiums can be complicated and costly.

Some funding issues have been alleviated since the nonprofit Puerto Rico Science Technology & Research Trust was established in 2004. However, other problems persist.

Power outages are a major headache for anyone running a lab.

During the first year of his lab in 2017, Rodríguez–Martínez spent most of his starter funds on expensive reagents and lab equipment. When Hurricane Maria hit Puerto Rico, Rodríguez–Martínez and his students had just finished successfully purifying their first protein. They stored their protein samples in refrigerators and evacuated, not knowing when they would return.

After the hurricane passed, they returned to find the generator had failed to start, the refrigerator had switched off and all their hard work was lost. They had to start all over again.

"Unfortunately, power outages are still common here," Rodríguez–Martínez said. "It's quite a scare for us when the power goes out. If the generator fails to start, we have to quickly come up with ways to save our research."

To solve these problems, his students have to spend time and energy they could have been using elsewhere, he added.

"On the bright side, these crises compel them to adapt quickly and keep their research going, irrespective of what issues might crop up."

Despite the challenges, Rodríguez–Martínez believes he's fortunate to work at his alma mater.

"Training and mentoring the next generation of Puerto Rican researchers is a privilege," he said. "I also love doing ciencia en español (science in Spanish). We understand English is currently the agreed language of science, but it feels great to be able to do and communicate science in your native language."

Promoting diversity

Rodríguez–Martínez joined the ASBMB Maximizing Access Committee in 2022 as a way of giving back to the society. "ASBMB has been an important organization for my and my students' development," he said. "We try to go to the annual meeting every year and present our latest work."

He noted the committee's focus on diversification of the scientific workforce and recognition of the contributions of researchers from traditionally excluded and marginalized groups. As a principal investigator, he makes sure all his teams have a mix of students from different backgrounds, and he takes them to conferences where scientists from diverse fields come together to share their research.

"After all, how can you solve diverse problems if you are never aware of them in the first place?" he said. "It is important that I teach my students to learn from diverse sources and to include everyone in all aspects, whether it is solving a research problem or running clinical trials for new drugs."

In his spare time, Rodríguez–Martínez enjoys traveling, cooking and reading science history books. An expression of pure wonder came over his face as he said, "I am always curious how different scientific fields came to be and to understand why we study the things we study today."

Farah Aziz Annesha (azizannesha98@gmail.com) is an aspiring science writer. She recently graduated from Yonsei University Underwood International College with a B.S. in biotechnology and a B.A. in comparative literature. She is an ASBMB Today volunteer contributor.

Touching the future from the bench

By Nicole Lynn

Odutayo "Tayo" Odunuga was introduced to science at a secondary school in his hometown in Southwest Nigeria when a chemistry teacher invited him to work on titrations and basic benchwork in the lab. It wasn't until his second year as an undergraduate at Olabisi Onabanjo University in Nigeria (then Ogun State University) that Odunuga's fascination with biochemistry inspired him to pursue a life of teaching.

"I loved everything about teaching," he said. "It was something that came naturally, and that was the beginning for me."

Odunuga's graduate journey was not straightforward. Nigeria experienced political instability between 1983 and 1999 during the military rule. Universities were frequently shut down due to student unrest and strikes by the academic staff union, demanding better working conditions and increased investment in higher education, thus delaying the progress of many students. After obtaining his M.Sc. in biochemistry, Odunuga began his Ph.D. in 1995 at the University of Ibadan, Nigeria, but left the country after four years without completing it.

"I used to say I did two Ph.D.s, but the one I finally completed was in South Africa," Odunuga said. "A big obstacle in Nigeria was the limited opportunities and limited resources. Because of the frequent academic strikes and student unrest in Nigerian universities, graduate programs that would normally take one to one-and-a-half years instead took three to four years or more to finish."

Odutayo "Tayo" Odunuga is a professor at Stephen F. Austin State University in Texas, where his lab focuses on a chaperone that guides a protein involved in muscle contraction.

Unwavering in his dream of becoming a university educator and a mentor, Odunuga began his Ph.D. again in 1999, this time with the aid of the Deutscher Akademischer Austauschdienst, or DAAD, a German academic exchange predoctoral scholarship.

In 2003, Odunuga received his Ph.D. in biochemistry from Rhodes University in South Africa. He then undertook two consecutive postdoctoral appointments, first at the University of Cape Town in South Africa, where he explored medical virology, and second at the University of Texas Medical Branch, where he studied the roles of chaperones in muscle biology. In 2008, he found his home as an assistant professor at Stephen F. Austin State University, or SFASU, in Nacogdoches, Texas, where he is now a full professor.

"It has been a journey," he said. "From a boy in a small town in southwestern Nigeria with a dream of becoming a scientist, to going all around the world to pursue it."

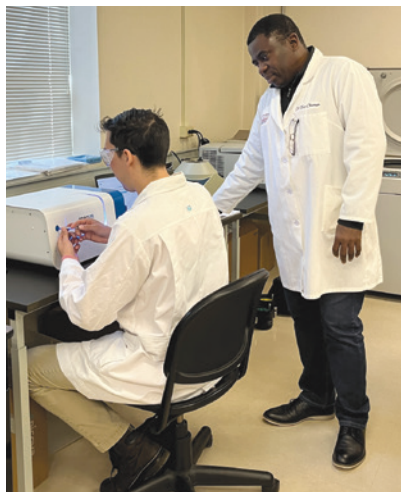
Wearing many hats

Now, as faculty adviser for the university's American Society for Biochemistry and Molecular Biology Student Chapter and interim chair of the chemistry and biochemistry department, Odunuga continues to find new ways to fulfill his commitment to pursuing research and guiding his students toward their futures.

"My Ph.D. adviser at Rhodes University wore many hats," he said. "He was more than a teacher; he was a mentor. I know how important this is in the lives of up-and-coming scientists. This is what I do for my students because I have experienced it."

Using the model organism Caenorhabditis elegans, a soil nematode, Odunuga's lab focuses on character-

Senior biochemistry major John Mullins, an ASBMB Student Chapter member, works on the OpenSPR instrument in the lab as Tayo Odunuga looks on.



PHILIP BAKER

PHILIP BAKER

Tayo Odunuga looks on as senior biochemistry students Ravyn Solis and Madison McFarland check out information on a computer screen in the lab. McFarland is president and Solis is vice president of the SFASU ASBMB Student Chapter.

izing and understanding UNC-45, a unique chaperone that guides the folding and function of myosin, the motor protein involved in muscle contraction. Odunuga and his colleagues recently published a review on the roles of UNC-45 beyond the chaperone as a part of the Subcellular Biochemistry book series. They are working on new projects to understand more about this chaperone family.

Odunaga was an organizer of the 2023 ASBMB Education Meeting. His commitment to education and continued faculty training can be seen in his 2023 collaborative publication in the International Union of Biochemistry and Molecular Biology Journal, where he and his co-authors address classroom pedagogy and faculty development for molecular and life science education.

"Balancing teaching and doing high-impact science is a very delicate art," Odunuga said. "Part of my research is preparing the next generation of scientists."

Laboratory research is carefully woven into the chemistry and biochemistry curricula at SFASU, with undergraduates working in a lab by the beginning of their second year. While the curriculum requires a minimum of two semesters of research, many students surpass this requirement with four to six semesters at the bench by the time they complete their undergraduate degree.

"We foster the right attitude towards research for our students," Odunuga said. "We have a system in place to support our students, and we also sponsor students for conferences and for their professional development."

Odunuga has taken several students to conferences organized by the ASBMB, in particular the former Experimental Biology conference. In February 2023, his department-sponsored 15 students to the Texas Academy of Sciences annual meeting, where they presented research, attended workshops and networked with other institutions.

In September 2023, SFASU officially became the 14th institution in the University of Texas system, a transition that will expand opportunities for students, including funding, research, networking and graduate education. Odunuga believes this is a push in the right direction.

Connections and attitude

Odunuga attributes much of his success in making professional connections to the ASBMB community, which he joined in 2009. A career spotlight in the seventh edition of Cengage's Biochemistry came to him through his ASBMB network.

"ASBMB has really helped me," he said. "The networking is excellent. I try to make my students see the value in organizations like this."

In addition to his efforts to increase ASBMB awareness at SFASU, Odunuga is also working with his daughter to revive the society's Student Chapter at the University of Texas, Dallas, where she is in her first year of college studying biochemistry.

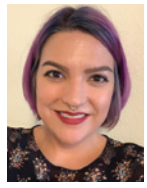
Five undergraduates and one master's student are working in Odunuga's lab this spring. He coaches each student to have a research mindset and assess their goals and challenges so they can succeed.

"I tell my students it is all about attitude," he said. "Everything else you do depends on that. Your level of commitment, for example; I ask my students, 'Do you really want to go all the way or to just check the boxes?' Once you discover this, you can open the doors for these students."

After 15 years as an educator and researcher at SFASU, Odunuga continues to push the boundaries of science while training students for their futures. He said his passion for all his roles grows stronger with each passing year.

"You want to spend your life knowing there is purpose to what you are doing," he said. "In this role, I can touch the future — something you have not seen yet but are already a part of."

Nicole Lynn (nalynn@ucla.edu) holds a Ph.D. from UCLA and is an ASBMB Today volunteer contributor.



Biophysical Society names fellows

The Biophysical Society has named seven 2024 society fellows, three of whom are ASBMB members: **Rommie Amaro, Ivet Bahar** and **Jennifer Doudna**.

AMARO

Amaro is a professor and endowed chair and co-director of the Airborne Institute at the University of California, San Diego. The society honors her work on developing methods to enable the simulation of biological molecules in situ and their applications to illuminate the role of glycans in biology.

Bahar is director and endowed chair of the Louis and Beatrice Laufer Center for Physical and Quantitative Biology and a professor at the Stony Brook University School of Medicine. The society honors her for pioneering novel models and methods in structural and computational biology, including the elastic network models for protein dynamics that helped bridge protein structure and function.

BAHAR

Doudna is an endowed chair and a professor at the University of California, Berkeley, and founder and chair of the Innovative Genomics Institute. The society honors her for her work in developing the CRISPR–Cas9 method for genome editing.

DOUDNA

Vallee selects visiting professors

Of the four scientists named 2023 Vallee Visiting Professors by the Vallee Foundation, three are ASBMB members: **Carlos Bustamante, Jeffrey Gordon** and **Gero Miesenböck**. The awardees may take a one-month sabbatical at a research institution of their choosing.

Bustamante is a professor at the University of California, Berkeley. His research focuses on the structural characterization of nucleo-protein assemblies as well as protein–DNA interactions and their control of gene expression. He will use his VVP sabbatical to organize an annual international summer course in advanced biophysics and structural biology at the University of Salamanca in Spain.

BUSTAMANTE

Gordon is a professor at the Washington University School of Medicine and founding director of the university's Center for Genome Sciences and Systems Biology. His lab explores the role of the gut microbiome in defining healthy growth of infants and children and in the pathogenesis of malnutrition. Gordon will spend his VVP sabbatical in Bangladesh working with colleagues at the International Centre for Diarrheal Disease Research.

GORDON

Miesenböck is a professor and director of the Center for Neural Circuits and Behavior at the University of Oxford. His current research investigates the biological function and neuronal control of sleep. He created the technique of ontogenetics and was the first to genetically modify neurons so their electrical activity could be controlled with light and use this form of optical remote control to insert artificial messages into the brain. For his VVP sabbatical, he will join distinguished scientists who share his interests in using the fly model to gain a mechanistic understanding of cognitive processes.

MIESENBÖCK

In addition to their sabbatical, the awardees will each receive a $25,000 honorarium.

FASEB announces advocacy fellows

The Federation of American Societies for Experimental Biology recently named its inaugural Howard Garrison Advocacy Fellows. Three ASBMB members were among the first nine fellows: **Kaitlyn Browning, Natalie Gehred** and **Katherine Lehmann**. FASEB created this fellowship to help trainees develop their skills as science advocates.

BROWNING

Browning is a graduate student in the lab of Houra Merrikh at Vanderbilt University. Her research is focused on understanding bacterial evolution and multidrug-resistant bacterial infections. She hopes to learn about science policy careers during the fellowship.

Gehred is a graduate student at UCLA in the lab of Thomas Vondriska. Gehred's work uses molecular


GEHRED

transcriptomics to examine the mechanisms that underlie cardiac fibrosis. She hopes to use the skills she gains through the fellowship to write an op-ed and lead a policy-writing workshop.

Lehmann is a postdoctoral fellow at Oregon Health & Science University in the lab of Marc Freeman. Lehmann's work aims to understand the neuron and glial cell signaling mechanisms involved in synaptic pruning. During her fellowship, she aims to advocate for grad student and postdoc benefits.


LEHMANN

Svaren appointed to research leadership

John Svaren is now the interim associate vice chancellor for research in the biological sciences at the University of Wisconsin–Madison. In this role, he oversees the biological sciences and interdisciplinary research across campus and is responsible for divisional area recruitment and retention, grant matches and awards.


SVAREN

Svaren is a professor at the UW School of Veterinary Medicine and director of the Waisman Center intellectual and developmental disabilities core. His research explores the genomic and epigenetic determinants of the myelination process, and his lab is developing therapeutics to treat myelination disorders such as the inherited peripheral neuropathy known as Charcot–Marie–Tooth disease.

Chandel wins Lurie Prize

Navdeep Chandel was one of two recipients of the 2023 Lurie Prize in Biomedical Sciences. The Foundation for the National Institutes of Health gives this award to researchers under age 52 who have made discoveries in mitochondrial science.


CHANDEL

Chandel is a professor at Northwestern University Feinberg School of Medicine. His lab studies mitochondria as signaling organelles in the context of cellular differentiation, cancer and immunity.

The Lurie Prize includes a $50,000 honorarium.

Khal receives Duke chancellor's award

Sai Kwan Khal was among the nine second-year Ph.D. students at Duke University School of Medicine to receive a 2023 Chancellor's International Award. The chancellor's awards support international students with a full year of tuition and fees and a stipend for living expenses. The award also provides opportunities for professional development.


KHAL

Khal is a graduate student in biochemistry and works in the lab of Michael Boyce at Duke. Khal's research focuses on protein glycosylation during health and disease. He completed his undergraduate degree at the College of Wooster in Ohio, where he served as a peer educator, teaching his fellow students about health issues such as alcohol use and stress management.

Gordon wins Princess of Asturias Award

Jeffrey Gordon is one of three researchers awarded Spain's 2023 Princess of Asturias Award for Scientific and Technical Research for seminal contributions to science showing that microorganisms are essential for life on Earth. According to the jury, Gordon was selected for "the discovery and understanding of the human microbiome … (and) enabling innovative therapeutic applications and the search for new effective treatments against antibiotic-resistant bacteria."


GORDON

Gordon is a professor and founding director of the Center for Genome Sciences and Systems Biology at Washington University School of Medicine. His research investigates the role of the gut microbiota in defining healthy growth of infants and children and in the pathogenesis of malnutrition. In addition, Gordon played a leading role in the Human Microbiome Project. His research efforts have led to microbiome-directed therapeutic foods for treating childhood malnutrition.

Bowman named AAAS local network liaison

Faith Bowman, a doctoral candidate at the University of Utah, is one of six people named by the American Association for the Advancement

of Science to its inaugural class of Local Science Engagement Network liaisons. The liaisons are building networks to mobilize scientists and engineers who are interested in science engagement and policy. They will engage with local communities to build trust in science.

BOWMAN

Bowman researches the role of a potential nutrient sensor and its effects on glucose metabolism in diabetes and heart failure in the Summers–Holland lab. She is an Indigenous scholar from the Stockbridge–Munsee Band of Mohican Nation in Wisconsin and a 2023 ASBMB Advocacy Training Program delegate.

Benkovic awarded honorary professorship

Pennsylvania State University has named **Stephen Benkovic** an Atherton professor. This title honors retired faculty who hold the Evan Pugh professorship, the University's highest faculty distinction, and wish to continue a high level of engagement as emeritus members.

BENKOVIC

George Washington Atherton was a Civil War veteran who served as president of Penn State from 1882 to 1906. Evan Pugh, an agricultural chemist, secured Penn State's designation as a land-grant institution and was the university's first president, from 1859 to 1864.

Benkovic was among the first scientists to hypothesize that conformational changes outside the enzyme's active site were necessary for achieving maximal catalysis. He is also noted for his studies on the T4 replisome and the discovery of the purinosome in purine biosynthesis. He has studied many enzyme systems critical to human biology, contributing fundamental findings to the design of cancer drugs and antibiotics.

Bumpus advances at FDA

Namandjé Bumpus has been named the principal deputy commissioner at the U.S. Food and Drug Administration. In this new leadership role with the FDA, she will work with a team to develop, advance and implement key public health initiatives and oversee the agency's day-to-day operations.

BUMPUS

Bumpus was previously the FDA's chief scientist. Before moving to the FDA, she ran a lab at Johns Hopkins University studying how P450 enzymes process antiretroviral drugs and antivirals used against hepatitis C. She served as associate dean for basic research and director of the pharmacology department at Hopkins and chair of a National Institutes of Health study section on xenobiotic and nutrient disposition and action.

Küster and Riley win HUPO awards

The Human Proteome Organization has honored two ASBMB members. **Bernhard Küster** won the Distinguished Achievement in Proteomic Sciences Award for his ongoing contributions to the field of chemical proteomics. **Nicholas Riley** won the HUPO Rising Star Award, which recognizes early-career researchers.

KÜSTER

Küster is a professor at the Technical University of Munich. His research focuses on the biochemical actions of therapeutic drugs, the molecular mechanisms that play a role in cancer and how information about these two aspects can be used for individual approaches to clinical treatment. Recently, his lab published a novel quantitative proteomic approach for decrypting drug actions and protein modifications by dose- and time-resolved proteomics. Küster is a deputy editor of the journal Molecular & Cellular Proteomics.

RILEY

Riley is an assistant professor at the University of Washington. The Riley research group investigates glycosylation patterns that govern health and disease using mass spectrometry-centric glycoproteomics and chemical glycobiology. His group is particularly interested in understanding how altered cell surface glycosylation phenotypes manifest in cancer progression and drive metastasis.

NAM names members

The National Academy of Medicine recently inducted 100 new members, including four ASBMB members: **Susan Baserga, Roger Davis, Timothy Springer** and **Brent Stockwell**.

Baserga is a professor at the Yale University School of Medicine. Her lab focuses on understanding how ribosomes are made in eukaryotic cells. In particular, they study the pathogenesis of ribosomopathies, diseases caused by abnormalities in ribosome biogenesis that can induce cancer. She is a 2023 ASBMB fellow and chairs the society's Women in Biochemistry and Molecular Biology Committee.

BASERGA

DAVIS

Davis is a professor and chair of molecular medicine at the University of Massachusetts Chan Medical School. His lab seeks to understand the role of JNK signaling in inflammatory diseases and how intervening in the pathway might address a wide variety of diseases. The Davis laboratory was the first to clone human cJun N-terminal kinase, or JNK.

SPRINGER

Springer is a professor at Harvard Medical School. His lab studies protein conformational changes in integrins, the von Willebrand factor, the transforming growth factor-β family and adhesins in malaria sporozoites. He discovered lymphocyte function-associated molecules, intercellular adhesion molecules, the first subfamily of integrins and the process of leukocyte diapedesis.

STOCKWELL

Stockwell is chair of the department of biological sciences and a professor at Columbia University. His lab uses small organic molecules in a systematic way to perturb cellular processes and discover their underlying mechanisms. Stockwell discovered ferroptosis and is particularly interested in understanding cell death mechanisms and how they intersect with disease mechanisms in cancer and neurodegeneration.

Booker wins Julian research award

The National Organization for the Professional Advancement of Black Chemists and Chemical Engineers honored Squire Booker with the 2023 Percy L. Julian Award, named for a Black American research chemist who pioneered the chemical synthesis of medicinal drugs from plants.

BOOKER

Booker is a professor at the Pennsylvania State University and a Howard Hughes Medical Institute investigator. His lab studies biosynthetic enzymes that use S-adenosylmethionine and iron-sulfur clusters as radical catalysts. He recently identified the final step and chemical mechanism in the formation of certain membrane lipids found in archaea, the first known biological reaction that couples two completely inert aliphatic carbons.

Booker has led the ASBMB Maximizing Access Committee and served on the Nominating Committee, Meetings Committee, Finance Committee and Program Planning Committee. In 2022, he received both the ASBMB Ruth Kirschstein Diversity in Science Award and the ASBMB–Merck Award.

Llinás receives honorary professorship

Manuel Llinás has been named the Ernest C. Pollard professor in biotechnology at Pennsylvania State University. This honor recognizes his outstanding research contributions, teaching and service.

LLINÁS

The Llinás lab studies the malaria-causing parasite Plasmodium falciparum to identify ways to disrupt its growth and lifecycle. The team is particularly interested in parasite gene regulation and metabolism during the red blood cell stages of parasite development in humans, when clinical symptoms of the disease occur during infection. Llinás established and co-directs the Huck Center for Malaria Research, a collaborative forum for researchers at multiple Pennsylvania campuses working on malaria and mosquitos.

Ernest C. Pollard was a physics professor who taught at Penn State from 1961 to 1971 and founded the Department of Biophysics. In 1979, that department merged with the Department of Microbiology and Biochemistry to form the present Department of Biochemistry and Molecular Biology.

Girirajan awarded honorary professorship

Santhosh Girirajan has been named the T. Ming Chu professor of biochemistry and molecular biology at Pennsylvania State University.

Girirajan's research explores how human genetics contributes to neurodevelopmental disorders such as autism, schizophrenia and congenital malformation. The lab uses techniques such as human genetics, functional genomics in model organisms and computational genomics.

GIRIRAJAN

T. Ming Chu earned his doctoral degree in biochemistry from Penn State in 1967 and went on to develop a widely used blood test for prostate cancer. He established this professorship in 1997.

ON THE WEB

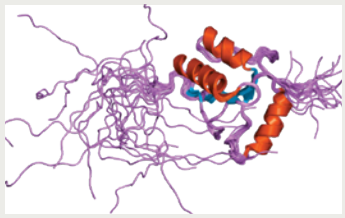
Read more member news at asbmb.org/asbmb-today.

IN MEMORIAM

Lucy Chang and Fred Bollum

Lucy Chang and Fred Bollum, personal and professional partners for more than four decades and longtime ASBMB members, both died in 2023: Bollum on March 2 and Chang on Nov. 13. Bollum was 95, and Chang was 81.

Bollum earned a Ph.D. in physiological chemistry at the University of Minnesota in 1956 and was a postdoctoral fellow at the University of Wisconsin. He worked at the Oak Ridge National Laboratory, the University of Kentucky and the Uniformed Services University of the Health Sciences in Bethesda, Maryland.



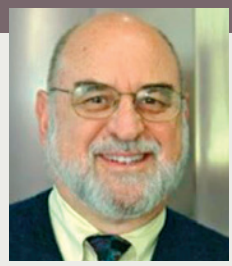
PDB

Lucy Chang and Fred Bollum built a business around their discovery of the mammalian terminal deoxynucleotidyl transferase, or TdT.

Lucy Ming Shih Chang earned a Ph.D. in biochemistry from Indiana University in 1968; she pursued postdoctoral research at the University of Kentucky and began her independent research career at the University of Connecticut before joining the faculty at USUHS.

During their joint research career, they discovered the mammalian terminal deoxynucleotidyl transferase, or TdT, a specialized DNA polymerase expressed in precancerous cells, developing immune cells and acute leukemia and lymphoma cells. In 1982, they founded Supertechs Inc., a biotech firm specializing in diagnostics for leukemia and apoptosis research. Together, they developed numerous patents related to TdT and other related enzymes.

Daniel Malamud



Daniel Malamud, an expert in salivary diagnostics and molecular pathobiology and an ASBMB member for almost 40 years, died June 23 at the age of 84.

Malamud received a Ph.D. from the University of Cincinnati and trained as a postdoc at the medical school at Temple University before beginning his faculty career at Temple. He went on to become the director of the HIV/AIDS research program at the New York University College of Dentistry.

Malamud's early research focused on the biochemistry of saliva. Later work focused on inexpensive point-of-care testing using saliva to diagnose HIV, tuberculosis, malaria and Zika in developing countries. Certain proteins in saliva can be linked to infectious diseases, making them good candidates to develop diagnostic testing.

These biomarkers led to Malamud's research on molecules that have antibacterial and wound-healing properties. Inspired by animals and humans licking their wounds to promote healing, his lab developed an anti-HIV drug using a saliva-derived molecule.

Malamud received the Albert Nelson Marquis Lifetime Achievement Award in 2017 and was named a fellow of the American Association for the Advancement of Science in 2022. He retired in 2021.

Charles Kasper

Charles Boyer Kasper, a professor emeritus at the University of Wisconsin–Madison McArdle Laboratory for Cancer Research and an ASBMB member since 1970, died Sept. 5 in Appleton, Wisc. He was 88.

Kasper earned a Ph.D. at the University of Wisconsin–Madison in 1962 and was a postdoc at the University of Utah and at UCLA, where he was hired as an assistant professor. He moved to the McArdle Lab in 1965 and remained there until he retired.

Kasper studied proteins of the endoplasmic reticulum and nuclear envelope. His lab discovered the CYP3A gene family and pioneered understanding of its contribution to the metabolism of more than half of all prescription drugs.

He served for many years on the editorial board of the Journal of Biological Chemistry.

John Hoover Hash

John Hoover Hash, who served for more than 30 years on the Vanderbilt University Medical Center faculty and had been an ASBMB member since 1965, died June 20. He was 94.

Hash earned a Ph.D. in biochemistry from Virginia Tech and was a postdoctoral fellow at Columbia University. He worked at Lederle Labs for six years before Vanderbilt hired him in 1964.

Hash was appointed associate dean of biomedical science and director of sponsored research at Vanderbilt in 1976 and began helping colleagues secure research funding. He retired as an emeritus professor of microbiology and immunology in 1994.

He was a fellow of the American Association for the Advancement of Science.

A genetic light switch for obesity lurks in the liver

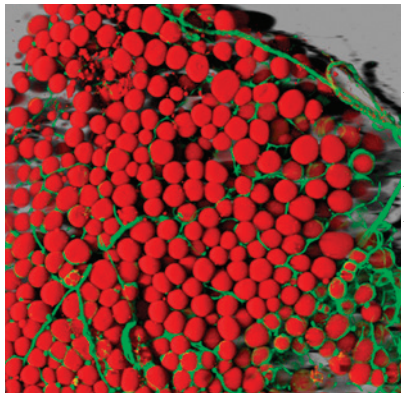
By Hallie Blevins

Obesity can be caused by a variety of environmental, lifestyle and genetic factors. Age seems to be a major contributor to obesity, causing a decline in liver function and progressive adiposity through mechanisms that researchers do not yet completely understand.

Age-induced obesity in humans is likely caused by our species' long history of food insufficiency and shorter life expectancy before advanced medicine was developed, as our ancestors' bodies worked to create an efficient metabolism and minimize energy expenditure. However, now that people live longer and food is more plentiful in most parts of the world, these innate survival tactics are no longer helpful and may cause more harm than good.

Kamal Mehta is a professor of biological chemistry and pharmacology at the Ohio State University. Since his training with Nobel laureates Michael Brown and Joseph Goldstein at the University of Texas Southwestern Medical Center, he has dedicated his research to finding the biological mechanisms behind age- and diet-induced metabolic diseases.

"I was interested in signaling pathways regulating cholesterol homeostasis," Mehta said. "By cell culture studies, we found a critical role of protein kinase C, or PKC, in cholesterol homeostasis. We pursued studies to define the specific isoform and narrowed it down to PKCβ. While studying whole-body PKCβ knockout



DANIELA MALIDE, NATIONAL HEART, LUNG, AND BLOOD INSTITUTE/NIH

A mouse's fat cells (red) are surrounded by a network of blood vessels (green). Fat cells store and release energy, protect organs and nerve tissues, insulate us from the cold and help us absorb important vitamins.

mice, we realized that PKCβ plays a critical role in obesity syndrome."

In 2008–2009, Mehta published his first papers in the **Journal of Biological Chemistry** and Hepatology about PKCβ's involvement in lipid homeostasis. In his early research, he fed a high-fat diet to mice that had been genetically modified to lack the gene for PKCβ. He found that the mice were resistant to weight gain and protected from insulin resistance.

"Realizing that PKCβ can be critical for regulating both cholesterol and fat homeostasis felt great," Mehta said.

However, it wasn't clear which tissue caused this effect. To answer this, Mehta's team created tissue-specific genetic knockouts of PKCβ and found that PKCβ in the liver is responsible.

This sparked Mehta's interest — how does PKCβ in the liver modulate other tissues? He has now answered this question. His lab's recent paper in the JBC reported the finding that hepatic PKCβ modulates β3 adrenergic receptor, or β3-AR, signaling in the brain and peripheral tissues, which is responsible for lipolysis and thermogenesis found in brown adipose tissue, the type of body fat that regulates the body's temperature and burns calories.

Mechanistically, age-induced activation of PKCβ can reduce the sympathetic nervous system (which is activated by metabolism) and therefore β3-AR signaling, which then decreases energy expenditure and the rate of mitochondrial oxygen consumption. This in turn leads to gradual weight gain and insulin resistance. Removing the PKCβ gene in the liver of mice reverses this effect, acting as a genetic light switch to turn off obesity.

In future studies, Mehta is interested in exploring how PKCβ regulates β3-AR signaling and how the liver communicates with the brain to achieve these effects. His lab's findings highlight a potential avenue for drug discovery and the development of novel therapeutics for age-induced obesity; however, no PKCβ inhibitors or β3-AR agonists are currently on the market as a treatment for obesity.

"We have developed PKCβ inhibitors," Mehta said, "and we're pursuing further studies on utilities through my start-up Instacare Therapeutics."

DOI:10.1016/j.jbc.2023.104917

Hallie Blevins (Hallie.Blevins@vcuhealth.org) is a postdoctoral fellow in the Department of Human and Molecular Genetics at Virginia Commonwealth University Massey Cancer Center. She is an ASBMB Today volunteer contributor.

Inflammation and diabetic kidney disease: Why mitochondria matter

By Nicole Lynn

Diabetes mellitus refers to a group of chronic conditions that affect the body's ability to effectively use sugar, specifically glucose, resulting in a buildup of sugar in the blood. In 2022, the Centers for Disease Control and Prevention estimated that 11.3% of the U.S. population was diabetic, and many more had higher-than-normal blood glucose levels.

The long-term health effects of diabetes mellitus can be grim. In addition to deteriorating vision, nerve damage and hearing impairment over time, diabetes can also affect larger organ systems. In the U.S., it is the predominant risk factor for cardiovascular and kidney diseases. Diabetics are at increased risk for hypertension, heart attack and stroke; furthermore, one in three diabetic adults have diabetic kidney disease, or DKD.

In DKD, prolonged elevated glucose in the blood damages blood vessels and nephrons, the cells in the kidney responsible for filtration. Often occurring in parallel with ailments such as high blood pressure, DKD damages kidneys increasingly over time. A recent study in the **Journal of Biological Chemistry** demonstrated a potential to mitigate this damage by improving the function of mitochondria, the organelles that maintain and generate energy.

Komuraiah Myakala, a research instructor at Georgetown University, uses animal models that mimic Type 2 diabetic disease progression, known as db/db mice, when testing his hypotheses for DKD.

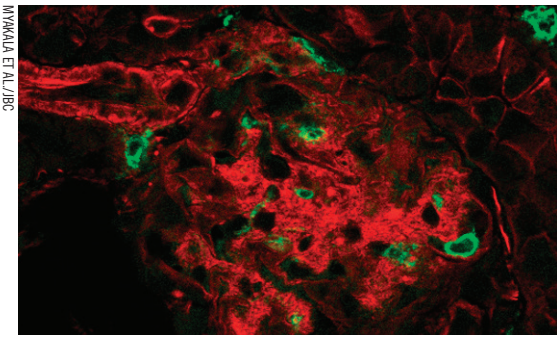
"We have to pick the right animal model to understand the disease," Myakala said. "Every metabolic disease is regulated by different signaling pathways; we need to understand, if there is a causal relationship in kidney disease progression, the signaling proteins involved."

During the study, db/db and healthy mice were given the supplement nicotinamide riboside, or NR. Also known as vitamin B3, NR is a precursor to the biologically functional form of nicotinamide adenine nucleotide, or NAD^+, and can increase its levels within the body. A critical co-enzyme in metabolic processes, NAD^+ is ubiquitous to every cell type, where it is essential to mitochondria metabolism and generating cellular energy.

The body naturally produces NAD^+. With age, levels decline naturally, and low NAD^+ also occurs with conditions such as diabetes, cardiovascular disease and neurological disorders.

"The etiology of kidney disease between diabetes and aging are very different," Myakala said. "Diabetes is usually a higher-grade kidney disease compared to age alone."

Inflammation is closely associated with damage to the mitochondria, and diabetic kidney disease. Giving NR to the db/db mice reduced inflammation and prevented many of the usual manifestations of kidney decline, for example, levels of blood-protein markers that rise in DKD progression were reduced after NR treatment.



MYAKALA ET AL./JBC

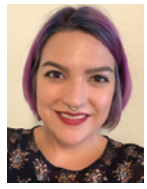
This immunofluorescence image shows a kidney cell derived from the diabetic mouse. Filamentous actin, a part of the cytoskeleton, is stained red to show cell structure. Macrophages, or immune cells, are green.

This research helps demonstrate the importance of mitochondrial function in renal disease, particularly in diabetes. Researchers still do not fully understand the mechanisms that link mitochondria and inflammatory disease, and they require further study. This research provides insight, however, into the potential of using supplemental NR to improve mitochondrial function and gives hope for DKD treatment.

Myakala describes his dedication to understanding the mechanisms of kidney disease as "unwavering." He and his colleagues hope to continue their research as they seek to bridge the gap in understanding that exists between inflammation, mitochondria and kidney disease.

DOI:10.1016/j.jbc.2023.104975

Nicole Lynn (nalynn@ucla.edu) holds a Ph.D. from UCLA and is an ASBMB Today volunteer contributor.



Circadian influences on lipid metabolism

By Elizabeth Stivison

Many biological processes are coordinated over time, creating rhythms of biological activity around the 24-hour day. In modern society, humans are often in situations when our behavior or environment — electric lights, food at all hours and shift work, for example — fights the circadian clock that coordinates these processes, a conflict that is implicated in a variety of health problems, including cancer and heart disease.

And it's not just in humans. A new study by researchers at Julius–Maximilians University in Würzburg, Germany, led by Agnes Fekete and Christian Wegener, provides insights into how the circadian clock and the external environment together regulate lipid metabolism in fruit flies.

The work, recently published in the **Journal of Lipid Research**, draws on Wegener's and Fekete's complementary fields: Wegener studies the circadian clock and Fekete lipid metabolomics. At the intersection were unanswered questions that intrigued them both.

"This combination of expertise that we have makes this special," Wegener said.

They were curious about lipid levels in hemolymph because this insect blood can serve as a window into metabolism at any given moment. "We were very surprised that there is no publication on the lipid oscillation in the hemolymph,"

Wegener said.

They had some doubts that they'd see circadian regulation of lipids this way because so many external influences affect what is in hemolymph at any time.

"When we started this project, we said, 'Oh of course it won't be rhythmic — we eat. We don't have any regulation from the body — it's all what we eat,'" Fekete said.

They addressed this by feeding the flies a diet lacking lipids; all lipids in the hemolymph had to come from biological processes.

When the flies ate this lipid-free diet, the researchers were amazed to see a clear rhythmicity of lipid transport, with peaks of lipids surrounding the times the lights were turned on in the morning and off at night (an effect that was hidden when the flies ate a lipid-containing diet), indicating underlying circadian control of lipid transport.

They then tracked the effects of activity, feeding, light and a circadian clock mutation. Flies kept in darkness cycled only once per day, while flies with a mutation in the circadian clock didn't cycle, indicating that the circadian clock drives rhythmic lipid transport, while light and dark cycling sets the timing. Activity and feeding behavior didn't drive the lipid peaks, so the peaks appear to prepare the body for predicted times when it needs to build and restore itself.

Next, Fekete and Wegener want to look into the source of lipids, as well as at other external influences, such as offset light and dark cycles to resemble shift work or a light-polluted environment.

Knowing that organisms regulate lipid transport around the circadian clock has implications for both human biology and the natural world. Flies, like those in the study, and pollinators such as bees also live in our light-polluted world, and we may inadvertently influence their metabolism.

Wegener summed up the relevance of constant clock disruption: "The clock is really good to optimize things but not required. We can live without the clock. However, if you mask the clock for a long time, then you will end up with problems."

DOI: 10.1016/j.jlr.2023.100417

Elizabeth Stivison (elizabeth.stivison@gmail.com) is a postdoctoral researcher at Vanderbilt University studying inositol signaling and a careers columnist for ASBMB Today.

More than one way to be good

A new role for HDL in the immune system

By Elizabeth Stivison

If you've had a blood test to check your cholesterol levels, your doctor probably told you both your so-called good, or high-density lipoprotein, and bad, or low-density lipoprotein, cholesterol levels. HDL is known for helping your body get rid of LDL, and this is great for your cardiovascular system; LDL is a component of atherosclerotic plaques that build up in arteries and lead to heart attacks.

However, researchers have begun to see that story as incomplete. Several groups at Cincinnati Children's Hospital Medical Center and the University of Cincinnati College of Medicine working together recently published a study in the **Journal of Lipid Research** showing one way that HDL does much more than remove LDL.

Claire Chougnet is the corresponding author on the study. "It has become clearer and clearer to the field that HDL is acting through other mechanisms," she said, "particularly through immune modulating capacity."

That the immune system influences cholesterol and health isn't news. In fact, macrophages taking up LDL is one of the first steps down the path to developing atherosclerotic plaques in the arteries.

Macrophages are part of the innate immune system, however, and Chougnet and her group were interested in the other arm, the adaptive immune system, which has a less clear role in metabolic disease.

Laura Atehortua is the first author on the paper. "It is well known that innate immune cells recognize HDL," she said, "so we wondered what is going to happen with adaptive immune response."

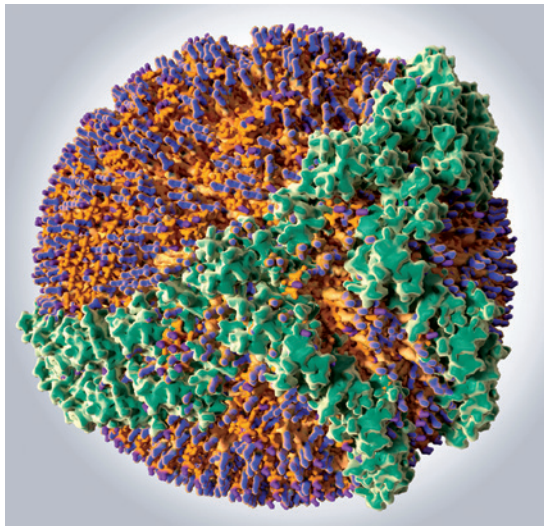
Using human samples from blood banks, which requires meticulously repeating the experiments many times to account for the inherent variability in the samples, the researchers found that HDL can prevent cell death in T regulatory cells, or Tregs, a type of $CD4^+$ T lymphocyte responsible for resolving inflammation.

Atehortua explained the role of Tregs. "They're very important for the immune system," she said. "They're the ones that say 'oh it's enough.'"

Researchers have shown that the number of Tregs, which is regulated by the balance between Treg proliferation and Treg death, influences the overall level of inflammation in the body, which in turn influences atherosclerosis, metabolic diseases and other conditions including autoimmune diseases.

Once they found that HDL prevented Treg death, but not that of other $CD4^+$ T lymphocytes, the researchers wanted to figure out what exactly in the HDL was having this effect, and they expected lipids to be the key. However, using reconstituted HDL particles lacking various components, they found that it wasn't the lipid, but the proteins in the HDL particles that acted on Tregs to prevent their death.

"This was not at all what we expected," Chougnet said. "The first surprise was that it was not the lipid but the protein, and the second surprise was that in the protein, it was a relatively minor protein not the major protein."



The researchers found the prosurvival effect was mediated by apolipoprotein E, a protein found less abundantly on HDL than the more common apolipoprotein A.

This work may help scientists design better treatments for cardiovascular and metabolic diseases, as it highlights a potential point of intervention to reduce systemic inflammation.

DOI:10.1016/j.jlr.2023.100425

Elizabeth Stivison (elizabeth.stivison@gmail.com) is a postdoctoral researcher at Vanderbilt University studying inositol signaling and a careers columnist for ASBMB Today.

Sibling study reveals mechanism for genetic disease

By Ken Hallenbeck

Genetic diseases pass from parents to children — often in surprising ways. The unpredictability of these transfers means that sometimes a disease skips whole generations, while other times it may affect only one sibling. Pairs of affected and unaffected siblings provide a unique opportunity for scientists to study the molecular mechanisms of genetic disease.

Unraveling the connection between the genetic mutation a person carries and the symptoms they have has been a decades-long focus of Yi-Wen Chen's laboratory, part of the Center for Genetic Medicine Research at Children's National Hospital in Washington, D.C. Chen's expertise is in genetic muscle disorders, which occur in 59 out of every 100,000 adults in the United States.

Muscle weakness can sometimes start early — even in the womb. Other times, as is the case with the second-most common muscle disorder, adult-onset facioscapulohumeral muscular dystrophy, or FSHD, symptoms begin much later, in adolescence or early adulthood. Why is this, and does it hint at a way to design treatment?

To answer these questions, Chen's laboratory teamed up with proteomics expert Jatin Burniston of the Research Institute for Sport and Exercise Sciences at Liverpool John Moores University. They studied affected and unaffected sibling pairs using proteomics experiments designed to reveal the underlying mechanisms of FSHD.

The researchers took cell cultures from each sibling and incubated them with deuterium, or "heavy water." Then, they tracked the lifespan of each protein in the cell with mass spectrometry. The results, described in a recent article in **Molecular & Cellular Proteomics**, implicate slower turnover of mitochondrial proteins, but more abundant mitochondrial proteins in the sibling with FSHD. Slower turnover means old proteins — which should be recycled — pile up in the mitochondria, triggering stress responses and interrupting normal cell function. The finding is a clever combination of atomic-level detail and good biological controls.

Yusuke Nishimura, a postdoctoral research associate in Burniston's lab is a co-first author on the paper.

"Mitochondrial dysfunction and mitochondrial stress in FSDH had been identified in previous studies," Nishimura said. However, that information alone wasn't enough to begin designing a treatment. Because FSHD varies widely between individuals, "studying (the) underlying biological mechanisms is challenging," he said.

Differences in protein turnover observed when comparing FSDH patients with healthy individuals may not be caused by the disease, but simply be normal variances between unrelated people. That's where the sibling pair comes in — by simultaneously analyzing a sibling with FSHD and a sibling without the disease, Nishimura and collaborators were able to unravel the FSHD mystery.

FSHD has no treatment or cure. "Our new data on mitochondrial protein dynamics in FSHD is particularly exciting because highlighting dysfunctions in protein turnover offers a potential new therapeutic route," Nishimura said.

If the evidence continues to mount, therapeutic strategies such as targeted protein degradation might be used to restore order to the mitochondria in FSHD patients.

DOI:10.1016/j.mcpro.2023.100605

Ken Hallenbeck (k.hallenbeck@gmail.com) is an early drug-discovery researcher. He is a member of the ASBMB Today editorial advisory board and a volunteer contributor.

Proteomics study isolates drug targets

By Oluwadamilola "Dami" Oke

Target identification is a major stage of early drug development — the point when researchers identify a biological element implicated in a disease that can be regulated by a therapeutic agent.

One research team in Germany has recently focused on myeloid-derived suppressor cells, or MDSCs, which are blood cells that are not fully differentiated. These cells suppress immune cell activities and promote cancer, infection and inflammatory diseases. By screening MDSCs from mice, the researchers took the first step in identifying potential targets that can modulate MDSC activity.

Johannes Krumm, a scientist at OmicScouts GmbH, and Bernhard Küster, a professor at the Technical University of Munich, collaborated with the pharmaceutical firm Merck & Co. on the study. They recently published their findings in the journal **Molecular & Cellular Proteomics**.

The research team used high throughput screening, a technique that allowed them to cross-test large quantities of compounds against several factors to identify potential drug targets. The screening narrowed the potential targets from 20,818 compounds in the MDSC mice cells to 104 compounds that also modulated MDSC activity in human cells.

Krumm and Küster both hope that this paper "motivates further research groups and biotech/pharma companies to consider proteomics as a tool for drug discovery," they wrote in an email.

Proteomics combines biological assays and computer software to analyze large numbers of proteins and their associated interactions. This characterization explores the whole data set and can uncover patterns that merit further investigation.

"The strong point about proteomics is that no initial hypothesis is needed," Krumm and Küster wrote.

In this study, their data showed that an unknown compound suppressed MDSC activity in the mouse cells. They tested this compound in immunoassays with human cells where its immune activity ranged from no effect to strong effect. Following a round of proteomic analysis, they found that the active compound upregulated the expression of proteins responsible for cell detoxification; this led to a reduction in reactive oxygen species, which play a role in promoting various diseases, including cancer. By studying this pattern, the researchers determined that a strong potential mechanism of action for new drugs to modulate MDSC activity would be to upregulate proteins that reduce reactive oxygen species.

"We were rather surprised to see how selectively the active compound upregulated proteins associated with detoxification functions," Krumm and Küster wrote.

In their analysis, they found two proteins that closely upregulated MDSC activity: acylphosphatase 1, also known as ACYP1, and a HLA class II histocompatibility antigen gamma chain protein, also known as CD74.

PROTEIN DATA BANK

Acylphosphatase 1 (ACYP1), one of the potential drug target proteins identified for attacking myeloid-derived suppressor cells.

In the future, drug developers looking to target MDSC immunosuppression could focus on the downregulation of ACYP1 and CD74 to attack MDSCs. This study is "a good example for how proteomics can be used for drug discovery in general and in mode of action hypothesis in particular," Krumm and Küster wrote.

"By making all data available to the public," they concluded, "we hope that biologists in the field of MDSCs will find our data and chemical tool compounds useful and enriching to their own research."

DOI: 10.1016/j.mcpro.2023.100632

Oluwadamilola "Dami" Oke (okeo@gwu.edu) is a Ph.D. candidate of biomedical engineering at the George Washington University with an interest in communication and outreach. She is an ASBMB Today volunteer contributor.

From the journals

By Ken Farabaugh, Elisabeth Adkins Marnik, Aswathy N. Rai, Marissa Locke Rottinghaus & Lydia Smith

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

Location matters in liver disease

Alcoholic related liver disease is a leading cause of chronic liver disease-related mortality in Western countries, but researchers do not yet completely understand the condition. Excessive alcohol consumption can lead to an imbalance in the biogenesis and breakdown of lipids and to mitochondrial dysfunction. Steroidogenic acute regulatory protein, or StARD1, regulates steroid hormone synthesis and mediates the transport of cholesterol from the outer mitochondrial membrane to the inner mitochondrial membrane. In addition, StARD1 has been shown to promote nonalcoholic fatty liver disease.

In a recent study in the **Journal of Lipid Research**, Raquel Fucho and Estel Solsona–Vilarrasa of the Institute of Biomedical Research of Barcelona, Spain, and colleagues investigated the role of StARD1 in chronic liver disease and alcohol-induced

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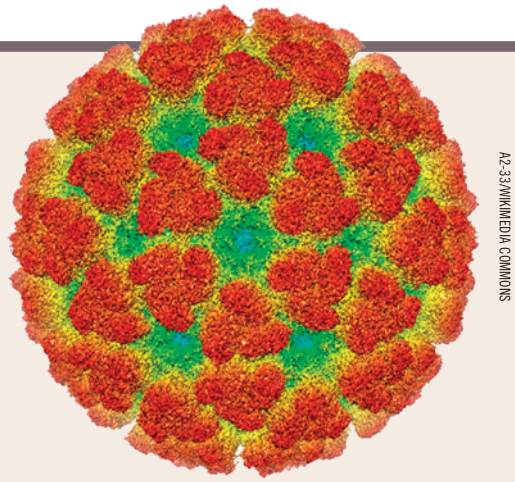
Cap-snatching viruses

Alphaviruses like the chikungunya virus, or CHIKV, are positive sense single-stranded RNA viruses that use a unique messenger RNA capping machinery distinct from that of host cells, which makes this machinery a great candidate for antiviral drugs. The N7-methylguanosine RNA cap can recruit cellular proteins to initiate translation, and its removal or "decapping" can lead to exoribonuclease-mediated degradation; as such, many viruses have evolved strategies to cap their own mRNAs, or even to decap host RNAs to create decoy noise and mask their own RNA production.

Recent cryo-electron microscopy structures of the CHIKV capping enzyme nsP1 indicated that the methyl group is first stolen from a host RNA and added to nsP1, and then it is transferred using nsP1's guanylyltransferase activity to the viral RNA. In their new study published in the **Journal of Biological Chemistry**, Michelle Cheok Yien Law and colleagues at Nanyang Technological University in Singapore explored this process using cryo-EM structures of their own with nsP1 bound to RNA substrates. They showed that not only can nsP1 remove the N7-methylguanosine cap from both host and viral RNAs, but that this decapping can trigger the host interferon immune response.



A2-33/WIKIMEDIA COMMONS

Using an RNA structure that mimics the native host cap, they used cell-based assays to demonstrate that nsP1 decapping activity activates RIG-I-mediated type I interferon signaling.

The authors theorize that CHIKV nsP1 may selectively decap certain mRNAs to prevent translation overload and alerting cells in the early stages of infection. It is also possible that the ratio of capped to decapped RNAs can impart some kind of signal crucial for viral replication or immune escape. Future work will be necessary to determine the roles of RNA decapping in relevant biological systems, as well as the roles of interaction of nsP1 with other viral and host proteins.

DOI: 10.1016/j.jbc.2023.105415

—Ken Farabaugh

liver injury. Using mouse models of alcohol-related liver diseases, the team showed that alcohol feeding induces StARD1 expression in perivenous zone liver hepatocytes. By contrast, animals that were not fed alcohol showed StARD1 expression in the periportal liver hepatocytes. Transmission electron microscope images revealed that alcohol feeding increased lipid droplet accumulation and mitochondrial number in the perivenous zone.

These results demonstrate that the role of StARD1 in hepatocyte mitochondrial metabolism depends on their location within the liver during alcohol-related liver disease.
DOI: 10.1016/j.jlr.2023.100413

Can nerves be made to regenerate?

After a peripheral nerve injury, specialized glial cells of the peripheral nervous system called Schwann cells change from their mature, stable form to adopt a phenotype that can migrate to sites of injury and proliferate to promote nerve regeneration. Therefore, scientists have been seeking ways to activate the Schwann cell repair response as a clinical treatment for peripheral nerve injuries.

In a recent article in the **Journal of Biological Chemistry**, Qianqian Chen and colleagues at Nantong University in China describe their finding that the transcription factor FOS-like 1, or FOSL1, is highly expressed at sites of nerve crush. Using short interfering RNA that suppressed FOSL1 expression, chromatin immunoprecipitation and proliferation assays, the researchers showed that FOSL1 binds to the promoter of the tyrosine protein kinase receptor-encoding gene EPHB2 and induces its transcription; the Schwann cells then proliferate and migrate. Following this line of evidence, these authors demonstrated that EPHB2 increases the proliferation rate and movement speed of Schwann cells.

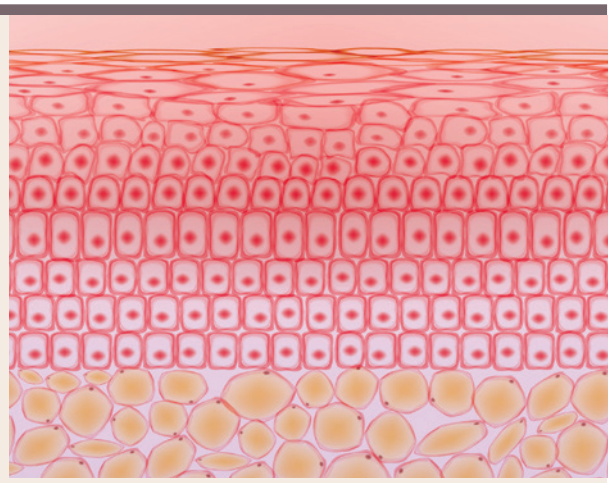
The researchers found essential roles of FOSL1 and EPHB2 in the Schwann cell repair response and suggest they are potential therapeu-

What activates T cells in psoriasis?

Psoriasis is a disease commonly identified by lesions; skin cells proliferate, white blood cells infiltrate and lipid metabolism is altered in the skin. In the past, researchers have shown that n-3 polyunsaturated fatty acids, or PUFAs, may suppress this inflammation, thus slowing disease progression. A recent study in the **Journal of Lipid Research** by Sophie Morin and a team at Laval University aimed to identify the role of n-3 PUFAs — specifically eicosapentaenoic acid, or EPA — in T cell activation and polarization in psoriasis.

Characteristically, psoriasis causes an increase in IL-17A, an inflammatory cytokine produced primarily by the Th17 subset of helper T cells, commonly known as $CD4^+$ T cells. Morin's team found that, in the presence of EPA, IL-17A production is reduced, and $FOXP3^+$ regulatory T cell production increases. They determined that EPA inhibition of STAT3, a signaling protein on the cell surface that activates and polarizes Th17 cells, prevented polarization to a Th17 proinflammatory phenotype. This inhibition was specific to STAT3; EPA did not reduce polarization to a proinflammatory Th1 phenotype via STAT1.

The researchers used a 3D model of psoriatic skin



to show that EPA reduced proliferation of skin cells, transduction protein phosphorylation and transcription activation. They also noted that the NF-κB pathway was altered, which led to increased concentrations of Fas, a death receptor located on the cell surface, causing increased cell death.

The researchers deduced that EPA and other n-3 PUFAs act as anti-inflammatory mediators of psoriasis by simultaneously producing regulatory T cells and reducing proinflammatory T cell phenotypes, as well as altering major signaling pathways promoting psoriasis symptom reduction.
DOI:10.1016/j.jlr.2023.100428

—Lydia Smith

tic targets for treating peripheral nerve injury. Scientists will need to do additional studies to identify whether and how to target this signaling axis to promote nerve regeneration.
DOI: 10.1016/j.jbc.2023.105444

New technique helps detect protease cleavage

Proteases are enzymes responsible for cleaving proteins into smaller polypeptide chains or individual amino acids. This cleaving can modulate specific proteins and regulate key cellular processes. One such process is apoptosis, a form of programmed cell death, where various proteases are instrumental in initiating the breakdown of cellular protein components.

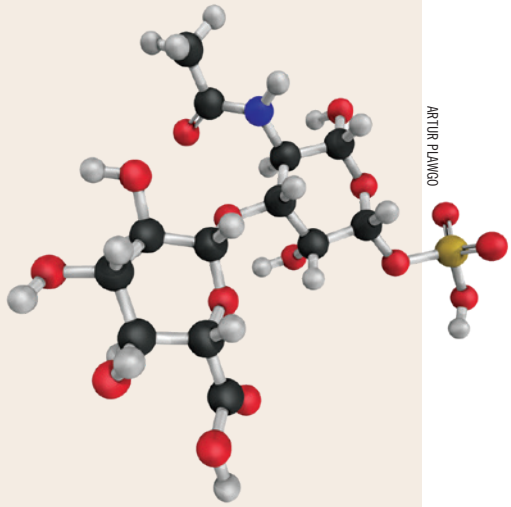
Proteases are important enzymes, and researchers need to be able to catalog their targets when studying the proteome. However, using mass spectrometry, or MS, to identify protein fragments generated by proteases is difficult.

To address this, Rawad Hanna and colleagues at the Technion–Israel Institute of Technology developed a new technique called LysN amino terminal enrichment, or LATE. This technique combines digestion with LysN and isotope labeling of the N-terminal end of a protein to better identify cleaved proteins in MS analysis.

The researchers recently described this work in the journal **Molecular & Cellular Proteomics**. By using LATE, they were able to identify novel targets of cleavage by caspase-3, a protease involved in apoptosis. They also discovered cross-talk between caspase-3 cleavage and N-terminal acetylation.
DOI: 10.1016/j.mcpro.2023.100584

Amino acids and sulfate signatures

Chondroitin sulfate proteoglycans, called CSPGs, are complex molecules that surround cells and provide not only structural and biochemical support to various tissues in the human body, including the nervous system, cartilage, bone and connective tissues, but also influence organ differentiation and regeneration. They are made up of a core protein to which chondroitin sulfate chains, or CS chains, are attached at specific serine residues. CS chains are long, linear sugars composed of repeating often sulfated units of glucuronic acid and N-acetylgalactosamine.



ARTUR PLAWGO

Chondroitin sulfate, shown here as a 3D structure, is a sulfated glycosaminoglycan composed of a chain of alternating sugars.

Sulfation can occur at different positions on the amino sugar and the uronic acid, leading to various sulfation patterns. These variations contribute to the diverse biological functions of chondroitin sulfate. Core protein structure, CS chain length and sulfation patterns vary widely in CSPGs, complicating the characterization of a standard representative sequence for a given CSPG. Chondroitin sulfate signatures may serve as biomarkers for certain diseases or conditions. Identifying unique patterns associated with specific health states can aid in the development of diagnostic tools.

Mass spectrometry is a powerful tool for sequencing CSPGs, but technical challenges still exist in determining how CS structures vary among them. In a recent article published in **Molecular & Cellular Proteomics**, Fredrik Noborn and colleagues from the Institute of Biomedicine at the University of Gothenburg, Sweden, report a novel glycoproteomics approach for characterizing the sequence of CS modification at specific sites of attachment to the core proteins.

With a combination of CS glycopeptide enrichment, using strong anion exchange chromatography, depolymerization of CS polysaccharides and nanoscale reversed-phase liquid chromatography-tandem mass spectrometry, the authors determined the sulfation patterns of CS in protein attachment sites of CSPGs in human urine samples. The approach showed that the acidity of amino acid sequences around the CS attachment site corresponds to higher sulfation levels in the CS chains. This approach will help researchers analyze the structure-function relationships of CSPGs in the future, which can guide the design of drugs for diseases with altered CSPG modifications.
DOI: 10.1016/j.mcpro.2023.100617

— Aswathy N. Rai

Enzyme activity in a crowd

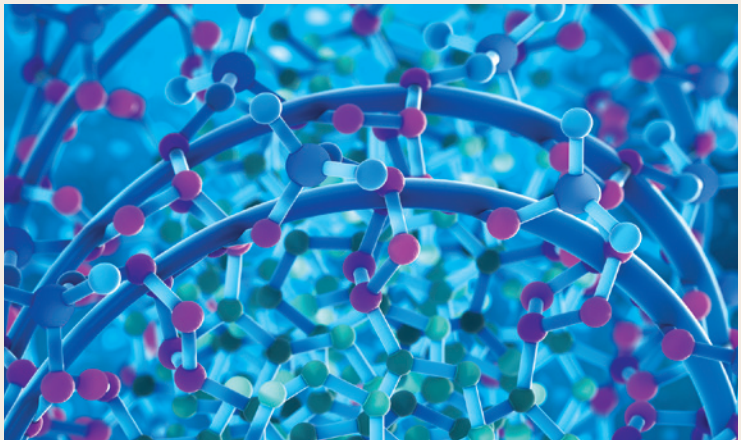
Macromolecular crowding, or an increase in concentrations of proteins and nucleic acids, can occur when limited water is available or a cell's volume is reduced. These cramped conditions can affect protein–protein interactions, protein–DNA interactions and rates of biochemical reactions. In addition, many enzymes behave differently in a laboratory compared with their native conditions of molecular crowding in living cells, particularly bacterial cells.

In a recent paper in the **Journal of Biological Chemistry**, Zifang Deng and colleagues at the Florida International University describe how they examined the activity of Mycobacterium tuberculosis, or Mtb, DNA gyrase, the enzyme responsible for maintaining the negative supercoiling of double-stranded DNA, under conditions of macromolecular crowding. They treated cells with polyethylene glycols, or PEGs, and polyvinyl alcohols, or PVAs, to induce intracellular crowding and then examined the activity of the DNA gyrase using enzymatic and gel-based assays. They then used molecular dynamics simulations to determine changes in the DNA gyrase structure.

These simulations showed that high PEG concentrations kept the gyrase in a closed or semiclosed conformation, keeping adenosine triphosphate, or ATP, molecules trapped in a binding pocket, likely leading to the enhanced binding of ATP and DNA and increased efficacy and speed of DNA supercoiling activity.

The authors conclude that DNA gyrase activity increases under conditions of macromolecular crowding likely because water is excluded from hydrophobic interaction surfaces, which typically promotes tighter binding. Also, activity can increase due to steric repulsion, which limits the enzyme's freedom to adopt additional conformations. The systematic and quantitative analysis of Mtb gyrase enzymatic activity highlights the importance of studying enzymes in their native environments, especially during stress, and could help inform research into drug strategies used to treat multidrug-resistant tuberculosis.
DOI: 10.1016/j.jbc.2023.105439

— Ken Farabaugh



Controlled diet targets heart disease risk

Saturated fatty acids, or SFAs, are found in foods such as full-fat dairy, red meat and poultry. Scientists have linked SFAs to production of low-density lipoprotein cholesterol, or LDL-C, which increases the risk of cardiovascular disease, or CVD. In the past, researchers have found that lipoprotein(a), or Lp(a), is similar to LDL-C, but poses an independent risk for CVD. While these factors are true for most ethnicities, individuals of African American descent experience a higher risk. For this reason, Hayley G. Law at the University of California, Davis, and her collaborators aimed to identify an SFA-dependent relationship between Lp(a) and CVD risk in African American populations. They wrote about their work in a study recently published in the **Journal of Lipid Research**.

Study participants ate two diets sequentially, each for five weeks. The first was similar to the average American diet, or AAD, while the second contained a decreased amount of SFA. This diet resembles the dietary approaches to stop hypertension, or DASH, diet, which was supplemented with carbohydrates. As expected, switching from an AAD diet to a DASH diet resulted in a significant reduction in cholesterol, specifically LDL-C. Lp(a) levels were increased upon switching to the DASH diet, which the researchers speculate may be due to the carbohydrate supplementation. In the future, they may examine this relationship more deeply, determine the specific mechanisms that cause Lp(a) increases with SFA reduction and identify appropriate nutritional replacements.
DOI:10.1016/j.jlr.2023.100420

The challenges and promises of biomarkers

Biomarkers, typically proteins detected in patients' blood or tissue, hold significant potential to help clinicians practice medicine more effectively. They can be used to diagnose and monitor disease progression, identify targets for drug development, monitor treatment effectiveness and predict which patients are at risk for drug side effects. Despite the promise of their utility, however, researchers have seen limited success and faced many challenges in bringing biomarkers to the clinic.

In a recent article in the journal **Molecular & Cellular Proteomics**, Jakob Bader and colleagues at the Max Planck Institute described challenges, technological advancements and success stories related to using mass spectrometry to identify biomarkers from body fluid samples. Many of the challenges were due to technological difficulties in high-throughput sample processing.

Researchers now address many of the challenges of biomarker discovery by using automation and simplified and improved protocols. Due to the many technological improvements the authors outline, it is possible to use larger cohorts of patients for better biomarker identification. This could mean the future is here, and with it, hopefully, the discovery of better biomarkers.
DOI: 10.1016/j.mcpro.2023.100577

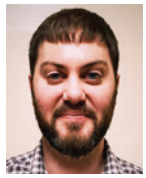
Preventing bacteria from sensing each other

A great struggle doctors and scientists face in fighting bacterial infections is using drugs without introducing selective pressure for those bacteria to develop drug resistance. One strategy to address this dilemma is developing molecules that affect bacterial quorum sensing, or QS, a process that allows bacteria to sense their population density and alter their gene expression once a quorum is reached.

In their new study published in the **Journal of Biological Chemistry**, Tahmina Milly and colleagues at the University of Nevada, Reno, explore the competence regulon QS circuitry in Streptococcus mitis, a commensal bacterium that would have pathogenic potential if it adopted virulence genes from the related bacteria S. pneumoniae. These authors used mutational scanning and circular dichroism spectroscopy to determine the structural motifs needed to bind the S. mitis competence-stimulating peptide to its receptor, and they even identified a peptide that could modulate QS in both S. mitis and S. pneumoniae.

These results demonstrate that the S. mitis competence regulon can modulate pathogenic phenotypes including biofilm formation. Using this QS-modulating scaffold, scientists can now further study the effects of temporal QS modulation in the natural bacterial environment and potentially find ways to inhibit bacterial competence.
DOI: 10.1016/j.jbc.2023.105448

Ken Farabaugh (kfarabaugh@asbmb.org) is the ASBMB's science editor.

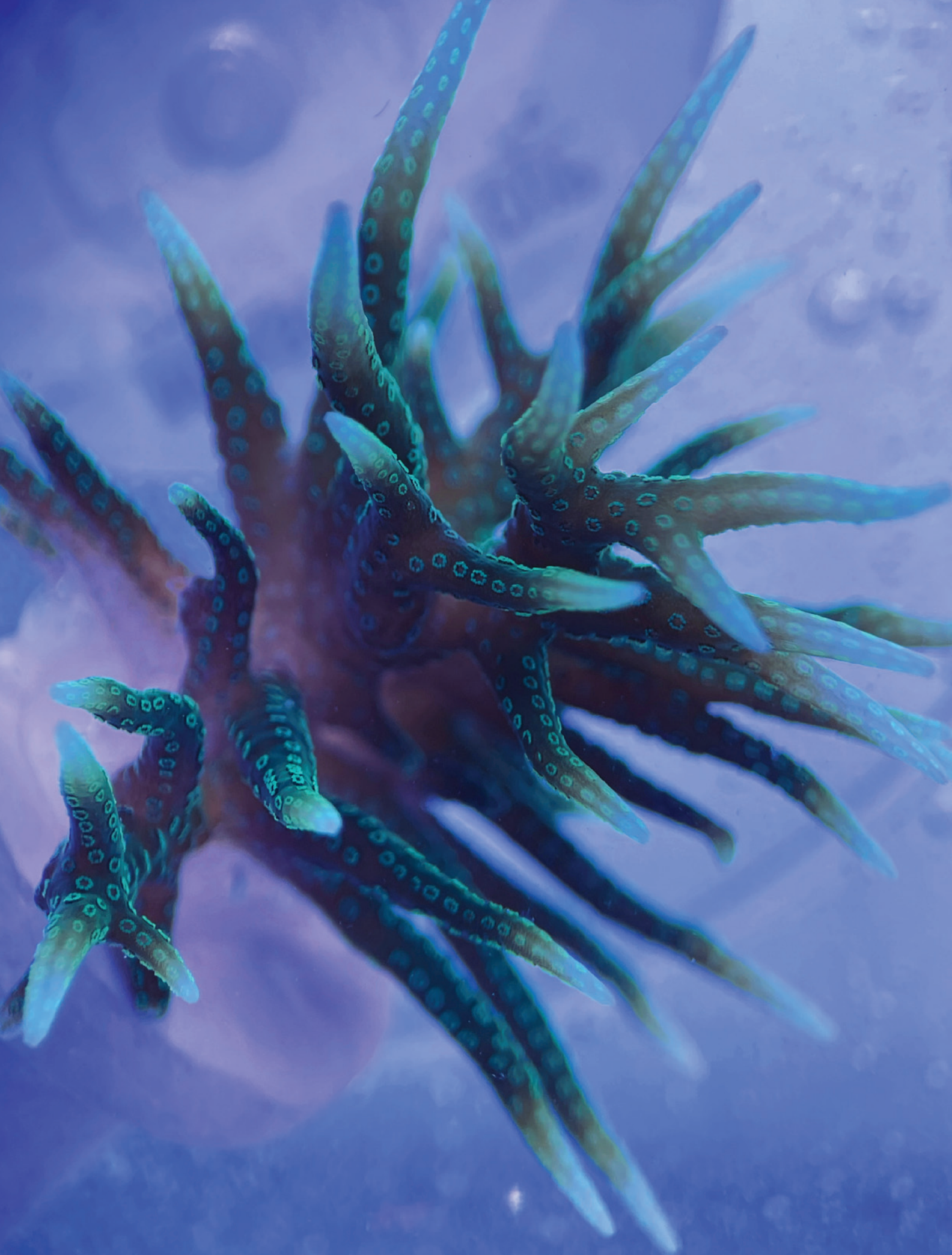


Elisabeth Adkins Marnik (marnike@husson.edu) is an assistant professor of molecular biochemistry at Husson University. She studies the mechanisms that help maintain germline stem cells and how these can be co-opted in cancer. She is an ASBMB Today volunteer contributor.

Aswathy N. Rai (aswathy.rai@msstate.edu) is an assistant teaching professor and undergraduate coordinator at Mississippi State University's department of biochemistry, molecular biology, entomology and plant pathology. She is an ASBMB Today volunteer contributor.

Marissa Locke Rottinghaus (mlocke@asbmb.org) is the science writer for the ASBMB.

Lydia Smith (lyd.smith2001@gmail.com) has a B.S. in molecular cell biology from California State University, Long Beach and is working toward a Ph.D. in microbiology and immunology at the University of Utah. She is an ASBMB Today volunteer contributor.



‘Cities under the sea’

Nanotechnology offers a way to restore and recreate coral reef biodiversity

By Marissa Locke Rottinghaus

Liza Roger grew up exploring the wonder and mystery of the oceans — in front of a television in her childhood home and in the rockpools along the coast of Normandy, France. She fell in love with the underwater world, guided by Jacques-Yves Cousteau, an award-winning filmmaker sometimes called the “father of scuba diving.” Cousteau’s documentaries reveal vibrant and diverse creatures such as corals, which inspired Roger to dive into marine biology.

Her first foray into scuba diving took her to the depths of the Mediterranean Sea.

“I loved being underwater and seeing marine life in action,” Roger said. “For me, it felt full of discoveries, adventures and treasures.”

Now an assistant professor and a senior global futures scientist at Arizona State University, Roger has devoted her career to the ocean invertebrates that populate coral reefs.

Roger takes an outside-the-box approach to ocean conservation and has partnered with nanotechnologists to protect and restore the thousands of coral species that make up the world’s remaining reefs.

“At ASU, we are oriented toward making the world better for future generations,” Roger said. “We are all about innovation and bringing multidisciplinary teams together.”

Ninety percent of the world’s coral reefs could be decimated by 2050 due to climate change, overfishing and coral disease outbreaks, Roger said, and saving these reefs is a daunting challenge because researchers lack foundational knowledge.

SAMANTHA CHOW, ARIZONA STATE UNIVERSITY NEWS

LIZA ROGER

Exploring uncharted waters

Corals are invertebrate animals that build complex underwater colonies. They contain specialized cells that harbor algae, forming a mutually beneficial endosymbiotic partnership. Corals and their jellyfish cousins top the list as

LIZA ROGER

NIKKI TRAYLOR–KNOWLES

Liza Roger scuba dives in Thailand.

LIZA ROGER

some of Earth's most ancient animals. However, coral research has long taken a back seat to other topics, according to Roger.

"The questions we've answered in mammalian systems need to be examined in corals, and the need is urgent," she said.

She likened these reefs to "cities under the sea," in which corals are the engineers that provide the structures supporting other living things. Coral reefs are home to thousands of species including fish, crabs, lobsters, clams and more, which feed an estimated 850 million people annually.

As in the legend of the lost city of Atlantis, most people overlook coral reefs because they don't occupy everyone's backyard, Roger said.

However, coral reefs contain potent chemicals, which medical professionals now use as treatments for cardiovascular diseases and cancers. In fact, the majority of all new cancer drug research focuses on examining marine organisms, many of which live on coral reefs.

In a lab, coral cells can be difficult to grow and require specialized equipment to maintain, Roger said. At ASU, she cultivates dozens of shallow-dwelling corals and related invertebrate species, such as sea anemones and jellyfish. These creatures grow under blue light in the lab, which mimics their natural light source in the ocean. As the depth of the ocean increases, colors such as reds and oranges are filtered out, and blue light remains.

Despite advances in molecular biology and genomic sequencing, most coral research has been limited to multicellular coral colonies or heterogeneous cell mixtures, Roger said, because isolating uniform cell cultures is challenging.

Recently, scientists identified the cell types that make up coral. In addition, researchers have adapted CRISPR–Cas9 technology to alter the genes in coral — almost two decades after scientists used a similar technique to create the first knockout mouse.

Much about basic coral biology still eludes researchers.

Nikki Traylor–Knowles, an associate professor in marine biology and ecology at Miami University, studies the coral immune system. She said she struggles to strike a balance between basic and translational coral research.

"We're often operating under an 'emergency scenario,' which makes it really hard to get answers," Traylor–Knowles said. "There's a constant feeling of playing catch up on a shoestring budget to save this really important ecosystem that we've just started to understand."

Stressed out

Corals comprise over 40 cell types and partner with algae, which give reefs their dazzling colors. In return for a protected home, algae provide their coral hosts with essential nutrients.

Thermal stress, irradiation, disease, ocean acidification as well as deoxygenation and other factors cause coral bleaching, which threatens coral survival and their endosymbiosis with algae. Bleaching triggers symbiosis breakdown and transforms corals into lifeless skeletons. Researchers have not completely ironed out the mechanisms behind coral bleaching, but most agree that free radicals play a

major role.

"When corals get stressed, like us, they release a burst of reactive oxygen species and go into oxidative stress," Roger said.

During stressful periods, nutrient transfer from algae to coral host breaks down, and the coral may starve without other nutrients from the ocean. In the algae, thermal stress disrupts photosynthesis and mitochondrial electron flow. This leads to toxin buildup, coral immune responses and cell membrane breakdown.

However, Traylor–Knowles said, it is difficult to know if a coral is stressed before it is too late.

"We often don't know if a coral is sick until it's bleached or basically sloughing off its tissue, which means it's dead."

Traylor–Knowles' lab develops tests to probe coral health so researchers can intervene and treat corals before bleaching.

"Corals are so fragile," Saborni Chowdhury, a graduate student in the Roger lab, said. "A slight change in pH or salinity can kill or affect their metabolism.… But they are so valuable. A lot of their basic biology has been understudied because the focus has been on ecology."

VIRGINIA COMMONWEALTH UNIVERSITY

NASTASSJA LEWINSKI

Nifty nanotech to the rescue

During her postdoc, Roger worked with Nastassja Lewinski, an associate professor of chemical and life science engineering at Virginia Commonwealth University. Their goal: use advances in nanotechnology to combat coral bleaching.

Nanotechnology is the understanding and control of matter at dimensions between approximately one and 100 nanometers and has been used in medicine for more than a decade, despite public skepticism. Examples include everything from drug delivery systems such as lipid nanoparticles to mineral-based sunscreens.

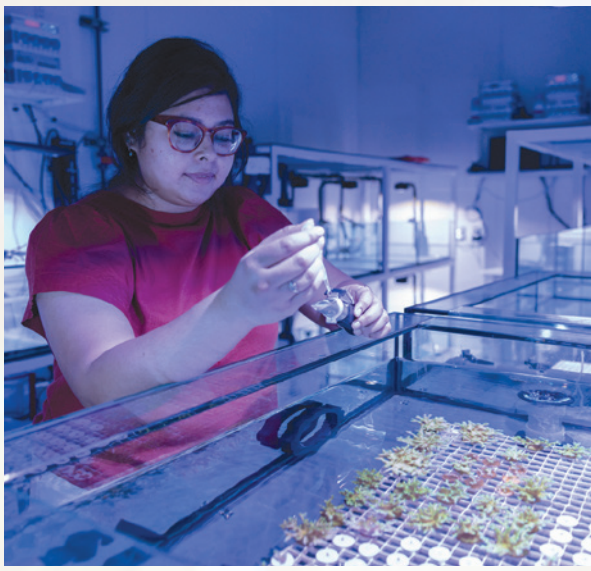
"The public is very scared of 'nano' things," Roger said. "But we need society to understand the science behind nanotechnology, and we are being very careful not to do any harm."

Roger and Lewinski used the antioxidant properties of nanoceria, or cerium dioxide nanoparticles, to eliminate toxins from stressed corals. Lewinski compared nanoceria's activity to that of the enzyme superoxide dismutase.

Unlike other metal oxides, nanoceria can exist in two different electron states depending on their environment. This means they can act as a free radical scavenger at a physiological pH and a reactive oxygen species generator in an acidic environment, such as inside a cancer cell or bacteria.

Since bleaching begins with the algae symbiont, Roger and Lewinski focused their study on a free-living algae, Breviolum minutum. They hypothesized that polyacrylic acid-coated nanoceria could reduce reactive oxygen and reactive nitrogen species in B. minutum under high temperatures.

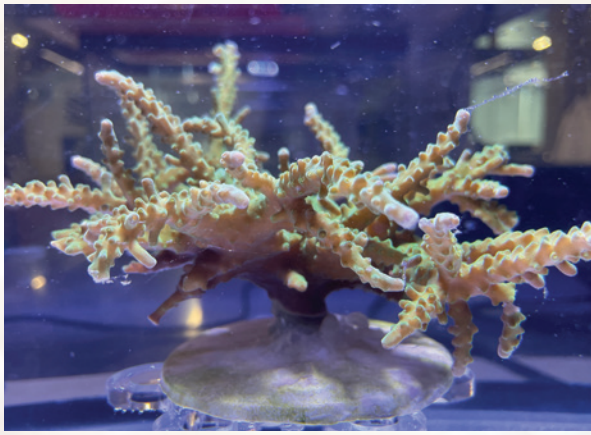
In the lab, the team exposed the



SAMANTHA CHOW, ARIZONA STATE UNIVERSITY NEWS

Saborni Chowdhury is a graduate student in Liza Roger's lab at Arizona State University.

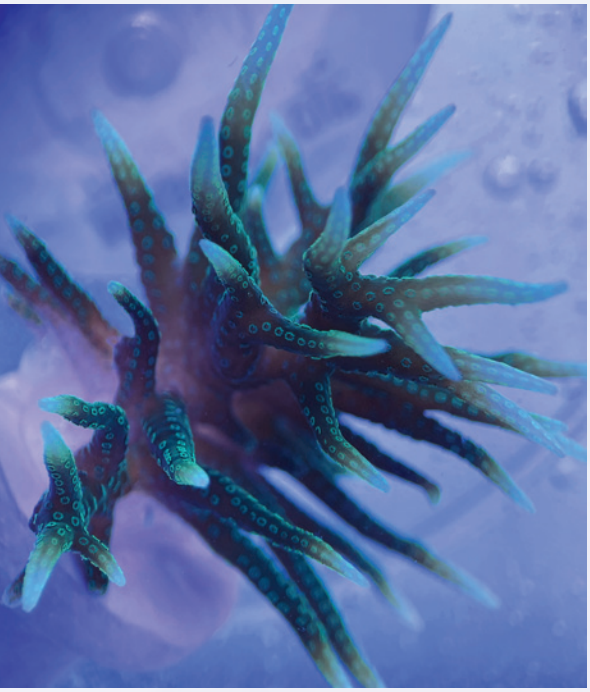
A green Acropora coral growing in Liza Roger's lab.



LIZA ROGER

JENNIFER MATTHEWS

A Seriatopoa coral growing in Liza Roger's lab.



LIZA ROGER

algae to two temperatures: 27 °C, a normal tropical water temperature, and 34 °C. After nanoceria treatment, they saw a fivefold decrease in intracellular reactive oxygen levels in B. minutum under hotter temperatures. Nitric oxide also diminished by 17%. These changes occurred after a one-hour treatment, and nanoceria did not hamper algae survival or growth.

"I don't see this as a 'miracle solution,'" Roger said. "I see this as a short-term treatment to help corals until humanity acts."

Roger and Lewinski will continue testing coral nanoparticle delivery methods. Lewinski said they may take inspiration from drug delivery methods such as microneedles, patches and hydrogels.

"My postdoctoral work was my first foot into the door of nanotechnology," Roger said. "It really opened up doors to a lot of other opportunities and ideas.… These techniques are quite advanced in plants and humans; it's not a big leap to develop them for corals. We just have to find the right targets."

In her lab, Roger said she will investigate how to improve coral model systems and mitigate bleaching using nanotechnology. Chowdhury is using her skills in molecular biology and proteomics to study heat shock proteins in corals and other invertebrates, such as jellyfish and sea anemones.

"Some marine organisms have a higher bleaching tolerance than others," Chowdhury said. "We want to understand the proteins and the underlying biochemical pathways that lead to bleaching tolerance in coral cousins like jellyfish and giant clams. Then, we could extract those special biomolecules, package them and deliver them to corals to give them a better chance of survival."

Heritage beneath the waves

More than 800 million people depend on coral reefs for food, coastal protection and tourism, especially in the Caribbean and south Asia, according to a study in the journal PLOS ONE.

"Coral reefs are a part of the communities that live in these areas," Roger said. "They are a part of their cultural heritage, a part of the history and a part of their economy. Coral reefs are how they feed themselves. With all of these needs, we can't let them be wiped out."

Jennifer Matthews, a research fellow at the University of Technology Sydney, fell in love with corals during a vacation in Thailand.

"I went on holiday to learn how to (scuba) dive," Matthews said. "I went underwater, and I saw corals for the first time. They were these neon yellows, pinks and bright blues. They were so beautiful."

Matthews later learned that she had seen a coral bleaching event. During bleaching, most corals turn white; but some can turn neon colors, creating a makeshift sunscreen, to shield themselves from excessive light exposure without their algal symbiont.

"I thought, 'If something could look that beautiful when it's that stressed, imagine what it could look like when it's happy,'" Matthews said.

Matthews now lives just around the corner from the world's largest tropical reef. Her team collaborates with local communities to mitigate pollution and reef damage by providing corals with nutrient supplements.

"The Great Barrier Reef has immense ecological, economic and iconic value for Australia,"

Matthews said. "All Australians feel a connection to the reef because it is just part of who we are."

The need is now

"So many American still don't believe in climate change," Roger said. "But climate change is the entire basis of my research, and it's all our fault."

Despite regulations designed to curb emissions, humans continue to harm the oceans and their inhabitants, sometimes unknowingly, Roger said. Most people think corals live in shallow, warm waters, but more than half of all coral species occupy dark and cold waters.

In January, Norway was the first to approve seabed mining, despite scientists' warnings. Deep-sea mining removes mineral deposits from the ocean floor and releases toxins that can kill corals and other species.

"It's high time we realize that we need to save and protect corals from further damage," Chowdhury said. "If their equilibrium is disrupted, humans will have to pay for the consequences."

While working in Madagascar, one of the world's poorest nations, for over 25 years, Christopher Golden, an associate professor of nutrition and planetary health at Harvard University and Oceana science advisor, saw firsthand the effects of climate change in the oceans.

"We are seeing the confluence of sea temperature rise, ocean acidification, pollution and over exploitation of fisheries," Golden said. "Because of this, we worry a lot about food security."

Most costal Malagasy people depend on the oceans for survival. However, due to the recent changes in the reefs, they can no longer sustainably feed themselves, Golden said.

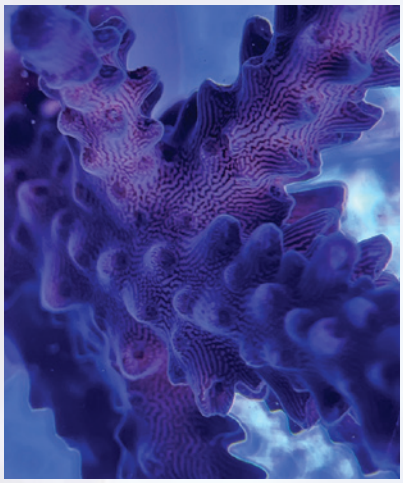
"About 85% of the Madagascar population live in rural and remote areas," Golden said. "A very large proportion of the population is severely poor; nearly half of the population are chronically malnourished. So, we are facing urgent lifestyle issues that really need to be dealt with now."

Golden and his team are constructing artificial reefs using limestone to create a new home for corals, algae and fish that have been displaced by reef destruction.

The team installed autonomous reef monitoring structures, or ARMS, in Madagascar near a healthy reef system. These cube-like structures consist of a stack of 10 rigid vinyl sheets.

Reef native species accumulate on the ARMS so researchers can take the pulse of the area. They can then collect the tiny organisms and transplant them onto artificial reefs, Golden said.

"Through this process, which obviously takes a long time, we can try to reshape ecological dynamics to rehabilitate what was once a healthy coral reef ecosystem," he said. "(In Madagascar), we're trying to build what will ultimately be the world's largest artificial coral reef to see if we

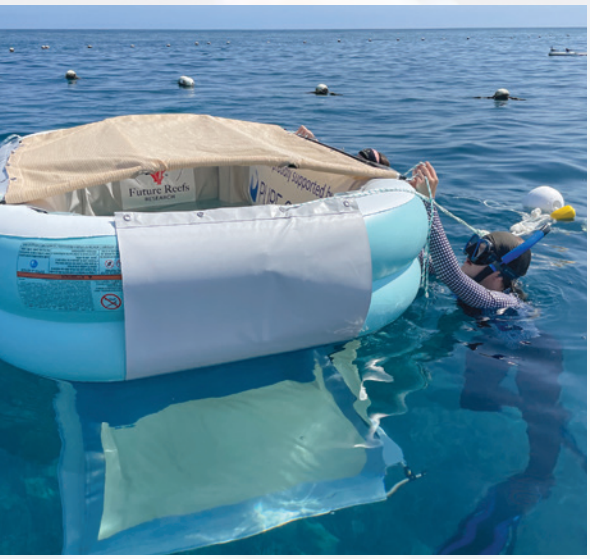


LIZA ROGER

A blue Acropora coral growing in Liza Roger's lab.

CHRISTOPHER GOLDEN

Christopher Golden and former undergraduate student from Harvard College, Akhsaya Annapragada, review research results in a small community in Southwestern Madagascar while local Malagasy children in the village look on.



JENNIFER MATTHEWS

Jennifer Matthews collects coral larvae at Moore Reef, Australia.

SAMANTHA CHOW, ARIZONA STATE UNIVERSITY NEWS

Liza Roger examines an adult Pocillopora acuta coral on a water table in her lab at Arizona State University. Corals can produce sexually and asexually. Therefore, the Roger lab propagates corals using microfragmentation, the method by which scientists break a coral colony into smaller pieces to induce rapid regeneration.

can rehabilitate fisheries as well as increase access to seafood."

Scientists, including Roger and Matthews, agree that coral reefs require human intervention to protect them against impending damages.

"I think the main thing to recognize is that there's never a perfect solution," Lewinski said. "There are always going to be trade-offs. I can always say we need more research, but what's very apparent with the coral reef decline is that there may be a crucial window of opportunity for us to act."

'Coral baby food'

When corals reproduce, they release millions of gametes into the ocean creating a colorful underwater blizzard. However, only 1% of these gametes survive, Matthews said.

"That's a critical bottleneck to restoring reefs because it's limiting genetic diversity and the potential to produce corals that might be better adapted to the changing environment," Matthews said. "If we could improve the survival of corals in their most vulnerable life stages, then we could potentially have a much greater pool, not just to rebuild coral reefs, but also to help restore their ecological functions and maintain them as the climates change."

To harness this source of genetic diversity, Matthews created what she calls "coral baby food," lipid-loaded lipid nanoparticles that promote coral larvae survival.

When the researchers exposed lab-grown coral larvae in elevated culture temperatures to the lipid nanoparticles, they boosted larvae survival from 1% to almost 50%.

Matthews is now planning to take her "well-fed corals" to the Great Barrier Reef.

The team collected coral larvae during a mass spawning event and took them back to the lab to be reared and fed. After they mature, the researchers will release the young corals back onto the Great Barrier Reef where they were collected. Matthews said she hopes these efforts will drive the restoration and rehabilitation of native coral populations in Australia.

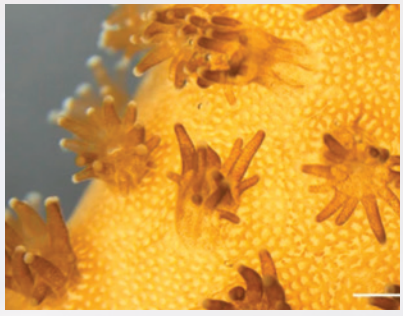
"Some of this research might sound a little out there," Matthews said. "But we need to start thinking outside of the box; we need to start taking on what may seem like 'risky' experiments like lipid nanoparticle feeding to buy time until we can get our act together on climate change. It can sound perhaps a little daunting that we're going to more extreme measures on reefs, but (the corals) require it."

Matthews plans to collaborate with Roger to adapt her coral baby food for adults to feed them without disturbing the local environment.

"We definitely appreciate that our work sounds like we're pumping the ocean full of chemicals," Matthews said. "But that's not what we're doing. Our work is very targeted."

Reef rehab

Corals structurally adapted over millions of years to use sunlight efficiently, according to Daniel Wangpraseurt, a principal investigator of coral reef ecophysiology and engineering at the University of California,



DANIEL WANGPRASEURT (DOI.ORG/10.1038/S41467-020-15486-4)

Close-up photograph of coral polyps on a colony of Stylophora pistilla growing off the coast of an island in Indonesia.

San Diego. He studies coral structures at the nano and micrometer scale to replicate them in the lab using 3D bioprinting. This tissue engineering technique harnesses the workflow of 3D printing using bioinks infused with living algae.

"We are creating a 3D cell culture environment that mimics the chemical and physical environment of how these cells grow in nature," Wangpraseurt said.

Roger teamed up with Wangpraseurt to bolster the coral model systems in her lab.

"We hope that some of these advances in bioprinting and nanomaterials research are able to shed completely new light on fundamental processes in corals," Wangpraseurt said. "Hopefully, this will help to facilitate the development of new technologies that can reduce and manage coral bleaching."

Using a multimillion-dollar award from the U.S. Department of Defense's Defense Advanced Research Projects Agency, Wangpraseurt and his team plan to build an artificial reef off the coast of Hawaii. They are constructing biomaterials, such as hydrogels, designed to enhance coral recruitment and attachment.

"Our team will develop new biomaterials that will kick-start the living reef by applying state-of-the-art medical tissue engineering approaches," Wangpraseurt said in a press release.

Lewinski's lab examines another aspect of corals that could be used for restoration: coral wound healing. Migrofragmentation, the method by which scientists break a coral colony into smaller pieces, is the gold standard for propagating coral colonies to plant back into the ocean. According to Lewinski, microfragmentation speeds up the tissue growth process and promotes rapid regeneration.

Which method of reef restoration and regeneration will ultimately be the most successful? Scientists don't have the answer, but Golden said working on multiple approaches simultaneously could be the key.

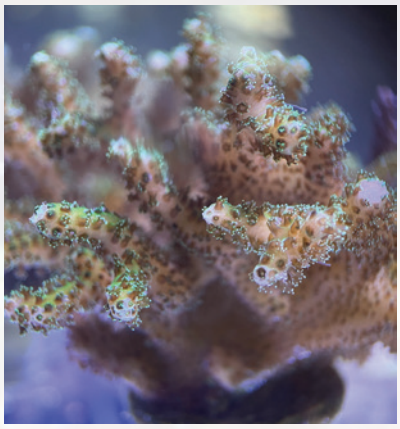
DANIEL WANGPRASEURT

Daniel Wangpraseurt and UC San Diego and Scripps Institution of Oceanography researchers Natalie Levy and Oceane Boulais deploy coral reef settlement-enhancing biomaterials for the Defense Advanced Research Projects Agency's Reefense project in Oahu, Hawaii.

"If there was a straightforward answer to climate change, it would already be fixed," Golden said. "We need to work with local populations on bettering their lifestyle and introducing conservation efforts so that we can create a happy future for all."

Ocean ecosystems are changing inevitably, Roger said, and mitigating these changes requires help from everyone. Without societal change, the coral reefs she marveled at in Cousteau's documentaries as a child will cease to exist.

"I want future generations to experience marine life the way I have," Roger said. "For this, we need to live in a more conscious way. Let's be more connected to the natural environment through education and lifestyle for a healthier planet."



LIZA ROGER

A green Pocillopora acuta coral growing in Liza Roger's lab.

Marissa Locke Rottinghaus (mlocke@asbmb.org) is the science writer for the ASBMB.

A road to survival

Cutting-edge genetic therapies offer greater promise for a sickle cell cure

By Marissa Locke Rottinghaus

Te'Avionna Rowe, or Te'A as most people call her, is a bright 14-year-old and captain of her junior varsity cheerleading squad in Florida. She also has sickle cell disease.

"Mostly my days are pretty normal, like any other kid," Te'A said. "When I'm in pain, that's when it changes."

A few months after Te'A's mother, Raytoyia Brooks, gave birth, she received an ominous letter stating her baby's blood might be abnormal. After a follow-up appointment, Te'A was diagnosed with sickle cell disease.

"I was completely devastated," Brooks said.

Sickle cell disease is a debilitating, genetic disorder that affects 100,000 individuals and 0.3% of Black or African-American births in the U.S. It causes normally disk-shaped red blood cells, which move easily through veins and arteries, to warp into a sickle shape.

The most common symptom is vaso-occlusive crises, when clumps of the crescent-shaped blood cells get stuck in vessels and block blood flow. These painful obstructions can lead to stroke, infection, eye problems and premature death.

The first six months of Te'A's life were uneventful, and then she had her first crisis. This episode marked the beginning of a tough period.

"We were in the hospital all the time," Brooks said, "sometimes every month."

JOHNS HOPKINS ALL CHILDREN'S HOSPITAL/ ALLYN DIVITO

Te'A Rowe has received care at Johns Hopkins All Children's Hospital for over 12 years. Now 14 years old, Rowe is learning to be a self-advocate in preparation for her transition from pediatric to adult care.

A traffic jam of red blood cells in her spleen caused Te'A's early crises. The solution: blood transfusions every three to four weeks for six months to replenish her normal red blood cells. At the time, her only other therapy was penicillin with potassium to prevent infections.

For many years, the treatment Te'A received as an infant was the norm for sickle cell patients. Since her birth, however, several drugs have been developed and approved, and stem cell transplants have been found to be effective in some patients.

In December, the U.S. Food and Drug Administration approved two gene therapies. One of these, Casgevy, is a CRISPR–Cas9 gene therapy from Vertex Pharmaceuticals and CRISPR Therapeutics, the latter co-founded by Nobel laureate Emmanuelle Charpentier. The FDA also approved bluebird bio's lovo-cel for sickle cell disease — a lentiviral-based gene therapy. Casgevy was approved in the United Kingdom in

November.

However, even these potentially curative treatments require chemotherapy that can have devastating and lasting side effects, so researchers press on in the quest for a safe and effective cure.

A new lease on life?

In 2019, Victoria Gray, a mother of four from Mississippi, became the first sickle cell patient to receive Casgevy at age 34. Before the treatment, Gray had to rush to the emergency room at least once a month and was often hospitalized for weeks at a time, she said; during one particularly bad period, she spent her children's birthdays, Thanksgiving and Christmas in the hospital.

"I wasn't living; I was just existing," Gray said. "I would just wake up and go from the bed to the couch."

Gray said she decided to pursue treatment options outside of FDA-approved therapies when her son began misbehaving at school.

"His behavior had changed because he thought I was going to die," she said. "So, I knew that I had to fight to survive for my kids. It wasn't just about me. I want to live for them."

Since receiving Casgevy, Gray said she has a "new lease on life" and her disease no longer gets in the way of working as a cashier at Walmart and caring for herself and her family.

Patients and carriers

As director of the Sickle Cell Disease Program at the Johns Hopkins All Children's Cancer & Blood Disorders Institute in Florida, Tamara New has seen how the disease gets in the way of patients living their lives. New oversees the care and education of Te'A and hundreds of other children. She also helps her patients become advocates for themselves as they move from pediatric to adult care.

"It's worse than having a kidney stone and worse than a woman in labor because it can be all over," she said of the pain individuals with sickle cell disease experience. "The vast majority of my patients … come to see me for their appointments; they take their medications; and they do their very best. But it is a very unforgiving disease. And many of my patients will suffer from complications despite doing all the right things."

TAMARA NEW

Sickle cell disease, the most common genetic disorder in humans, is caused by a mutation in the hemoglobin beta globin chain gene, which then causes beta-globin subunits of hemoglobin to stick together. The mutant gene is recessive; an individual needs two copies, one from each parent, to be affected.

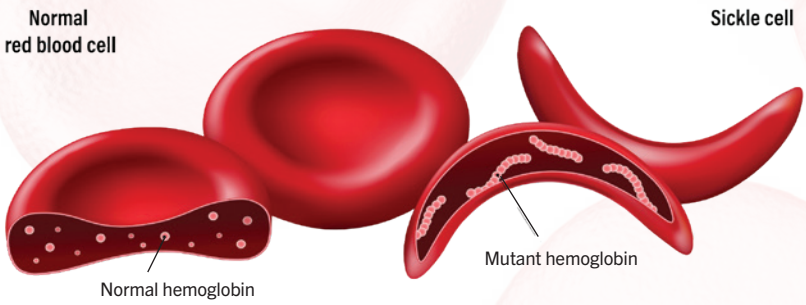
Though Brooks knew she carried the trait, Te'A's father was not aware

MAX PLANCK INSTITUTE FOR INFECTION BIOLOGY

Emmanuelle Charpentier is the scientific and managing director of the Max Planck Unit for the Science of Pathogens in Berlin, an institute that she founded with the Max Planck Society. In addition, she is a Nobel laureate and cofounded CRISPR Therapeutics.

Victoria Gray, the first participant in a gene-editing sickle cell disease clinical trial, on her infusion day in July 2019 with her doctor Haydar Frangoul, an investigator at the Sarah Cannon Research Institute.

SARAH CANNON RESEARCH INSTITUTE



Sickle cell disease is caused by a mutation in the hemoglobin beta chain gene. This mutation causes the beta subunits of hemoglobin to stick together, resulting in warped, or "sickle"-shaped cells, which can lead to impaired blood flow and cause stroke, infection, eye issues, severe pain crises and premature death.

that he did.

"Her father thought I did something wrong during my pregnancy," Brooks said.

In countries where the disease is more common, people often find out their carrier status at a young age. Nigeria is the most sickle cell endemic country in sub-Saharan Africa with approximately 2% to 3% of the total population affected. About 25% of Nigerians carry the trait, compared with just 7% of African Americans in the U.S.

Oluwaseyefunmi Adeniran grew up in Nigeria and now teaches biochemistry at Sefako Makgatho Health Sciences University in the Republic of South Africa. She found out she was a carrier when she was eight years old and was educated about how the disease is passed down.


OLUWASEYEFUNMI ADENIRAN

"It has been drummed into my mind that, as a carrier, I must not marry someone who has the same genotype," Adeniran said.

The disease carries little stigma in Nigeria and West Africa, she added; it is discussed openly within and outside of health care settings.

"Before a lot of my contemporaries go into a relationship, they are aware of each other's genotype," Adeniran said. "Once you start developing romantic feelings for anybody, you ask for their genotype. If it's not a match, you do not let the relationship progress."

A drug success — and side effects

Before the two gene therapies were approved in December, just four effective pharmaceuticals were available to sickle cell patients. None is curative, and only one, hydroxyurea, significantly reduces mortality, the frequency of painful crises and the need for blood transfusions.

Most physicians suggest patients with sickle cell disease take hydroxyurea daily.

Griffin Rodgers is one of the researchers who discovered the therapeutic benefits of the drug. Now the director of the National Institute of Diabetes and Digestive and Kidney Diseases at the National Institutes of Health, Rodgers has studied hemoglobinopathies for more than 40 years. He became interested in hematology when three of his friends died of sickle cell disease before they graduated from college.

"I wanted to see if I could break some ground in this area to help improve the lives of people affected with sickle cell disease and related disorders," he said.

After Rodgers finished his medical training in 1982, he began researching sickle hemoglobin with Alan Schechter, a senior investigator at the NIDDK.

He likened the aggregation of sickle hemoglobin molecules inside a red blood cell to a "reinforced steel pipe," which causes the cell to lose flexibility.

Adult hemoglobin has four components, two alpha and two beta globin

subunits, while fetal hemoglobin is made up of alpha and gamma globin. Most babies with sickle cell do not exhibit symptoms until they are about six to nine months old, Rodgers said, because fetal hemoglobin persists in their bloodstream and does not cause obstructions. As infants age, fetal hemoglobin is replaced by adult hemoglobin and with it the mutant beta globin protein. Sickle cell patients who express abnormally high amounts of fetal hemoglobin into adulthood often show little to no disease.

Based on these data, Rodgers and Schechter hypothesized that fetal hemoglobin might hold therapeutic potential.

"We thought, if we could turn fetal hemoglobin back on, that might inhibit this sickle hemoglobin polymerization and thereby change the course of disease," Rodgers said.

In a 1990 study, Rodgers and Schechter showed that hydroxyurea increased fetal hemoglobin levels and decreased destruction of red blood cells in 70% of sickle cell patients. A follow-up study in 1995 showed the drug also decreased crises and the need for blood transfusions. The FDA approved hydroxyurea for sickle cell disease to treat adults in 1998 and children in 2017.

"Thinking back now, had this drug been available when I was in high school, I still might have my friends to talk to today," Rodgers said.

Hydroxyurea is generally affordable, New said, but some patients and their families choose not to use it because it is a chemotherapeutic drug and can occasionally cause side effects, including abdominal pain, discolored nail beds and hair thinning.

Brooks hesitated to put Te'A on the drug.

"I kept her off of hydroxyurea for about a year or so because of the chemo aspects of it," Brooks said. "Then, her blood numbers kept coming back all wacky. The doctors told me the drug would really help stabilize her. So, eventually, I didn't really have a choice but to go ahead and put her on it. I just want what is best for her."

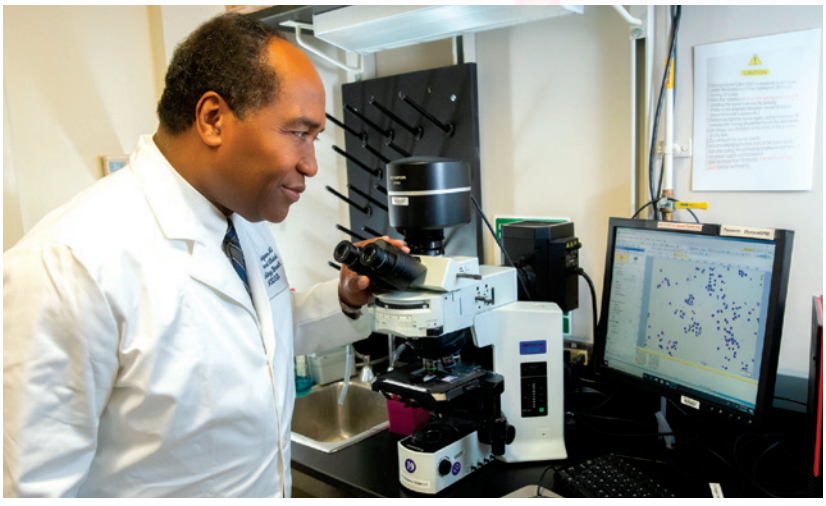
Since Te'A started taking hydroxyurea, she has far fewer emergency room visits, Brooks said.

According to a study published in the journal Blood Advances, 30% of adult patients who are prescribed hydroxyurea choose not to take it for fear of adverse effects.

"The community is advocating for medications outside of the chemotherapy family," New said.

RAYTOYIA BROOKS

Te'A Rowe, 10 years old in this photo, and her mother Raytoyia Brooks pose for photos together often. "Te'A loves taking pictures," Brooks said. "She is always the star of any photoshoot."



NATIONAL INSTITUTES OF HEALTH

Griffin Rodgers has studied hemoglobinopathies for more than 40 years.

> "If you're a kid with cancer, your fertility preservation is paid for. If you're a kid or adult with sickle cell disease, it's not. We need to fix this problem."
>
> — SOPHIE LANZKRON

Infertility and inequities

Until late last year, the only potential cure available to sickle cell patients was a hematopoietic stem cell transplant. In children, this replaces the abnormal stem cells in bone marrow with healthy cells from an eligible brother or sister. Only a sibling can donate hematopoietic stem cells to a pediatric patient. However, scientists are evaluating the safety and efficacy of a transplant from a half-sibling, parent or unrelated donor.

Before receiving a stem cell transplant, patients must undergo myeloablative therapy, a treatment with harsh chemotherapeutic drugs and radiation to eliminate their own bone marrow stem cells to make room for the transplanted cells. Due to the havoc that sickle cell has wreaked on adult patients' vital organs throughout life, this regimen is risky, Rodgers said, so adults are rarely considered for a transplant.

Also, though a stem cell transplant may offer a cure, the myeloablative chemotherapy that often precedes it causes infertility in more than 80% of patients.

Sophie Lanzkron, director of the Sickle Cell Center for Adults at Johns Hopkins Hospital in Baltimore, oversees the treatment of over 600 patients.

SOPHIE LANZKRON

"We know these (myeloablative) drugs absolutely cause infertility, both in men and women," Lanzkron said.

Furthermore, men and women with sickle cell disease usually have lower baseline fertility than the general population, and medical insurance rarely, if ever, covers fertility preservation for these patients.

"If you're a kid with cancer, your fertility preservation is paid for," Lanzkron said. "If you're a kid or adult with sickle cell disease, it's not. We need to fix this problem."

Some researchers are working to devise nonmyeloablative transplant strategies that use less toxic chemotherapy and/or radiation, which will do less damage to reproductive organs. Rodgers has successfully treated more than 60 adults with nonmyeloablative hematopoietic stem cell transplants using sibling donors.

Lanzkron blames structural racism within the medical system for the inequities faced by sickle cell patients. The disease receives more than three times less federal research funding and 75 times less foundation funding than other genetic diseases, such as cystic fibrosis, which primarily affects white individuals.

"It's not rocket science," she said. "We need to make sure people have access to care and understand their disease."

Gray has experienced racism within the medical system firsthand, she said. She sometimes hesitated to visit the emergency room during her crises because providers would refuse to administer adequate care.

"I've had doctors tell me that I was just addicted to drugs and that my pain isn't real," Gray said. "You just get tired of trying to explain your pain because it doesn't show on the outside. (Doctors and nurses) would second guess it all the time."

In the face of this discrimination, Gray said, people rarely advocated for her.

"I've even had nurses that wanted to say something" about the mistreatment, Gray said. "But they were afraid that speaking up would cost them their job."

Gene therapy to the rescue

Casgevy and lovo-cel, approved in December by the FDA, are the first potentially curative therapies for sickle cell patients who are not eligible for traditional stem cell transplants.

Both therapies edit a patient's own hematopoietic stem and progenitor cells, outside their body. After the cells are edited and the patient is conditioned with myeloablative drugs, physicians reintroduce the millions of edited cells. These progenitors expand and differentiate into white and red blood cells over several months. Unlike a traditional stem cell transplant, this strategy curbs the risk of the patient developing graft-versus-host disease, which occurs when the transplanted immune cells recognize the patient's own tissues as foreign and attack them.

Casgevy and lovo-cel use different strategies to combat the disorder caused by the mutant beta globin gene.

Like hydroxyurea, Casgevy takes advantage of fetal hemoglobin's properties.

Specifically, Casgevy uses CRISPR–Cas9 to target BCL11A, a repressor of the fetal hemoglobin gene, using a guide RNA. The precise target site is a residue within the BCL11A enhancer region, which, once modified by the Cas9 nuclease, takes the brakes off the fetal hemoglobin gene, allowing transcription and later translation to occur. Therefore, in addition to carrying sickle hemoglobin, patients who have received Casgevy also express high levels of functional fetal hemoglobin, which drowns out the sickle's damaging effects.

In the latest safety and efficacy clinical trial, patients who received Casgevy sustained high levels of total hemoglobin, similar to what is seen in healthy adults. Most needed no blood transfusions and were free of painful crises for at least one year after treatment.

Gray, who volunteered to be the first patient with sickle cell disease to receive Casgevy, has had no emergency room visits, hospital stays or crises for more than four years.

"I feel cured," Gray said. "I can do anything I want now. … My life has changed dramatically with just a leap of faith."

Since receiving Casgevy, Gray said she has become an unofficial spokesperson for gene therapy and patient education.

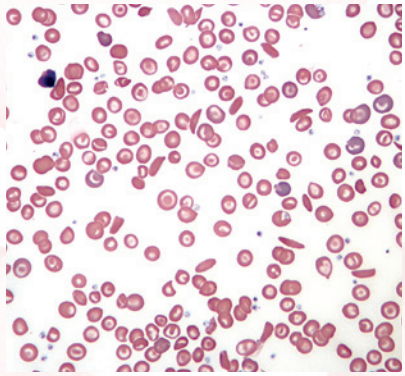
"It has been a joy, and it has changed my outlook on sickle cell and life."

The other recently approved therapy, lovo-cel, uses a lentiviral vector to introduce a modified beta globin gene into patient stem cells. This modified gene produces an antisickling hemoglobin protein, which is designed to inhibit the polymerization of mutant sickle hemoglobin, making it less likely to form blockages in the circulation.

After lovo-cel treatment, 96% of the 36 sickle cell patients enrolled in a safety and efficacy clinical trial were free of crises and, on average, showed effective DNA editing in over 80% of red blood cells for at least two years. Furthermore, patients sustain persistent expression of the antisickling hemoglobin for more than 5 ½ years after lovo-cel treatment.

SARAH CANNON RESEARCH INSTITUTE

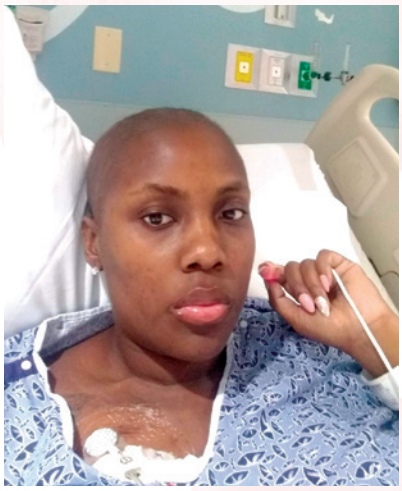
Victoria Gray, the first participant in the Casgevy sickle cell disease clinical trial, on her infusion day in July 2019 at the Sarah Cannon Research Institute.



KEITH CHAMBERS VIA WIKIMEDIA COMMONS

Microscopy image of a blood smear from a patient with sickle cell disease.

COURTESY OF VICTORIA GRAY



While receiving myeloablative chemotherapy to prepare her body for Casgevy, Gray developed painful mouth sores and lost her hair.

Risks and costs

Gray, and many other people, are saying these gene therapies are cures for sickle cell disease patients. However, Lanzkron urges caution.

For a patient to be cured, Lanzkron said, they must be free not only of crises and the need for transfusions but of signs of hemolysis as well. Hemolysis, or the destruction of red blood cells, is a fundamental feature of sickle cell disease and underlies many symptoms.

"(After receiving gene therapy), these patients have ongoing hemolysis, and we know that is a big problem," Lanzkron said. "These therapies aren't truly curative, but I think they are transformational. We don't know how long these effects last yet."

Lanzkron also said she is concerned about the long-term effects of fetal hemoglobin after Casgevy treatment. According to a perspective published in the journal Blood, patients with high fetal hemoglobin levels can still exhibit severe disease.

"I've had patients with high levels of fetal hemoglobin who have had multisystem organ failure," Lanzkron said. "(Gene therapies) seem to decrease vaso-occlusive episodes. I just think we have a lot more to learn about these therapies."

Despite her reservations, Lanzkron said she would "absolutely" recommend gene therapy to her patients who could benefit from it. However, she emphasized that, before deciding on gene therapy, patients must consult with a sickle cell expert physician.

"Let us not forget what a horrible disease it is," Lanzkron said. "We need these therapies. I will offer these therapies, and I will talk to my patients about them. But it's really a shared decision model with the limited amount of information that we have available."

Of the five gene therapies approved by the FDA before December, most cost between $1 and $2 million. However, some can have price tags of up to $3.5 million.

According to the Institute for Clinical and Economic Review, Casgevy and lovo-cel could be priced at up to $1.93 million to be cost-effective, a measure that estimates how much it costs to gain a unit of a health outcome, such as a year of life gained or a death prevented.

In 2022, each patient with sickle cell disease incurred out-of-pocket medical costs totaling up to $44,000, with insurers covering approximately $1.7 million per patient. Economists predict that these new drugs could cost a single state Medicare program more than $30 million per year.

Many of her patients at All Children's already incur thousands of dollars in medical expenses each year, New said, and a curative treatment may offer families a reprieve from lifelong medical costs.

However, Rodgers said gene therapies are not going to end sickle cell disease worldwide.

"The cost associated with these therapies with curative intent would be cost prohibitive, particularly if you needed to scale it to the 100,000 people that have the condition in this country and millions worldwide," Rodgers said. "So we still need therapies like pills or small molecules that you would be able to effectively distribute and manufacture to change the health of all of these patients."

On the horizon: one and done

Many research groups and companies are working to make gene therapies safer, more accessible and cheaper for patients around the world. Several of these initiatives aim to eliminate myeloablative conditioning from the

treatment regimen.

Gray said she developed mouth sores from the myeloablative chemotherapy while receiving Casgevy.

"I couldn't eat for over a week," she said. "It was too painful. It even hurt to swallow water. I was extremely tired. But I was already tired with my sickle cell. So that wasn't really new to me."

A team of researchers at the University of Pennsylvania, including Laura Breda and Osheiza Abdulmalik, showed that it is possible to genetically modify blood stem cells directly within the bodies of mice in what they call a "one-and-done" therapy. This could eliminate the need for currently used harsh myeloablative conditioning treatments.

Breda, a research assistant professor at the Children's Hospital of Philadelphia, said the researchers hope to develop treatments for genetic diseases, including sickle cell, available to patients in developing nations.

Abdulmalik is a research associate scientist at the same hospital. "The prevalence of sickle cell disease outside of the United States, in places like sub-Saharan Africa and India, is just not acceptable in the world we currently live in," he said. "Therefore, some of us have started to focus our careers on trying to alleviate some of these inequities."

Their gene editing approach uses lipid nanoparticles, or LNPs, and various cargoes to condition the bone marrow as well as deliver the gene therapy.

To make room for edited cells to expand, Breda and colleagues delivered an a messenger RNA encoding a pro-apoptotic protein, p53 upregulated modulator of apoptosis, to hematopoietic stem cells using an LNP conjugated to CD117, a molecule that binds a receptor on hematopoietic stem cells. This binding can facilitate LNP update by the cell.

Their gene therapy approach uses a Cas9 fused to an adenine base editor and a single guide RNA, all encapsulated in an LNP conjugated to CD117 to edit diseased genomes. In their study, the team showed that these LNPs can efficiently edit sickle cell hematopoietic cells in a dish to reverse their sickling phenotype.

The team said this therapy would likely be more affordable and better tolerated by the patient and have fewer side effects than myeloablation with chemotherapy.

"This approach would circumvent all the issues with the traditional ex vivo gene editing approach," Breda said.

More research will show whether the team can optimize and combine their conditioning and gene therapy strategies in a human to one day treat sickle cell disease.

Breda described their strategy as a "plug and play approach" that could easily be adapted to treat other genetic diseases.

Engineering an enzyme

Outside of academia, companies including Scribe Therapeutics are also developing gene therapies for diseases such as sickle cell.

"The prevalence of sickle cell disease outside of the United States, in places like sub-Saharan Africa and India, is just not acceptable in the world we currently live in. Therefore, some of us have started to focus our careers on trying to alleviate some of these inequities."

— OSHEIZA ABDULMALIK

OSHEIZA ABDULMALIK

LAURA BREDA

> "Scribe's main focus is on how to bring genome editing in vivo and to larger patient groups, so that we all have access to this amazing technology."
>
> — BENJAMIN OAKES

After pursuing his Ph.D. in Jennifer Doudna and Dave Savage's labs and a brief stint as an independent investigator, Benjamin Oakes co-founded Scribe Therapeutics in 2018 to use molecular engineering to bring CRISPR-based genetic medicines to the market.

Benjamin Oakes

"Scribe's main focus is on how to bring genome editing in vivo and to larger patient groups, so that we all have access to this amazing technology," Oakes said.

Their technology focuses on making the next generation of CRISPR–Cas safer and more efficient. During his Ph.D. studies, Oakes and colleagues described the CasX protein. At baseline, CasX does not edit the human genome well, Oakes said, but he saw this as an opportunity to mold it into a better genomic editor because this protein is naturally smaller, making it easier to deliver, and behaves differently than Cas9.

"Over the past four or five years, we have tested every single change you can imagine making to this enzyme," Oakes said. "We have iterated again and again and again using protein evolution, RNA evolution and the coevolution of both together to do things like improve protein stability, DNA binding and DNA unwinding as well as improving the therapeutic characteristics of cleavage and ability to target a location of DNA and create a double-strand break."

Oakes said Scribe's version of CasX is more than 120 mutational steps away from the original protein. Their engineered enzyme can target a single nucleotide polymorphism on one allele.

"We're really dramatically altering the landscape of how these enzymes look on both the protein and the RNA front," Oakes said.

Scribe is partnering with the pharmaceutical company Sanofi to encapsulate their CasX gene therapy, composed of CasX and a programmable guide RNA, into targeted LNPs to make these genetic medicines easy to deliver.

Scribe's gene therapies would not require a stem cell transplant and could be "undertaken anywhere in the world," Oakes said. "It's no more complicated than getting an infusion."

Gray said she is thankful for all the scientists behind gene therapy.

"The long hours and sleepless nights put into these types of treatments really makes a difference," she said. "So, keep doing what you are doing and keep researching."

Patient takeaways

The FDA approved Casgevy and lovo-cel only for individuals 12 or older. However, future clinical trials may test the two gene therapies in pediatric patients.

New said gene therapy could be transformational for children with sickle cell disease.

SCRIBE THERAPEUTICS

Christopher Duncan–Lewis, a scientist at Scribe Therapeutics, loads a microplate into a machine used to quantify the concentration of RNA extracted from cells.

"If gene therapy is able to lead to a lasting cure for patients, it is something that I think a lot of our families would be grateful to have," she said. "I hope it opens up a cure for a lot more of our patients."

However, the field still has a long road ahead to make sure this treatment is safe and effective for children, New said.

"It's not always easy to switch from a therapy that works well in adults to children. In adult medicine and clinical trials, they may be looking five to 10 years down the road. In pediatrics, we need to look 15, 20 or 25 years beyond treatment because, if I get rid of your sickle cell, I want to know that it's gone. I don't want it to suddenly come back when they are older."

Scribe Therapeutics leverages molecular engineering to create novel CRISPR-based genetic medicines.

At 14, Te'A qualifies for the new gene therapies, but she and Brooks said they would only consider them if an approach came along that did not require myeloablation. Brooks said it would be amazing if Te'A could receive a potentially curative gene therapy.

Gray said she has encouraged other patients to pursue gene therapy, and many have gone on to enroll in clinical trials.

"The opportunity for them to cut ties with the hospital is big," Gray said, "because we do experience a lot of stigma when we go into the ER. So to be relieved of that, relieved of the pain and able to get rid of our huge medicine baskets that we are tied to is life-changing."

COURTESY OF VICTORIA GRAY

Victoria Gray with her children Jaden, Jadasia and Jamarius on Thanksgiving in 2022.

She added, "I think it is a fair trade: (temporarily) giving up your hair for the chance of having a full life."

In Nigeria, Adeniran has lost friends and family to sickle cell disease when they were young, but she said she is optimistic because affected individuals in her community are living longer.

"People with sickle cell disease can have a healthy, fulfilled life," Adeniran said. "It's not a death sentence. Even though we are looking for solutions, people with sickle cell go on to have long beautiful lives."

Gray said she is happy to have helped open the door to gene therapy, and she advised all sickle cell patients to "hold on and don't give up yet."

"Change is coming. What once was science fiction is now fact."

Marissa Locke Rottinghaus (mlocke@asbmb.org) is the science writer for the ASBMB.

WHAT'S NEXT?

To address the weaknesses and side effects of CRISPR-Cas9 therapies, researchers have developed two new methods for gene editing. Read about these recent developments in "New kids on the block: Base and prime editors" at asbmb.org/asbmb-today.

‘A career challenge’

Marqusee balances her time between running a lab at UC Berkeley and leading one of the largest initiatives at NSF

By Marissa Locke Rottinghaus

> “NSF is kind of like a university. We have directorates that are like colleges, and we have divisions that are like departments ... But science doesn’t fall into those neat boxes ... Young scientists don’t box themselves in, and I want to adopt that mentality here.”
>
> — SUSAN MARQUSEE

For much of the last year, Susan Marqusee has made juggling bicoastal job responsibilities a breeze by hacking her work schedule. After long days working on governmental affairs, she switches gears to biochemistry in time for dinner.

“Since I’m located on the East Coast and my lab is in California, I use the time change to my advantage,” Marqusee said. “I start meeting with my students around 6 p.m. Eastern time.”

Marqusee is a professor in the Departments of Molecular & Cell Biology and Chemistry at the University of California, Berkeley. Since June 2023, she has also been the assistant director of the Directorate for Biological Sciences, or BIO, at the U.S. National Science Foundation.

An American Society for Biochemistry and Molecular Biology member since 1995, Marqusee won the ASBMB William C. Rose Award in 2012, served on the society’s Council from 2015 to 2018 and was named an ASBMB fellow in 2023.

Driven by a passion for giving back to the scientific community, Marqusee, in 2000, helped establish and direct the California Institute for Quantitative Biosciences, also known as QB3, to fortify science and the economy in California. Last year, Marqusee decided to use her skills to enable nationwide scientific success by taking the assistant directorship at the NSF.

However, stepping into a leadership role at the NSF hasn’t stopped her from maintaining a productive research lab at UC Berkeley. ASBMB Today spoke with Marqusee about how she manages it all. This interview has been edited for length and clarity.

U.S. NATIONAL SCIENCE FOUNDATION

“If you want to be involved in research and policy, get a really solid scientific training and follow your passion,” Susan Marqusee advises.

Q: How did you become the assistant director of the directorate at NSF?

Marqusee: I’ve always tried to enable other people’s science through mentorship or administration. I spent a lot of time at Berkeley building and directing QB3. I’ve had the pleasure to serve as part of many scientific societies with roles as simple as running annual meetings and as complex as being on the societies’ councils. Through these experiences and others, I discovered that I find enabling the science of the community and others, as well as mentoring, just as rewarding as the scientific discoveries themselves.

When I stepped down from running QB3, I didn’t know what I was

going to do next. But I knew it would probably involve enabling science and the scientific process in some way. At the time although I had some interaction with NSF, I didn't fully appreciate the intricacies of the agency and its impact.

In fall 2022, I got some phone calls asking if I was willing to be considered for the role of assistant director at NSF. I realized it was a special opportunity, and I had the potential to have a lot of impact. I felt it was my time to give back.

There's also something very attractive about this role, both for me and for the NSF, in that I could take it as an Intergovernmental Personnel Act hire without shutting down my lab. This isn't a career change; it's a career challenge because I have two jobs right now. I hope that I will have a positive impact on the NSF and science in the nation. I'm absolutely sure the NSF is going to have a major impact on me as a scientist.

Q: What is your role at the NSF? What does your day-to-day look like?

Marqusee: My role as the assistant director is overseeing the Directorate for Biological Sciences. Each directorate has a budget of about $1 billion. So, I spend a lot of time with the budget. I also work with the NSF director and other staff to examine how to move the NSF mission forward. The mission of the BIO Directorate is to enable discoveries for understanding life. So, I spend time thinking about that both locally within BIO and broadly as a part of the agency mission. I also think at a very detailed level about how to get money into scientists' hands.

What I do day-to-day changes and it's been a very steep learning curve. I spend about half my time working on BIO-specific issues, including the aspects of science that will further our mission. NSF has a global and holistic approach to science in the community, and that appeals to me. We think about what science we need to support to move BIO forward as well as how we create a scientifically competitive nation. The other half of my time is spent as the BIO voice at the agency level and across the government as a whole. For example, last year there was an executive order on advancing biotechnology. Our job is to turn executive orders like this one and other initiatives into reality in a coordinated fashion.

Q: What are some of your goals for the BIO directorate?

Marqusee: NSF is kind of like a university. We have directorates that are like colleges, and we have divisions that are like departments. Those divisions are important for administration. But science doesn't fall into those neat boxes. So, what I want to do is enable cross-interactions among these areas. Young scientists don't box themselves in, and I want to adopt that mentality here.

NSF has a great history of focusing on fundamental research, but we do not do a great job of letting society know about the tangible benefits from that research. So, another one of my goals is to communicate that.

I also want to enable the rapid translation of our discoveries into societal benefits without compromising the need for curiosity-driven research. We want to make sure we're funding the most exciting new areas of science, but science is getting so expensive. I just want to encourage people, when they apply for a grant, to ask for what it takes to do the research in the grant. Finally, a big goal of ours is widening access to science so we can be competitive as a nation. For example, cryogenic electron microscopes are very expensive, and we can't have them in every little corner of the country. So, we are working on creative solutions.

Q: How do you maintain your research lab in addition to holding a position at NSF?

Marqusee: I spend about 80% of my time on NSF duties. The rest I spend focusing on my laboratory. Since I'm located on the East Coast and my lab is in California, I use the time change to my advantage. I start meeting with my students around 6 p.m. Eastern time.

I probably overestimated the amount my students need to rely on me. They have really risen to the occasion. They're all quite independent. The science is ongoing, and it hasn't suffered. I worried about leaving my lab for this position, but it has been a risk worth taking.

I've never not been in academia, so this dual role is very out of my comfort zone. It's exhausting. For me, the main challenge has been this work–work balance. It reminds me of when I was a young parent and an assistant professor, and I felt like I was terrible at everything. I feel overcommitted, but that is just because everything is new. In the beginning of this role, when people asked me how I felt about it, I think I just felt proud of getting outside my comfort zone.

Q: What are your favorite and least favorite parts of your job at NSF?

Marqusee: My favorite part of the job is the people I work with. They are amazing and very mission-driven. They want to get money into everybody's hands and make sure everyone has access to what they need to do science. To do these things, the people

> **"When you're working within the federal government, momentum is hard to gain. The system is reluctant to change ... some of my impact will play out after my time."**
>
> — SUSAN MARQUSEE

here make data-driven decisions to impact science broadly. It's very different from academia, where you're very focused, in your own laboratory, on every publication.

It's a crazy time in biology right now. We are grappling with what the role of a graduate student is, proper compensation, the role of a postdoc and the rising cost of science. We are at a disequilibrium right now, and these problems need to be seriously considered.

NSF is an exciting place to work. I've been to the White House, and I got to take a selfie with Tony Fauci. I actually did not grow up in the U.S.; I grew up and went to high school in Europe. So it's been an amazing experience to learn about the government and live in Washington, D.C.

When you're working within the federal government, momentum is hard to gain. The system is reluctant to change. Getting things done on a budget is difficult and we're always working on multiple budgets at one time — the one we're spending and the ones were planning; some of my impact will play out after my time. But I think academia has the same frustrations.

In academia, we have a rare privilege of being able to think about whatever we want to think about at whatever time of day. But now, I have no control over my schedule. I find it difficult to find time to think about and absorb what I've been given. When you're on a college campus, there's a sense of potential at the beginning of the school year. As a forever student, I miss being able to experience that.

Q: What advice would you give young scientists interested in a career like yours?

Marqusee: If you want to be involved in research and policy, get a really solid scientific training and follow your passion. Make sure to surround yourself with mentors who see a big picture, who really appreciate people, science and society.

I believe a Ph.D. is a really important thing that allows you to become an expert. Ph.D. research is a very privileged time when you get to think about one thing.

Look for things to bring you joy and remember that nothing is forever. I like to think things could change at any moment. Be willing to stretch yourself.

Marissa Locke Rottinghaus (mlocke@asbmb.org) is the science writer for the ASBMB.

Embracing serendipity

NIGMS Deputy Director Dorit Zuk describes her scientific journey and offers tips on making career changes

By Marissa Locke Rottinghaus

Dorit Zuk says she joined the ASBMB's Education and Professional Development Committee in 2005 for two reasons: "To remind everybody that 'BMB' stands for molecular biology, as well as biochemistry, and to remind everybody that there's more than one career outcome and to stop using the term 'alternative.'

"I used to stomp my feet in those meetings and say, 'They're all careers; there's nothing alternative about any of them.' There are many things you can do with a Ph.D. in biology. I know this because I've done most of them."

Zuk, deputy director of the National Institute of General Medical Sciences of the National Institutes of Health since 2021, likes taking chances and embarking on new career adventures.

After finishing her Ph.D. at the Weizmann Institute of Science and a postdoc studying the messenger RNA turnover at the University of Massachusetts Chan Medical School in the laboratory of Allan Jacobson, Zuk left academia to pursue a role in publishing.

After six years at Cell Press, she thought she'd try her hand at science policy, and that field has stuck.

ASBMB Today spoke with Zuk about her dynamic career and her advice for today's young scientists. The interview has been edited for length and clarity.

Q: How did you become NIGMS deputy director?

Zuk: First, I'd like to say I am a card-carrying molecular biologist. My training is in RNA biology and genetics. And I'm the type of person who's always wondering what's around the corner, even when I'm in a job I love.

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

In her career journey, Dorit Zuk has learned that "Every single place of work, whether it is a company or academia or government, has its own rules. You have to learn those rules and operate within them."

My path was all about serendipity. But serendipity has two important segments. You have to recognize it, and then you have to act on it. During my postdoc, I was applying for academic positions and interviewed at a couple of places. I was also writing an article about RNA turnover. I needed a Molecular Cell paper, and I found that the entire journal issue was missing from PubMed, so I had to go to the Molecular Cell website to get the paper. There, I saw an ad for a molecular biology editor at Cell, which I would never have seen if I didn't have to go to their website. So, that's the serendipity.

The part where I acted on the serendipity was that I thought, 'Oh, I wonder what that would be like?' I also thought, 'I could do that job for a year, and if it's interesting, I'll stay. If it's not, I will have learned a lot, and I'll come back to academia.' So, I applied, and two weeks later, I got the job.

I could have been happy in that job until the end of my days. But one day, the topic of the American Association for the Advancement of Science & Technology Policy Fellowship came up. I was interested so I looked it up, and it said, right at the top: not just for early-career folks. I applied, and I got a position at the National Institutes of Health in the Office of Extramural Research and the Office of Director. I really enjoyed that.

I did a short stint at the American Academy of Arts and Sciences, and then I went back to NIH. I've been here ever since. I was a division director at NIGMS for six years before I became the deputy director, so, I know the institute, its values and how it runs. I have spent a lot of time on the policy and communications sides of NIH, so I bring my knowledge in policy, outreach and legislative affairs to the position as well.

Q: What is your role as deputy director? What does your day-to-day look like?

Zuk: As deputy director, I think about the institute as a whole. I work with Jon Lorsch, the director of NIGMS, to implement the institute's missions and values.

> **"Remember that your next job is likely not your last job. You want to do your best to find the right career fit, but it's not the only thing you'll ever do."**
> — DORIT ZUK

On a day-to-day basis, I talk to a lot of different people. This is so I can keep up with what is happening around the institute, make sure that we're on track and look for ways to improve operations.

I'm involved with NIH-wide activities as well. I try to make sure that I bring the NIGMS perspective to the table and ensure that our values and our interests are represented.

Q: What are your favorite and least favorite parts of your job?

Zuk: I've always liked thinking broadly. My favorite part of my job is being able to think about the whole institute and about the entire biomedical research enterprise. I always say, 'We do more or less the same things as academics: We write emails and documents; we go to meetings. The main difference is what we are thinking about every week.' Sometimes having lots and lots of meetings can be tiring. But I really do like talking to people.

Q: How is scientific leadership in government different from academia or publishing?

Zuk: I think the biggest difference is the level at which we think about things. When you're in academia, at the bench, you're digging deep into something really small. It's part of a whole, but you have to go really deep.

As soon as I switched to publishing and then to policy and programming, I had to start thinking more broadly. You have to be able to see how things fit together. You can't worry about whether the experiment was done well or not. You have to think about, 'What question was asked, and do the experiments proposed or done answer those questions?'

I think this is true about any career. As soon as you step away from the bench, even if you stay in academia or go to industry, you have to start thinking more broadly. But I think there are a lot of similarities between the fields. You work with people, and you have to get along with them.

Every single place of work, whether it is a company or academia or government, has its own rules. You have to learn those rules and operate within them.

Q: What advice would you give young scientists interested in a government career?

Zuk: Fellowships are really useful. Most of them pay a decent salary, and the goal of the fellowship is to learn and contribute to the organization at the same time. There's the AAAS fellowship; the Presidential Management Fellows Program, which is not just for scientists; the National Academy of Sciences six-week Science Policy Fellowship; and the National Human Genome Research Institute Genetics and Public Policy Fellowship. Some states also have fellowships, so you don't have to come to Washington, D.C., if you want a career in policy. Another suggestion is: talk to people. Most people, if you send them an email saying you are interested in what they do, will be happy to talk with you. So, look around for what you think you might be interested in doing, find someone doing it and contact them.

A piece of advice that I always give people is that you have to know yourself. You have to know if you're the type of person who needs to envision a career mapped out. If so, you probably wouldn't be able to have a career path like mine. But, if you're the type of person who wants to always learn new things, you can. Throughout my career, I always thought I could take a chance, and I would always learn something from it. You can always go back to a job you love if you aren't happy with what you are doing.

Also, remember that your next job is likely not your last job. You want to do your best to find the right career fit, but it's not the only thing you'll ever do. Looking back at my career at this stage, it really looks like it all made sense. It looks like there was a trajectory. But that's only in hindsight. I never envisioned it.

I certainly did not imagine that I would end up working for the U.S. government when I came to the U.S. (from Israel) for my postdoc 30 years ago. I made my choices one by one, according to what looked interesting at the time. Every time I made a choice, I accumulated more skills that all culminated in what I'm doing right now.

I don't want people to think the only way to get to a place like mine is by planning it all out. My way was not planned. This is just how I did it, but there are so many ways to end up here.

Marissa Locke Rottinghaus (mlocke@asbmb.org) is the science writer for the ASBMB.

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ASBMB NAMES 2024 FELLOWS

By Marissa Locke Rottinghaus

The American Society for Biochemistry and Molecular Biology has named 17 members as 2024 fellows of the scientific society.

Designation as a fellow recognizes outstanding commitment to the ASBMB through participation in the society as well as accomplishments in research, education, mentorship, diversity and inclusion, advocacy and service to the scientific community.

Edward Eisenstein, an associate professor of bioengineering at the University of Maryland and ASBMB Membership Committee chair, and Judith Bond, an adjunct professor of biochemistry and biophysics at the University of North Carolina at Chapel Hill and chair of the ASBMB Fellows Program Subcommittee, wrote in a joint statement: "The 17 ASBMB fellows in the 2024 class have shown immense commitment to ASBMB and represent an outstanding group of scientists that push the boundaries of scientific research, mentorship, education and advocacy. It is an honor to have these individuals represent ASBMB, and we look forward to their continued contributions as role models and mentors to current and future members of the biochemistry and molecular biology community."

This is the fourth year the ASBMB has named fellows. The society planned to recognize the 2024 class at its annual meeting, Discover BMB, in San Antonio in March.

Learn more about the 2024 fellows in the following pages.

Toni M. Antalis

Toni M. Antalis is a professor of physiology at the University of Maryland School of Medicine, where she is also associate director for training and education for the Greenebaum Cancer Center and director of the graduate program in molecular medicine. Her lab studies signaling mechanisms in vascular disease and cancer.

Antalis was the ASBMB president from 2020 to 2022 and served as treasurer, chair of the Publications Committee and a member of the Finance Committee. She is a past member of the Journal of Biological Chemistry editorial board. At UMB, she is the co-director of the T32 Training Program in Cancer Biology, supported by the National Cancer Institute, and a co-principal investigator of the Post-Baccalaureate Research Education Program supported by the National Institute of General Medical Sciences.

Dudley Strickland, a professor at the UMB School of Medicine, nominated Antalis and wrote she has "a strong record of exemplary service to the ASBMB, research excellence, mentorship of the next generation of diverse scientists and service to the national scientific community."

David A. Bernlohr

David A. Bernlohr is a professor and chair of systems biology of human metabolism at the University of Minnesota. His lab studies the biology of adipose tissue and the metabolic relationships with obesity, metabolic disease and cancer. They focus on cytoplasmic fatty acid binding proteins and their roles in mediating fatty acid metabolism in adipocytes and macrophages.

Bernlohr is a member of the Journal of Lipid Research editorial board and a past member of the Journal of Biological Chemistry editorial board. He served as cochair for the ASBMB's 2019 annual meeting.

Douglas Mashek, a professor at UM, who nominated Bernlohr wrote: "In addition to his exceptional research accomplishments, Dr. Bernlohr has been a pillar of leadership in the ASBMB community and the University of Minnesota during his unprecedented 27-year tenure as department head of the biochemistry, molecular biology and biophysics department." Nominator James Ntambi, a professor at the University of Wisconsin, described him as a "triple threat — exceptional research scholarship, outstanding professional leadership via mentoring and career development and commitment to the educational mission devoted to the next generation of biochemists."

Joan W. Conaway

Joan W. Conaway is a professor of molecular biology and the vice provost and dean of basic research at the University of Texas Southwestern Medical Center. Conaway and her husband, Ron Conaway, previously co-led a research lab at the Stowers Institute for Medical Research.

Conaway is the ASBMB president-elect. She is a past Council member and treasurer. She has served as chair for the meetings, nominating and finance committees, and on the editorial board of the Journal of Biological Chemistry. Conaway is a former Howard Hughes Medical Institute associate investigator and a member of the National Academy of Sciences and the American Academy of Arts and Sciences. The Conaways jointly received the ASBMB–Amgen award in 1997.

Barbara Gordon, former ASBMB executive director, nominated Conaway and wrote: "Joan Conaway is exactly the type of member the committee had in mind when the fellows program was established. She has given her time, enthusiasm and expertise to the Society freely and generously."

Kathleen Cornely

Kathleen Cornely is a professor of biochemistry at Providence College. Her research focuses on the genetic diversity and evolution of bacteriophages, including mycobacteriophages.

Cornely led her department's efforts to gain ASBMB accreditation for the biochemistry program. She is also chair of the ASBMB Undergraduate Poster Competition Committee and directs Providence's Student Chapter. She has served on the Education and Professional Development Committee.

Marilee Benore, a professor at the University of Michigan-Dearborn and a 2023 ASBMB fellow, nominated Cornely, writing, "It's not possible to fully share how wonderful she is, how hard she works, and how passionately she shares her knowledge and expertise. At meetings she goes out of her way to find the person who might be sitting alone to make sure they are welcome and engaged."

Martha S. Cyert

Martha S. Cyert is a professor and chair of biology at Stanford University. Her lab uses systems biology techniques to study the calcium-dependent phosphatase calcineurin. Immunosuppressive drugs such as cyclosporine A inhibit calcineurin through a mechanism defined by Cyert's research.

Cyert was a co-organizer of the 2022 ASBMB annual meeting and is a member of the Meetings Committee. She served on the Public Affairs Advisory Committee from 2015 to 2021. She has been awarded fellowships from the American Cancer Society, the Life Sciences Research Foundation and the Lucille P. Markey Charitable Trust.

Alexandra Newton, a professor at the University of California, San Diego, who nominated Cyert wrote: "Dr. Cyert is a passionate biochemist who has served ASBMB and who has made seminal contributions in phosphatase signaling. She is also an exemplary teacher and mentor and role model." Matthew Gentry, himself a 2024 ASBMB fellow, also nominated Cyert and wrote: "Her service to the society as well as to the broader biochemistry and signaling communities as well as her fundamental discoveries has had and will continue to have high impact."

Nicholas O. Davidson

Nicholas O. Davidson leads the gastroenterology division and digestive disease research center at Washington University School of Medicine in St. Louis. He holds professorships in the departments of medicine and developmental biology. His research focuses on the genetic regulation of intestinal and hepatic lipid metabolism, including the pathogenesis of obesity, gallstone disease and fatty liver.

Davidson is co–editor-in-chief of the Journal of Lipid Research. He served as an associate editor for JLR since 2011 and an editorial board member of the Journal of Biological Chemistry. He received his medical degree at Kings College Hospital Medical School before taking a position in the laboratory of cholesterol metabolism at Rockefeller University fellowship at Columbia–Presbyterian Medical Center.

Kerry-Anne Rye, a professor at the University of New South Wales Sydney, ASBMB fellow and co–editor-in-chief of JLR, nominated Davidson and wrote: "Over the course of more than three decades, Dr. Davidson has made a major contribution to the ASBMB. He has mentored future generations of scientists and physician–scientists and contributed to knowledge with a sustained and impactful body of seminal discoveries that have broad scientific impact." Stephen Young, a professor at UCLA, and ASBMB fellow, also nominated Davidson and described him as an "exceptional ASBMB leader" and a "role model for trainees."

Matthew S. Gentry

Matthew S. Gentry is a professor and chair of biochemistry and molecular biology at the University of Florida College of Medicine. He studies how glycogen metabolism goes awry in cancer and neurodegenerative disorders. In collaboration with multiple groups and companies, his lab has developed potential therapeutic approaches for Lafora disease, a glycogen storage disease and childhood dementia.

Gentry is a member of the ASBMB Council, former chair of the Public Affairs Advisory Committee and a Journal of Biological Chemistry editorial board member.

Blake Hill, a professor at the University of Colorado, nominated Gentry and wrote: "Throughout his career

in biochemistry and molecular biology, Dr. Gentry has consistently advanced scientific knowledge, fostered collaborations, nurtured the next generation of scientists, and advocated tirelessly for our scientific community." Martha S. Cyert, herself a 2024 fellow, also nominated Gentry and described him as an "outstanding mentor, leader and scholar on multiple fronts."

Marina K. Holz

Marina K. Holz is the dean of the Graduate School of Biomedical Sciences and a professor of cell biology and anatomy at New York Medical College. Her lab studies mechanisms of hormone and growth factor signaling in breast cancer and lymphangioleiomyomatosis, a rare lung disease.

Holz is a member of the ASBMB Women in Biochemistry and Molecular Biology Committee and served as a mentor for the Interactive Mentoring Activities for Grantsmanship Enhancement, or IMAGE, program. She was a session organizer for the 2021 ASBMB annual meeting. She established a Student Chapter at the Undergraduate College of Arts and Sciences of Yeshiva University and has authored articles for ASBMB Today.

Sonia C. Flores, a professor at the University of Colorado Anschutz Medical Campus, who nominated Holz, wrote that she is "an exemplary member of ASBMB, a respected leader, scientist and educator, and she has worked tirelessly to advocate for students, advance the (diversity, equity and inclusion) mission, create innovative educational programs, and serve the greater scientific community."

Mary O. Huff

Mary O. Huff is the dean of the Bellarmine College of Arts and Sciences. Her research focuses on the role of estrogen and estrogen-like substances in lung cancer. With collaborators, she studies the effects of cigarette smoke on lung cells.

Huff has been a member of the ASBMB Student Chapters Steering Committee for nine years. In this role, she chaired the Regional Meeting Awards Committee and served on the ASBMB Honors Society, Outreach Grant and Marion B. Sewer Scholarship committees. Huff has also been extensively involved in the Undergraduate Poster Competition, having served as a judge and head judge for many years. In addition, she has authored multiple articles for ASBMB Today.

Celeste Peterson, an associate professor at Suffolk University, nominated Huff and wrote: "She has integrity and high ethical values. Her exceptional and sustained service to ASBMB and her leadership skills in higher education make her an inspiring and deserving candidate."

Peter J. Kennelly

Peter J. Kennelly is a professor of biochemistry at the Virginia Polytechnic Institute and State University. His lab uses archaea to dissect the development and evolution of protein phosphorylation and dephosphorylation.

Kennelly has been a member of the ASBMB since 1986. He served on the Education and Professional Development Committee and Membership Committee for many years and chaired each. He was a member of the Journal of Biological Chemistry's editorial board. He won the 2024 William C. Rose Award for Exemplary Contributions to Education, and he contributed to the development of the accreditation program and the ASBMB exam. He has authored multiple articles for ASBMB Today.

S. Gaylen Bradley, a dean at Virginia Commonwealth University, who nominated Kennelly wrote: "Peter has invested an impressive and significant portion of his personal and professional career in service to the ASBMB.… It takes a unique and devoted person to dedicate so much time while facing the intense demands of being the head of a large and vibrant department."

Bettie Sue Masters

Bettie Sue Masters is an adjunct professor of biochemistry at the Duke University Medical Center. She is best

known for her research on the structure–function relationships of the nitric oxide synthase and characterization of cytochrome P450 reductase.

Masters served as president of the ASBMB from 2002 to 2004 and was a member of the Membership Committee. She also has served on the Journal of Biological Chemistry editorial board and Publications Committee and chaired the Public Affairs Advisory Committee. She was the 1992 recipient of the Federation of American Societies for Experimental Biology Excellence in Science Award and is an elected member of the National Academy of Medicine and a fellow of the American Association for the Advancement of Science.

Fred Guengerich, a professor at Vanderbilt University and a 2021 ASBMB fellow, nominated Masters and wrote: "There is no one else more qualified to be an ASBMB Fellow, just on the basis of service to our society. Adding Bettie Sue's accomplishments in research, teaching/training, and other service, seals the deal, so to speak."

Richard C. Page

Richard C. Page is a professor of chemistry and biochemistry and the associate vice president for research and innovation at Miami University. His lab studies the structural and biophysical basis of protein quality control and antibiotic resistance.

Page served on the Public Affairs Advisory Committee for eight years. In addition, he has mentored trainees through the Interactive Mentoring Activities for Grantsmanship Enhancement, or IMAGE, program. At Miami U., he advises the ASBMB Student Chapter and he has judged the Undergraduate Poster Competition. He has authored multiple articles for ASBMB Today.

Ann West, a professor of chemistry and biochemistry at the University of Oklahoma, nominated Page and wrote: "Rick has a distinguished record of service as a faculty member and administrator at Miami U. and, I can say first-hand, as an exceptional leader of the Public Affairs Advisory Committee (PAAC) for 8 years."

Jennifer Roecklein–Canfield

Jennifer Roecklein–Canfield is a professor of chemistry and physics at Simmons University. Her lab focuses on a systems approach to studying the mechanisms of viral-host interactions and the use of synthetic biology principles to create DNA devices used to introduce new functions into cells. She has also focused much of her career on providing opportunities for girls and women to excel in science.

She is a past member of the Women in Biochemistry and Molecular Biology Committee and contributed to the ASBMB accreditation program and exam, including establishing core concept areas and exam questions. Roecklein–Canfield is a member of the Massachusetts Governor's STEM Advisory Council, which works to expand access to high-quality STEM education for students across the state.

Victoria Del Gaizo Moore, a professor at Elon University, and Michael Wolyniak, a professor at Hampden–Sydney College, jointly nominated Roecklein–Canfield, writing that her career "can only be described as one of selfless dedication to the betterment of those around her with a special emphasis on providing opportunities for girls and women to excel in STEM fields. She has never shied away from challenges to build scientific opportunities at local, regional, and national levels that provide improved access to opportunities in STEM fields to all students regardless of background."

Christopher E. Rohlman

Christopher E. Rohlman is a professor of chemistry and biochemistry at Albion College. His lab studies RNA structure and function, with a focus on the role of transcription, aptamers and ribozymes in health and disease.

Rohlman has been heavily involved in undergraduate education at Albion and through the ASBMB. He has been involved in the Undergraduate Poster Competition since 1997 and served as an organizer, judge and lead judge. In addition, he is a past member of the ASBMB Education and Professional Development Committee.

Craig Streu, a professor of biochemistry at Albion, who nominated Rohlman wrote: "I have personally witnessed his strength as a mentor and his deep commitment to ASBMB's educational programming.

I believe, and others have confirmed, that it is possible to trace the success that ASBMB has had in undergraduate education directly to a number of his foundational contributions. Just as importantly, it is possible to trace the success of a generation of biochemists to his instruction and mentorship."

Walter A. Shaw

Walter A. Shaw founded Avanti Polar Lipids, Inc., which supplies academic and industry professionals with lipid-based products and tools. He served as its president and CEO until 2020 when Croda, Inc. purchased the company. Through Avanti, he has developed important research tools as well as lipids for U.S. Food and Drug Administration-approved pharmaceuticals.

He is the namesake and sponsor of the ASBMB's Walter A. Shaw Young Investigator Award in Lipid Research, which recognizes outstanding research contributions in the area of lipids by a young investigator who is an assistant professor or equivalent with no more than 10 years of experience. Shaw has sponsored this award for more than 10 years. He has also sponsored many other awards such as the ASBMB Avanti Award in Lipids and the Avanti–Biophysical Society Award, established in 1997 with the Biophysical Society.

Alfred Merrill, a professor of biological sciences at the Georgia Institute of Technology, nominated Shaw and wrote: "Walt (and Avanti) have always been more than just a company that sells lipids through their assistance at meetings as well as provision of helpful tips on the company website."

John T. Tansey

John T. Tansey is a professor of chemistry and the director of the biochemistry and molecular biology program at Otterbein University in Ohio. The Tansey laboratory examines the role the PAT proteins play in lipid storage and disease. This work is almost exclusively conducted by undergraduates.

Tansey is the faculty adviser of the ASBMB Student Chapter at Otterbein University, which won the 2023 Outstanding Chapter Award. They also won the award in 2012, 2014 and 2018. In addition, he has served on the ASBMB Education and Professional Development Committee. In 2004, he won the Best New Teacher award, and, in 2012, he won the Teacher of the Year award at Otterbein.

Peter Kennelly, also a 2024 ASBMB fellow, nominated Tansey and wrote: "He stands out as an influential leader of both his university community and of the ASBMB's scientist–educator community. The impact of John Tansey's multiple and sustained contributions as a thought leader and advocate both at Otterbein and beyond clearly and vividly embody the core values of the ASBMB Fellows program."

Brian W. Wattenberg

Brian "Binks" W. Wattenberg is a professor of biochemistry and molecular biology at Virginia Commonwealth University. His lab studies the biochemistry and trafficking of lipids, such as sphingolipids.

Wattenberg is a founding member and the membership director of the ASBMB Lipid Research Division. He is a member of the ASBMB Today editorial advisory board and has authored articles for the magazine. Wattenberg was a member of the Journal of Biological Chemistry editorial board from 2006 to 2020. At VCU, he won the biochemistry and molecular biology department Outstanding Teacher Award in 2018 and 2019.

Daniel Raben, a professor at Johns Hopkins University; Yusuf Hannun, director of the Stony Brook Cancer Center; Vytas Bankaitis, a professor at Texas A&M University; and Teresa Dunn, a professor at the Uniformed Services University of the Health Sciences, nominated Wattenberg. In their nomination letter, they wrote: "In addition to his stellar record of scientific achievement it is important to note his major impact on the ASBMB and the lipid research community at large. Scientifically, in addition to his seminal contributions to our understanding of vesicular trafficking, Dr. Wattenberg is an internationally recognized leader in lipid biochemistry, sphingolipid biochemistry in particular."

When mentor and mentee switch roles

In 2022, the Federation of American Societies for Experimental Biology introduced its Leadership Engagement and Appreciation of Differences, or LEAD, reverse mentoring program pairing senior-level professional mentees with junior-level mentors "to gain different perspectives of individual, group, and cultural views within the workplace and scientific research communities," per a FASEB announcement.

Among the 2023 LEAD participants were two members of the American Society for Biochemistry and Molecular Biology. Tina Tootle, a professor and department chair at the University of Iowa, was a mentee. Saket Bagde, a Ph.D. candidate at Cornell University was a mentor. Tootle and Bagde were not paired with each other in the mentoring program.

We invited each of them to write about their experience.

Relearning the trainee's view

By Tina Tootle

I am a first-generation college graduate, a female scientist, a professor and a department chair. My lab's research focuses on uncovering the connections between lipid signals, termed prostaglandins, and actin — both in the cytoplasm and the nucleus.

When I learned about LEAD, I was immediately intrigued. What, I wondered, is reverse mentoring? As I read about the program, I thought, "Wow, what a perfect time in my career to do this." I was in the process of moving departments and taking on a new leadership role — department chair. I rapidly applied and was paired with Fasilat Hassan, an international biomedical sciences graduate student at the University of Tennessee Health Sciences Center.

Like many researchers, as I progress in my career, I've lost some understanding of the issues facing trainees. LEAD breaks down the separation and power dynamic between senior faculty and trainees and provides a safe space to talk about these issues. I can learn how faculty and collegiate leaders can help, what makes the trainee experience worse and what makes it better, without Fasilat risking negative consequences for speaking up. It keeps me in touch with the trainee reality.

Fasilat has helped me understand the challenges international Ph.D. students face when moving to a new

FASEB will start accepting applications for the 2024 LEAD program in late spring. Check the Diversity, Equity and Inclusion page at faseb.org for details.

country: the financial burdens, the difficulties in finding housing and navigating transportation, the isolation until they make community connections and the struggles due to visa limitations on spousal employment.

This better understanding has pushed me to learn what resources are available on my campus; to share those resources with applicants, incoming students and current students; and to think about how to better integrate international students' cultures into the lab, department and program and vice versa. I still have much to learn.

From Fasilat I've relearned that trainees don't magically know about the process of science: How is authorship order determined? What does co-first authorship mean? Why would a principal investigator discourage one trainee but encourage another to apply for a specific funding opportunity? How can one determine lab expectations?

I now take more time to explain processes to my trainees and make fewer assumptions about what they know. It is easy to forget they don't just know how manuscript submissions, reviews and revisions go. I now walk them through the whole process at the beginning and remind them of the process at each step.

Recently, editors rejected one of our manuscripts after two weeks at a journal. I sat down with the trainee author and was honest about how disappointing this was, why the editors might have made this decision and what we would do about it. This gave the trainee a place to discuss their feelings and ask questions. It made a difficult situation much easier. We submitted the paper to another journal, where it is now being revised after largely positive reviews.

This program reminded me that trainees don't know everything about lab expectations. Often, students get so focused on doing research that they skip a lab meeting or a departmental seminar. I've learned to pause before reacting, to consider why they might think this is okay. I can now have more productive conversations about my expectations.

In LEAD, it is sometimes hard for me to be the mentee and not the mentor. When Fasilat told me she wanted to delay her first committee meeting because she had limited data on her project, I immediately jumped in. I told her about the purpose of committee meetings and how talking through the questions you want to address and how you plan to address them is often more important for project success than talking about your data.

To combat this urge to mentor, I try to enter each meeting with a few questions or issues I want Fasilat's perspective on. She is an amazing scientist, who is always willing to give me a hand and share her view.

I look forward to seeing where Fasilat's career takes her and hope to maintain our mentoring relationship — in both directions — for decades to come.

Tina Tootle (ttootle@uiowa.edu) is a professor and chair of the biology department at the University of Iowa.

The impact of nested identities

By Saket Bagde

Throughout my academic research career, I have found myself in the role of mentee or mentor, often both at the same time. Navigating these roles as a person with multiple intersecting identities is both rewarding and challenging.

As a LEAD participant, I mentored Allison McKenzie, a tenured professor and lab director at Chapman University in Irvine, California; a project scientist at the University of California, Irvine; and a physical therapist. At the time, I was a Ph.D. candidate at Cornell University.

Intersectionality occurs when the interplay of multiple social and political identities dictates a unique set of challenges, inequalities and privileges for an individual. It became apparent in our conversations that the concept of intersection may not provide a full picture of the relationships among multiple identities.

While my South Asian identity dominates my appearance, I am also a member of the Dalit minority within the South Asian community. And my queer identity makes me a minority within a minority. What I call a "nesting doll" concept describes how some identities may be more apparent than others. Navigating nested identities can be even harder in an environment where some identities are less visible due to a lack of awareness, as in the case of international researchers.

My identity as a member of the historically marginalized Dalit community may not be obvious or considered relevant in the U.S. Many people here think casteism only prevails in South Asia. I explained to Allison that the repercussions of

caste-based marginalization continue when people move to the U.S. from South Asian countries. A 2018 report, published by Equality Labs, a U.S.-based South Asian Dalit civil rights organization, and covered by the mainstream media, described incidents of caste-based discrimination in the workplace and education in the U.S.

I told Allison that my peers, in both India and the U.S., have questioned the merit of Dalit students who benefit from affirmative action in India. Hearing this prevents me from freely expressing my Dalit identity. The absence of role models around me, due to the lack of Dalit representation among my peers and faculty, compounds the problem. Talking about this helped us realize how marginalization can easily spill across borders.

To reduce the burden of performing my identities and to streamline our meetings, I created a document summarizing our conversations. I made lists of my identities and academic roles to guide our discussion of how each of my identities influenced my progress at different milestones in my career. We talked about how navigating my high school and undergraduate studies as a closeted queer student in India was very different than my graduate studies in the U.S. as an out queer person.

Having open discussions about my identities helped me realize the effort I have made over the years in navigating difficult circumstances. Allison told me about navigating her career as a woman in academia, and this encouraged me to share my experiences without the fear of being judged.

The LEAD program helped me realize that in mentoring we learn from the experiences of both the mentor and the mentee. Both can embrace perspectives informed by each other's identities and backgrounds and work toward improving learning and productivity.

In practice, the power imbalance in mentor–mentee relationships may hamper the free exchange of ideas. And while our goals may be clear, often the path to achieving them is not, mainly because each mentor or mentee comes with a different learning background and identities.

The reversal of mentoring roles allows the power balance to shift to a diversified approach toward problem solving. Most importantly, reverse mentoring could inspire institutional measures that allow the mentors who are decision-makers to step into the shoes of mentees and understand the vast implications that our identities and backgrounds have on learning.

Saket Bagde (sbagde@crystal.harvard.edu) is a postdoctoral research fellow in cellular and molecular medicine at Boston Children's Hospital and in biological chemistry and molecular pharmacology at Harvard Medical School.

Equitable hiring strategies for a diversified faculty

By Allison C. Augustus–Wallace

Most institutions of higher education report that diversifying their faculties continues to be a challenge. To address this challenge, 21 biomedical engineer–researchers have developed an evidence-based road map that describes six important strategies for a plan of action to hire faculty from historically marginalized and excluded backgrounds.

The first strategy these authors offer in their recent paper in Nature Biomedical Engineering is to prepare the work environment. They articulate the importance of this seemingly obvious detail and thereby set the foundation for the effectiveness of the other five strategies.

In "Preparing the Department," the authors suggest that academic departments should conduct a self-reflection by evaluating five areas: growth, academic leadership, current department climate, improvement of the department's culture and accountability and past mistakes. Each of these areas offers an opportunity to reimagine the current environment into one that is conducive to great achievement by actively and intentionally creating an overall inclusive culture; thereby, setting a department onto a path for greater overall well-being and productivity for all of its members.

The second strategy, "Preparing for the Search," also seems obvious; however, it is a much greater undertaking than many academics may realize. The authors identify and evaluate challenges and then provide seven specific approaches to mitigate them.

As I read this strategy, one approach, "train the search committee," stood out — this important detail often goes unnoticed. However, to mitigate behaviors caused by unconscious or implicit biases — or as I identify them, microaggressions in decision-making — training search committee members and, as the authors suggest, using a candidate selection rubric, can be critical to the overall outcome in selecting faculty from historically marginalized and excluded backgrounds. As presented, the authors have clearly considered such circumstances and provide thoroughly measured mechanisms to mitigate this primary source of historical, systemic exclusion.

Also, the authors recognize the potential counterattack regarding such diversity, equity and inclusion training. Hence, they suggest that such training be "coupled with activities that help the committee recognize and address potential defensiveness." Furthermore, the authors address the need to "embrace new hiring practices" as well as "revision of application materials" to be holistic, transparent and inclusive to mitigate disparities.

Additional strategies offered by the authors include "Recruiting a Diverse Applicant Pool," "Conducting Holistic, Equitable Assessments" of candidates, "Conducting Inclusive Interviews," "Making the Offer" and "Recruiting Candidates" as well as a "Call to Action." Like the prior strategies described in this article, each of these is presented with its own approaches and provides tactical solutions to address identified challenges in the field of biomedical engineering, which are applicable throughout the academy, to address challenges to equitable hiring.

As presented, this road map provides solutions that have the potential to lead us to a more perfect, inclusive union in an academy that reflects us all.

Allison C. Augustus–Wallace (awall1@lsuhsc.edu) is an associate professor-research and director of Undergraduate Academic Pipeline Programs for Diversity at the Louisiana State University Health Sciences Center-New Orleans, School of Medicine, Office of Diversity and Community Engagement and a member of the ASBMB Maximizing Access Committee.

The legacy of Geraldine P. Woods

She helped create NIH programs to broaden participation in STEM

By Raechel McKinley

I want to highlight a remarkable scientist whose actions led to the development of two of the most successful diversity training programs at the National Institutes of Health, NIH: Geraldine Pittman Woods.

I was one of the thousands of students who have benefited from these programs.

In 1964, Woods became the first African American woman appointed to the National Advisory General Medical Sciences Council at the NIH. In this position, she improved science education and research opportunities at historically Black colleges and universities by establishing two programs: Maximizing Access to Research Careers and Research Initiative for Scientific Enhancement, both components of Minority Biomedical Research Support at the NIH.

In the more than four decades since their founding, these programs have diversified the biomedical science, technology, education and mathematics workforce by supporting academic, research and professional development activities for undergraduate students from underrepresented groups.

Ruth Kirschstein, former acting NIH director and director of the National Institute of General Medical Sciences, called Woods "a person ahead of her time."

"She received a Ph.D. in biology from Radcliffe long before any other African American scientist could so qualify," Kirschstein said. "Yet, she never forgot her roots and worked tirelessly to assist in establishing the MARC and MBRS programs."

Seeing her aptitude for science, Geraldine Woods' professors at Howard University urged her to continue her education. She earned both a master's degree and a Ph.D. in neuro-embryology from Radcliffe College.

The program facilitator

Born in Florida in 1921, Woods began her journey in higher education at Talladega College and transferred to Howard University where she earned her bachelor's degree. Seeing her aptitude for science, her professors at Howard urged her to continue her education in graduate school. She earned both a master's degree and a Ph.D. in neuro-embryology from Radcliffe College, now Harvard University, in 1945.

After her time at Radcliffe, Woods was briefly an instructor at Howard before she and her husband moved to California, where she raised her family. When her children were teenagers, she volunteered for social services, equality of opportunity, and civil rights efforts in Los Angeles and later served in the California Department of Employment where her work caught the attention of President Lyndon B. Johnson's wife, Lady Bird Johnson, who invited Woods to help launch the Head Start program for preschool-age children.

In 1969, Woods was appointed to the NAGMSC at NIH as a special consultant advising the council's director and staff on ways to improve and increase biomedical science research and training at HBCUs.

"I noticed that, NIH and NIGMS, receive thousands and thousands of grant applications, but so few of them were from Black colleges," Woods said in the book "Black Women Scientists in the United States." "And of those few that did come from Black colleges, even fewer were awarded funding."

Woods contributed to the founding of the MARC and RISE programs in 1977, working with a group of colleges and universities toward the goal of developing a strong undergraduate curriculum and gathering undergraduate interest in the biomedical sciences. By the end of the first year, 120 students had matriculated in undergraduate research through both programs and in 1981, the MARC

program opened awards to doctoral trainees.

As a scientist–activist, Woods worked with lawmakers to improve research facilities and science curriculums at historically Black colleges and universities, and she conducted outreach to minority-serving institutions, or MSIs, through seminars and tutorials to assist with preparing federal grant applications. By serving as a liaison between MSIs and the NIH, Woods helped improve the approval rate for funding to these institutions.

About the programs

Woods died in December 1999. The programs she worked to create live on.

Since 1977, over 9,000 trainees have participated in the MARC program, with over half ultimately pursuing doctoral degrees and scientific careers. The RISE program has expanded to serve undergraduate, master's and doctoral students: the Undergraduate Research Training Initiative for Student Enhancement, or U-RISE; the Bridges to the Doctorate Student Training Program; and the Graduate Research Training Initiative for Student Enhancement, or G-RISE, programs. Both programs have provided mentorship, stipends, and opportunities to present at research conferences for underrepresented trainees.

Through institutional awards, the MARC and RISE programs have reached dozens of colleges and universities, supporting academic, research and professional development activities for underrepresented undergraduate and doctoral students in the biomedical sciences.

"Many people just call me a scientist," Woods said, "and I've been named one of the famous Black scientists, but I don't consider myself a true scientist, just a facilitator, a science-trained academic who has worked to make science available for others by developing a program to provide better access for those who, historically, have been bypassed."

> **"I don't consider myself a true scientist, just a facilitator, a science-trained academic who has worked to make science available for others."**
>
> — GERALDINE P. WOODS

Personal impact

As a former RISE scholar myself, I feel honored to write about Woods and her many accomplishments.

Through RISE, I was able to get the vital research experience and professional development needed for graduate school that I would have not been afforded otherwise. The program provided mentors who saw unlimited potential in me and nurtured my love of science. Through RISE, I was able to attend my first scientific conference, learn effective networking strategies and explore a variety of research fields. Without the exposure to research so early on as an undergraduate, I never would have thought pursuing a career in science was possible.

Raechel McKinley (rmckinley@asbmb.org) is the ASBMB's science policy manager.

ASBMB supports diversity training programs

The American Society for Biochemistry and Molecular Biology public affairs team has advocated for increased funding for the Maximizing Access to Research Careers and Research Initiative for Scientific Enhancement programs.

In February 2022, the society recommended that the National Institute of General Medical Sciences expand the programs, which fund college sophomores through seniors, to also support first-year students.

In May, the society submitted written testimony to the House Appropriations Subcommittee on Labor, Health and Human Services, and Education in support of NIGMS funding dedicated to training and capacity-building programs that attract talent from underrepresented populations in science, technology, engineering and mathematics.

The society also contributed to a "Dear Colleague" letter sponsored by U.S. Sen. Ben Ray Luján, D-N.M. That letter specifically noted that the MARC program, and others like it, "implement effective, evidence-informed approaches to biomedical training and mentoring that will keep pace with the rapid evolution of the research enterprise."

In addition, when 26 ASBMB members attended the society's annual Hill Day and held 59 meetings with their lawmakers and legislative staffers, they advocated for appropriators to increase funding at NIGMS and other agencies with impactful STEM training programs.

With appropriation season coming up, the public affairs team plans to continue to make the case for increasing funding for these programs.

Rethinking the promotion letter

A strategy for retaining underrepresented faculty

By Yass Kobayashi

The number of qualified underrepresented candidates for university faculty is increasing; however, 60% of those newly hired as assistant professors still identify themselves as white, according to a recent study by the American Psychological Association. The racial disparity increases as faculty progress in academic rank, with approximately 71% of associate professors and 76% of full professors self-identifying as white. This trend is a systemic issue across academia, regardless of the type of institution.

One factor that contributes to the attrition of underrepresented faculty is the letter of support or evaluation that candidates for promotion receive from senior colleagues. Although these letters are intended to support faculty members, many of them fail to convey that message because they are written using narrowly defined standards that are often racially biased and arbitrarily established.

The 2022 eLife article "Equity, Diversity, and Inclusion: A Guide for Writing Anti-racist Tenure and Promotion Letters" tackles this issue and suggests a different approach. The authors state that letter writers should start by reflecting on their own background and identities. They should ask for the institutional and departmental priorities on categories used for evaluation (teaching, research and service). They should also research departmental and institutional demographic information and examine how the candidate influences both within their field and outside their expertise with work in areas such as diversity, equity and inclusion, collaboration and leadership.

The authors state the importance of addressing the candidate with their formal title or academic rank rather than using generic terms. They advise writers to use a broad definition of productivity, describing all the candidate's achievements in detail and recognizing their contributions to different areas of service by elaborating on their efforts in mentoring and community development.

The writer of the letter, the authors suggest, must be aware of and address the issue of racial bias and the narrow and arbitrary nature of how productivity is defined. After the letter is complete, the authors suggest that support for underrepresented faculty members should continue by citing the candidate's work whenever possible, showing appreciation for their work and their effort in mentoring and enhancing their visibility through award and speakership nominations.

Writing an inclusive and anti-racist letter does not support the notion that standards for evaluating underrepresented faculty members are lower, the authors stress, and they acknowledge that changing the white-centric culture pervasive in academia is extremely difficult.

Writing an unbiased letter of support that reflects the excellence and contribution of underrepresented faculty to the department and the institution may be the first step in stopping the harmful trend of underrepresented faculty attrition and improving their retention and promotion.

If universities and colleges are to become more inclusive, we must continue to advocate for departmental and system-level changes. We also need to evaluate and support the excellence and efforts of underrepresented faculty members, not only within our institutions but also in our society.

Yass Kobayashi (ykobayashi@uga.edu) is an associate professor at the Augusta University/University of Georgia Medical Partnership of the Medical College of Georgia and a member of the ASBMB Maximizing Access Committee.

From the known to the unknown

Tips and tricks for writing a manuscript introduction

By Emily Ulrich

Preparing a manuscript can be daunting. Maybe you're under a time crunch. Maybe you're managing experiments for another project. Maybe this is also your first time writing a research paper.

I recently shared with you our tips for writing titles and abstracts. Now, we are moving on to the introduction.

Here, I am covering what I learned about writing introductions from "Writing Science: How to Write Papers That Get Cited and Proposals That Get Funded" by Joshua Schimel and "Essentials of Writing Biomedical Research Papers," Second Edition, by Mimi Zeiger.

Basic structure

Your introduction needs to tell us, your readers, what you set out to learn in your research and why we should be invested in the results. How do you organize your thoughts to accomplish this very important task?

Zeiger suggests structuring your introduction around three key components: stating the known information in your field, identifying the unknown information and posing a research question.

Schimel organizes these three elements of an introduction into what he calls an "opening" (known and unknown information) and a "challenge" (the research question).

Here are step-by-step instructions:

1. Start with the broadest biological significance that is appropriate for your project. Tell us why your topic matters.

2. Steadily add more detail to give us the facts we need to understand your particular manuscript. Keep this information focused and concise.

3. Point out where more research is needed. Say exactly what specific information is unknown.

4. Extend the unknown information to define the research question you want to answer. Do not leave this part out, even if it seems obvious what the question is; that just means you wrote a clear opening.

5. Explain how you will answer the question. What experimental approach did you use in your research, and what were the objectives?

6. Make your research question and approach the focal point of the introduction. No one wants to hunt for the main point. This statement is usually very distinct: "Here, our goal was to fill X knowledge gap by using Y method to characterize/analyze/measure Z."

Things to consider

- Who is your intended audience?
  - Are you planning to submit to a general science journal or a field-specific journal?
  - Consider how big of a picture to convey in your opening and what terminology to use up front.
- Keep in mind that an introduction is not a review article. Take your readers as directly as possible from what is known to what is unknown.
- Construct a logical narrative that builds to the challenge; the research question. If you notice that you are bringing up new concepts in the challenge, find a way to introduce these concepts in the background information of the opening.
- For manuscripts about a new method:
  - Communicate the current limitations for investigating the topic of interest.
  - Then, propose the new method as a way to address these limitations and advance technology.

Emily Ulrich (eulrich@asbmb.org) is the ASBMB's technical editor.

Career reinvention and reinvigoration: four stories

Four members of the American Society for Biochemistry and Molecular Biology's Women in Biochemistry and Molecular Biology Committee, known as the WIBMB, have written personal essays about their career journeys.

Pursuing the call to change

By Karlett Parra

I fell in love with research the day that I began working on my undergraduate research project. I had a mentor, designed experiments, set goals, learned to troubleshoot, developed new skills and had a new challenge every day. I enjoyed every aspect of the experience and aspired to do research forever, but after getting my master's degree I saw the end of this career path at home in Venezuela.

KARLETT PARRA

I had an overwhelming desire to go to graduate school to continue studying biochemistry after I graduated, but a wall separated me from my future. Like the families of many first-generation college graduates, mine didn't have resources.

For two years, I applied to a scholarship program in Venezuela. Each year, after many examinations, I made it to a final interview that was in English. However, I did not speak English and failed this last test.

I ultimately applied to U.S. graduate schools directly and joined the Ph.D. program of the State University of New York Upstate Medical University in 1992. This was the first time I traveled outside my home country and was away from my family. The moment I woke up on my first day in Syracuse, New York, I realized that I had finally arrived, and I was afraid. I was alone in an unfamiliar culture where everyone spoke a different language. However, I then envisioned the future — a future where I could move forward doing biochemistry research and discovery — and started the day. I felt reborn.

The ensuing three decades have been both challenging and highly rewarding. I have experienced being half of a dual-career couple, an underrepresented minority woman, an immigrant and a caregiver — all while working as a scientist. I have taken unexpected turns and directions, reinventing myself a few times.

Early in my career, I wished to be a researcher in the private sector. I had a family, however, and that constrained me geographically, so I accepted a lecturer position at a liberal arts college. I found undergraduate classroom instruction rewarding, and connecting with the students energized me.

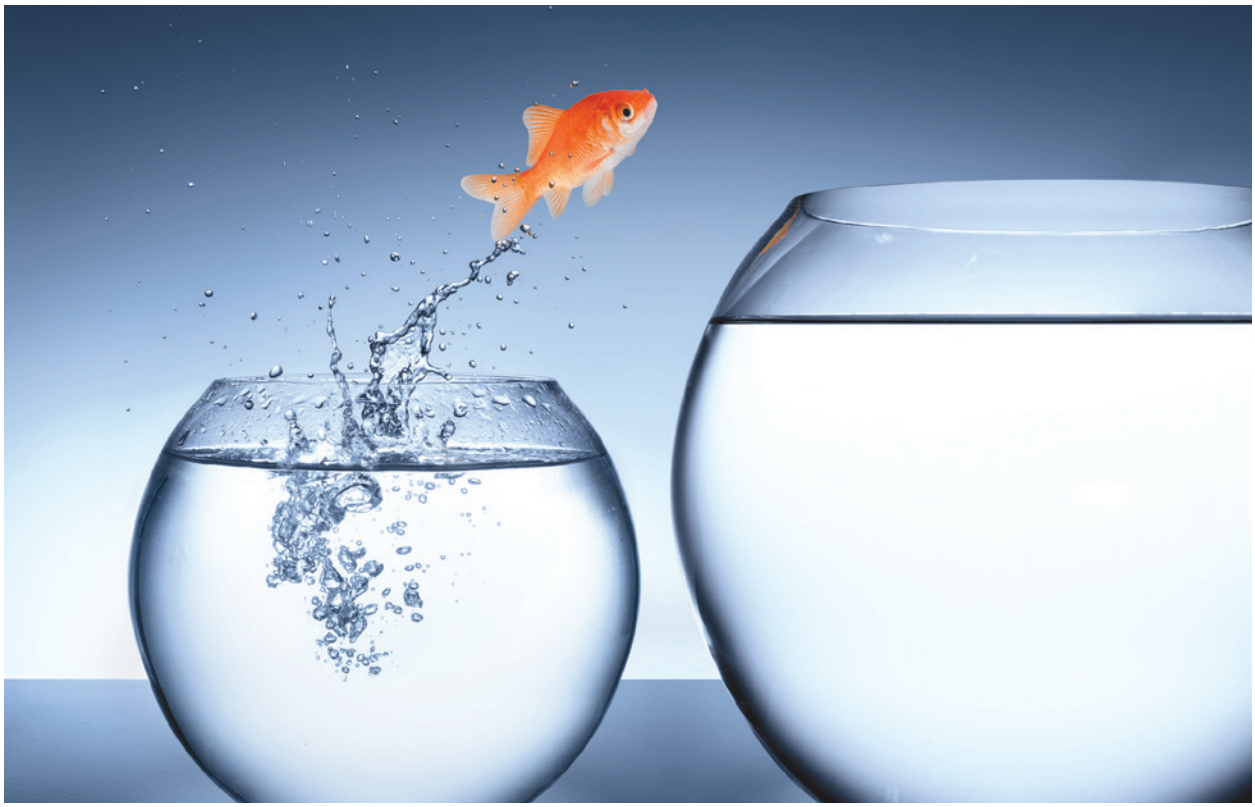
I joined the faculty of Ball State University, a primarily undergraduate institution, with the purpose of motivating students to pursue advanced research degrees. For six years, I taught and mentored students in my research laboratory. Many of them now hold faculty positions and practice medicine, which gives me great satisfaction. However, the demands of this position narrowed the scope of my opportunities to build a research program, and I wanted a position in a more research-intense environment. I found this at the University of New Mexico School of Medicine, where I moved in 2007. After five years, I was appointed chair of the department. Being a chair has expanded my academic visual field, showing me how things look from 30,000 feet. Notwithstanding, it has come at the expense of my own research program's productivity.

The COVID-19 pandemic was a time for me to reflect on my values. I wanted to do something less focused on myself, with the goal of helping people in meaningful new ways. I subsequently joined the ASBMB WIBMB Committee to help women in science navigate career challenges.

Although I was still working full-time and caring for a family, I also pursued and earned my executive MBA degree. Formal training on business management and administration was a logical direction, given that I enjoy the high-impact aspects of being department chair.

The past two years have been demanding, but worthwhile. I have refocused with a new purpose and the means to have a broader impact helping people to thrive. Looking ahead, I'll continue to embrace new directions as I did that first cold morning in Syracuse, envisioning the future and enjoying the ride.

Karlett Parra (kjparra@salud.unm.



edu) is a professor and chair of biochemistry and molecular biology at the School of Medicine of the University of New Mexico. She is a member of the ASBMB WIBMB Committee.

Catalyzing change and redefining purpose

By Sudha Sharma

I arrived in the U.S. from India for my postdoctoral training enticed by the prospects of exciting science and an incredible environment at the National Institutes of Health. Instead of being a temporary stop, this country became my newfound home, where I envisioned building my professional career and raising my family. The journey to secure a faculty position for a dual-career scientific couple was a long, rocky road that ultimately brought me to Howard University College of Medicine in 2011.

SUDHA SHARMA

Establishing an independent research program, navigating the tenure process and striving for promotion consumed my focus, and those early years seemed to pass in a blur. However, I also felt a strong desire for change, and a deeper sense of purpose emerged within me. Occupied with interim leadership responsibilities, coordinating medical courses, teaching and mentoring students, participating in committees and managing my research endeavors and grants, I had little time or need to contemplate revitalization — or so I convinced myself.

One day, during the early pandemic lockdown, I received an unexpected email from an investigator at the National Human Genome Research Institute, inviting me to join a collaborative study probing the genetic basis of COVID-19 susceptibility and manifestations. Howard University Hospital primarily serves patients from underrepresented communities, so recruiting our participants for this study was pivotal in comprehending the disproportionate impact of COVID-19 on African Americans and other ethnic groups.

Although it was challenging, spearheading this project — obtaining institutional review board approval, assembling a clinical team and leading the endeavor — promised not just a learning opportunity for a basic scientist like me; it also gave me a profound purpose. The samples we collected from our patients held the potential to unravel the underlying health disparities in COVID-19.

I directed the project at our site, gathering samples from COVID-19 patients that contributed to an important publication. Representing How-

ard University and our patients in this work was a humbling experience. With this scientific detour during an unprecedented time in history, I was able to shift focus from the constraints the pandemic imposed on my lab's research progress and productivity. I was given an extraordinary opportunity to make a substantial impact. Above all, this experience highlighted my yearning to be an active member of a broader community, where I could both contribute to and benefit from the expertise and knowledge of my peers.

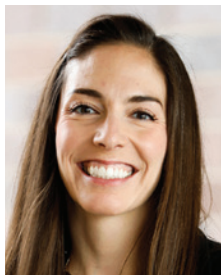
Early on, my success as a scientist meant acquiring deep expertise to address crucial research questions, measured by grants and publications. Transitioning to a faculty role broadened my focus to include teaching and service, critical for promotion and shaping the perception of success. As I reflect, I realize that my definition of success has changed over time, propelled by professional and personal circumstances, and I have needed to embrace the challenges and redefine my purpose.

Sudha Sharma (sudha.sharma@howard.edu) is a professor of biochemistry and molecular biology and interim director of the National Human Genome Center of the Howard University College of Medicine. She is a member of the ASBMB WIBMB Committee.

Building community

By Megan Filbin

I always knew I wanted to be a teacher. As an undergraduate and graduate student, I tutored and worked in afterschool programs at four inner-city middle and high schools, and I taught weekend workshops and summer camps at the Denver Museum of Nature and Science. However, I also loved research — bench work, peer review and even grant writing. How could I pursue a career path that satisfied both passions?



MEGAN FILBIN

In 2014, I happily accepted a tenure-track faculty position at Metropolitan State University of Denver, an urban, open-enrollment and Hispanic-serving primarily undergraduate institution, or PUI. In my mind, this was the place where I would teach, mentor and promote the next generation of scientists. For the first five years, that's what I did. I developed and taught courses, worked with students in the lab and took them to conferences — mentoring them toward science careers.

But it didn't work for me. I felt like I was continuously pouring from my cup, without refilling it. I lacked support, and I felt intellectually isolated and simply drained.

So, how could I fill my cup, reinvigorate my career and perhaps help others do the same? Build community.

I figured the best way for me to find the support I needed was to find others who had overcome these challenges and could share their advice and mentorship, who could critically review my research and share curriculum design, and whom I could help as well.

I started by creating a Women in STEM Faculty Group at MSU Denver where we shared challenges we faced in the tenure and promotion process. During the pandemic, I formed what I called a "peer review" group of former lab mates to share our research and tips for professional development (published in this A-Today article). I also joined the WIBMB Committee to gain advice, mentorship and professional development focused on women in STEM. More recently, I cofounded the RNA@PUI Supergroup, an international community of scientists who are PUI faculty members, or who aim to be, to share teaching and research resources to enhance undergraduate education and training.

Each of these communities has reinvigorated my career in different ways and expanded my network so I do not feel intellectually isolated. I've found that the energy I once split among teaching, research and service — the trifecta of academia — is replenished knowing I have support structures from my community of peers.

Megan Filbin (mfilbin1@msudenver.edu) is a professor of chemistry and biochemistry at the Metropolitan State University of Denver. She is a member of the ASBMB WIBMB Committee.

The power of sabbaticals

By Nick Rhind

One of the great opportunities in academic science is reinventing one's research program. In my case, sabbaticals have not led to dramatic shifts in fields. Instead they have allowed me to visit three collaborators' labs and learn new techniques that have empowered my lab to pursue new questions.

My first "sabbatical" actually happened before I started my independent career. I was hired by the Univer-

sity of Massachusetts Medical School in July 2001, but my lab in the new research building would not be ready until November. So, I accepted a generous invitation to spend three months at the Institut Pasteur learning how to comb DNA, an elegant single-molecule technique that changed the way I thought about the regulation of DNA replication.


NICK RHIND

Fast forward 11 years: I was a tenured associate professor and interested in the biochemical mechanism underlying the regulation of DNA replication that we have characterized by DNA combing. By this time I had a family, which made a foreign sabbatical impractical. I looked closer to home and arranged to spend a year in Johannes Walter's lab at Harvard Medical School, learning how to do replication biochemistry in frog embryo extracts. It was like being a postdoc again, trying to figure out how to make a project work in an environment with all of the support and expertise I needed.

After my first two visiting-scientist experiences, I was keen for a third. Constrained still to Eastern Massachusetts, nine years after my stint at HMS, I arranged to spend a year in Jeff Gelles' lab at Brandeis University. Gelles has pioneered single-molecule fluorescence microscopy, and I wanted to use the approach to test models we had about the loading of proteins at replication origins. I had another fantastic experience. A student has since established the technology in our lab, allowing us to test models we have been speculating about for years.

My primary takeaway: Sabbaticals are a precious resource.

All sorts of constraints can make them tricky to pull off — I delayed my third sabbatical a few years because of funding and staffing consideration — but the effort is well worth making. I was amazed at how much time I had to think and work when I was away from my office. I knew that not having teaching or committee responsibilities would free up lots of time. An unanticipated benefit was that not reviewing papers or grants for a year created more free time, and free mental energy, than I could have imagined. And none of the journal editors or granting agencies complained. They all said, "That's great. Have fun. Let me know when you are back in your office."

Being local, I was able to spend one day a week at UMass to have group meetings, talk with folks and look at data. My lab carried on fine, and I am sure they would have been just as fine if I had been somewhere else, meeting by Zoom.

If you're fortunate enough to have access to a sabbatical, don't waste it. Use it to reinvent your lab in some small way, and enjoy yourself while you do so.

Nick Rhind (nick.rhind@umassmed.edu) is a professor of biochemistry and molecular biotechnology at the University of Massachusetts Chan Medical School. He is a member of the ASBMB WIBMB Committee.

Books we love for future scientists

By Marilee Benore

I have always loved books, libraries and the stories captured between their spines and walls; heroines and heroes, love, remorse and hope. Storytelling is not just the most ancient of arts, but a reflection of what came before us. The lives stories describe provide a roadmap as we navigate our future.

The American Society for Biochemistry and Molecular Biology's Women in Biochemistry and Molecular Biology Committee occasionally hosts a popular book club event. I recently asked WIBMB committee members to highlight books that were important to them during their formative years — stories that empowered them on the way to becoming the cool scientists and advocates they are now.

Some of these stories are true, others are fictional, but all resonated, and so we recommend putting them on a reading list for budding citizens of planet Earth.

Did I get lost in books? Sure, but importantly, I found clues for my own path.

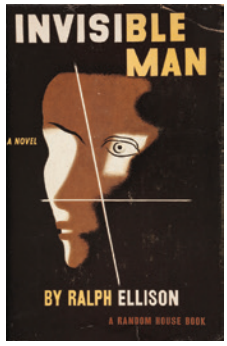
Reader's Digest best-loved books for young readers 1967: "Madame Curie"

When I was younger than 10 years old, knowing that Marie Curie was a successful scientist made it possible for me to believe that girls like me could also be successful scientists. This was a condensed version of the biography Eve Curie wrote about her mother in 1937. Since then, I have read several other biographies of Marie Curie, for example "Marie Curie: A Life" by Susan Quinn, and they never fail to inspire.

— Susan Baserga, Yale University

"Invisible Man" by Ralph Ellison

"Invisible Man" was entirely transformative for me as a high school student because, at its core, it is a book about identity — which is something each of us struggles with as we carve out our paths in this world. It also opened my eyes to subtle and not-so-subtle racism and inequitable social constructs that our society still faces today.

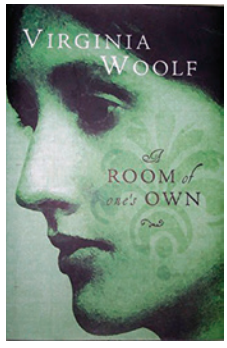


Narrated by an unnamed Black man, the masterful plot recounts the winding path of a man who navigates abuse and racism in education and the workplace, as well as power and social dynamics within the Black community. As you read, you get the sense that the narrator tries to conform to each group, but because he does not fully identify, he ultimately feels invisible.

As a scientist and educator, I see and have experienced, these same inequities and "invisibility" of particular and intersectional groups. This book is my reminder and call to action to help my students feel seen and supported on their personal and professional paths.

— Megan Filbin, Metropolitan State University of Denver

"A Room of One's Own" by Virginia Woolf



I first read Virginia Woolf's essay "A Room of One's Own" as a high school student. Woolf opens with a story of visiting the (not entirely) fictional campus of Oxbridge, where she is ushered off the lawn and not allowed access to the library because she is a woman unaccompanied "by a Fellow of the College or furnished with a letter of invitation."

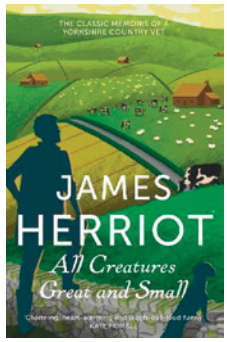
These passages increasingly resonated with me as I observed the environment around me and listened to the experiences of female friends and colleagues moving through their education and careers in the sciences. Woolf wasn't referring to scientists when she wrote "a woman must have money and a room of her own if she is to write fiction." But, I realized this could be just as easily rewritten as "a woman must have a grant and a lab of her own if she is to do science."

This essay has a permanent place on my office shelf

for its thoughtful — and often wryly humorous — articulation of how differentials in resources and access affect participation in the sciences.

— Don Elmore, Wellesley College

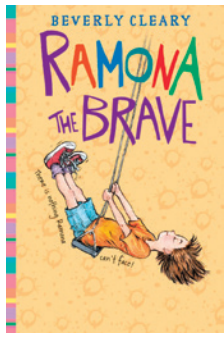
"All Creatures Great and Small" by James Herriot



I read this whole series of books about a country veterinarian and the difference he made in the lives of both the animals he treated and the humans he encountered along the way. This book made me think that I wanted to become a veterinarian (which eventually morphed into becoming a scientist).

— Kelly Ten Hagen, National Institutes of Health

"Ramona the Brave" by Beverly Cleary

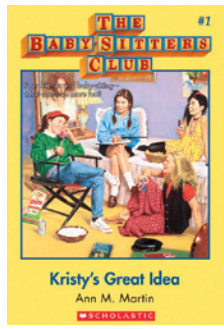


Ramona was an independent young girl with a great imagination who was fiercely determined to do things on her own terms. I could relate to her adventures around the neighborhood, her desire to wear pajamas to school, and her creativity in suggesting alternative homework for herself at school; making paper shoes instead of a paper turkey for Thanksgiving.

Ramona made it okay to see things differently, speak up and find the fun in everyday situations.

— Nicole Koropatkin, University of Michigan–Ann Arbor

"The Baby-Sitters Club" series by Ann Martin

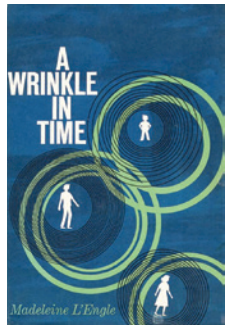


I read the Baby-Sitters Club series by Ann Martin when I was a young girl in elementary school. The books focus primarily on the friendships and adventures of the characters.

I loved these fictional books because they were about a group of friends who started a babysitting business. From a science point of view, the books promote critical thinking, problem-solving skills and emotional intelligence.

— Kanika Pulliam, ASBMB

"A Wrinkle in Time" by Madeleine L'Engle



Reading "A Wrinkle in Time" as a girl had a tremendous impact on me, assuring me that my weirdness and love of science were normal, instilling confidence and courage and allowing me to accept who I truly am as an individual.

Both Meg and her mother, Kate, were terrific role models. Kate dared to be different while conducting experiments in the kitchen, while Meg, admittedly an odd and unpopular kid, struggles with her identity and faults. Those crazy cool witches? A tesseract? Connection to family? Mesmerizing.

This 1964 Newbery medal awardee inspired a 2010 Newbery winner, "When You Reach Me," about a girl who loves "A Wrinkle in Time" and reads it constantly. I also reread L'Engle's book regularly, and it resonates.

— Marilee Benore, University of Michigan at Dearborn

Escape to the ice

Two scientists strap on their skates and grab their sticks

By Joseph Provost & Ed Eisenstein

The Zamboni finishes its last lap around the rink, and the doors clang shut as we look upon the surface for the last traces of water to freeze. Our group is stretching, chatting nervously and focusing on a few moments from now when we'll step onto the fresh ice and begin our ritual of skating the perimeter of the rink to warm up before our adult league ice hockey game.

The feel of that first step, the glide of steel on smooth ice, is exhilarating. After a few minutes of warmup laps, someone dumps a five-gallon bucket of pucks at center ice. One by one, skaters each scoop one up with their stick and you can hear the carom of hard rubber being shot against the boards and bouncing off the surrounding plexiglass.

Once we set foot on the ice, we no longer have any thoughts about deadlines, paper reviews, grant proposal submissions, papers to grade or lectures to prepare. All of our focus is on finding a rhythm and getting a feel for the ice and the puck. That's all that matters

The game itself is immaterial. Our teammates shout a lot of encouraging cliches from the bench, and we engage in enthusiastic talk of "strategy" between periods. Sure, we are trying hard and want to win. But that isn't the point. The idea is to let go, to find delight as we play and to decompress by leaving behind everyday pressures.

Each shift on the ice has the potential for success or failure: Do we score a goal? Or will we be scored on? Sometimes it takes a lot of effort to focus on the game and to relax from the day-to-day pressures of running a lab. But the game is fast — even for us.

We try hard to let go of our day jobs so we can make snap decisions to win a puck battle, outmuscle an opponent for position and make the perfect pass to a teammate for a shot on goal. Like the lab, doing the small things right is important for obtaining great results, and good execution on the ice can lead to victory.

The euphoric high we feel on the ice is a little different than what we experience in academia.

After the game and off the ice, elderly men and women tell stories about their younger glory days, boasting about the great play they made, pointing out how somebody else cost us a goal or how our goalie made an unbelievable save that they've never displayed before. And, of course, there are usually some adult beverages to stoke the exaggerations and help to make them more believable.

Our teams are diverse: plumbers, attorneys, electricians, pilots, business folks, landscapers, postal workers and professors like us. We have profound differences of opinion on some important issues. But, in the locker room and on the ice, the camaraderie is real and meaningful and genuinely reflects the broad spectrum of our community.

After the stories and adrenaline

Joseph Provost and his daughter, Kristina Provost, cross sticks in the Fargo Pond Hockey Tournament.

Joseph Provost plays in an all-military team tournament over Veterans Day in Las Vegas with the San Diego Patriots team.

Ed Eisenstein holds the Mullet Invitational Hockey League trophy awarded to his championship team, the Danglers.

Ed Eisenstein and his daughter Ariana attend an MIT hockey alumni game.

Ed Eisenstein's senior (60+) hockey team, the Silverkings, were the 2020 league champions. Eisenstein stands second from right.

fade, we finish packing our gear, throw our bags over our shoulders, pick up our sticks and head out into the crisp night air. We are content with our effort, and we're already thinking about the next game.

From time to time, maybe because the rink is cold, our eyes tear up when we take to the ice and start our laps. Or maybe we're recalling some of our glory days, when we were skating alone on a pond in winter, dangling a puck at the end of a hockey stick, dreaming about scoring the winning goal in the Stanley Cup final and shedding a tear of joy.

Joe Provost (josephprovost@sandiego.edu) is a professor at the University of San Diego, and **Ed Eisenstein** (eisenste@umd.edu) is a fellow at the Institute of Bioscience and Biotechnology Research and in bioengineering at the University of Maryland. When they aren't in their labs, offices or working for ASBMB, you can find them in the pro shop of an ice rink getting their skates sharpened.

My guitar companion

A musical journey through time and around the world

by Blaise J. Arena

The folk music revival of the 1960s gave me a great gift: I became held in thrall by the acoustic guitar.

I had no real passions during high school until I got a guitar. Then I couldn't stop. I spent hours every day learning and playing songs by Bob Dylan, Joan Baez, Doc Watson and Pete Seeger. By the time I went off to college, I was proficient at bluegrass, blues and folk — enough to be invited to join a moneymaking rock and rhythm & blues band. This was a huge ego booster for a freshman, and I became flush with cash.

After college, I continued playing, but by then I had only a couple of guitar-playing friends. Over the years my playing was mostly a solitary activity. Life came along — grad school, home, family, kids and a demanding career. My guitar playing faded into the background but I never abandoned it. It was always there, like an old friend — a companion.

When my children were grown and gone, I went back to the guitar. I decided to improve my playing and explore new musical challenges. I had always loved the rock 'n roll of the 1950s and early 1960s. I began learning some of these songs and making my own arrangements, solo instrumentals capturing the melody (no singing).

While on this path, I noticed something I'd forgotten. Many early rockers had their roots in American gospel music and hymns; they spent their youth soaking up church music in the South. Little Richard, Jerry Lee Lewis and Elvis Presley all recorded classic gospel songs they'd heard on Sundays. Blues legend B.B. King recorded a gospel album early in his career. I began learning some of these songs and learning about the history of classic gospel music in America. That history is especially rich in Black culture. And it is rich in its influence on American rock 'n roll and blues. This music has stood the test of time. On YouTube, you can find Jerry Lee Lewis performing "Life is Like a Mountain Railroad" — a beautiful melody written in the early 1900s and still performed today.

Around this time, I got involved with the Old School of Folk Music in Chicago. Founded in 1957, the school holds iconic status in the teaching and performing of folk and traditional music. I asked to teach some of my arrangements of classic rock and gospel songs.

Over the next dozen years, I taught workshop classes for adults on how to fingerpick the songs that I had arranged. I enjoyed sharing my music and its history with the students, and this was a good spur to move forward musically. Besides teaching, I also learned at the Old Town School.

I joined a Mexican mariachi ensemble group that met weekly at this school, opening a new musical world for me. The group needed a vihuela player. I bought one of these Mexican stringed instruments, similar to a guitar, and learned it well enough to get by. The songs of mariachi have beautiful flowing, lilting and soaring melodies. I felt uplifted playing

Blaise J. Arena's vintage classical guitars include, in front, a Tatay made in Spain around 1964 and, in back, a 1968 Gibson.

COURTESY OF BLAISE J. ARENA

with the group. I met interesting new people and immersed myself in the songs of the revered Mexican composer Augustin Lara. I worked out my own solo arrangements of many of these songs and taught them in my classes.

Several years before I brought my guitar out of stagnation, I'd made a couple of business trips to Japan. I became fascinated by Japanese culture, but it took a while for this interest to include Japanese music. Years later, during my involvement with the Old Town School, I decided to see if traditional Japanese folk songs could be adapted to the guitar. Again, a whole new world.

I became interested in songs from the 1800s and early 1900s written to be played on Japanese instruments of that era, such as the three-string shamisen or the zither-like koto. Their only similarity to the guitar is strings that are plucked. After some hunting, I found two good sources of sheet music for these traditional songs. One was a website (daisyfield.com) that provided free Japanese sheet music. The library of the Japanese consulate in Chicago had a thick book of sheet music for Japanese songs dating from the 1800s. They allowed me to borrow this great resource.

COURTESY OF BLAISE ARENA

This stamp represents the Japanese song, "Kojo no Tsuki."

Some of these songs are very simple. "Gonbe ga Tanemaku" tells of Gonbe sowing his seeds while scaring off the crows that are picking up his seeds as he sows them. "Koito-Utatote" is a simple haunting melody that tells of a man who cannot come to the island of Sado because the waves are too high and the distance too far.

COURTESY OF BLAISE ARENA

Blaise J. Arena holds one of his guitars, a 1966 Epiphone steel string.

"Kojo no Tsuki," a more elaborate song, has such a revered place in Japanese folk music that it was commemorated on a Japanese postage stamp showing the first line of melody beneath the ruins of a moonlit castle.

These songs have stood the test of time, and their melodies all sound wonderful when played on the guitar. I brought my arrangements to the Old Town School and taught them in many small classes over the years — trying to open some eyes and ears to this music.

One song turned out to have a surprising history. My wife and I enjoyed the Japanese Netflix series, "Midnight Diner." Each episode begins with a beautiful Japanese song, "Omohide" sung and accompanied by a guitar. After listening to the song many times, I noticed that it sounded a little Irish. Rather odd. I decided to learn the song. Along the way, doing background research, I found that the melody is a traditional Irish tune from 1790 about a pretty milkmaid. Japanese lyrics were added much later — a cross-cultural embrace between Ireland and Japan.

The gift from the 1960s folk revival turned out to be a life-long journey. A companion, always there. Along with giving me the joy and satisfaction of playing the guitar, it opened doors to new experiences and people I wouldn't have known otherwise. It led to dalliances with the music of other cultures and eras.

I still have that first guitar from 1966 and others I've gathered along the way. They are my companions.

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

A paleolithic grant review

By Bill Sullivan

You might think review panels have only been around for the last century or so. You would be mistaken. Archeologists recently discovered the following etched into the wall of a cave deep below the campus of Flintstone University, an R1 research institution.

Research Plan

Midday fatigue is a significant problem affecting the majority of our tribe, reducing our ability to hunt and gather effectively.

Our preliminary studies show that when goats eat the berries of plants in the genus Coffea, they become more energetic.

We hypothesize that coffee berries may be used to brew an energy drink for humans.

Our research plan will involve steeping the grinds from the coffee berry fruit or seed (or placebo) into heated water for 10 minutes. Samples will be blinded and consumed by age-matched participants. Energy levels of participants will be quantified 30 minutes later, assessed by how far each subject can run.

Unfortunately, the proposal was not discussed, delaying the discovery of coffee for many years. Here are the reviews:

Reviewer 1

- The premise is flawed as what happens in goats is not guaranteed to happen in humans.
- The PI has no experience grinding seeds.
- Water source is not specified.

Reviewer 2

- Leaves are already used to brew tea. Proposal lacks innovation.
- It is surprising that the PI did not determine whether goats are more energetic after consuming other foods.
- Only oral dosing is proposed. The PI should include alternate routes of administration.

Reviewer 3

- PI did not ensure that all participants would have equal leg lengths, complicating interpretation of the data.
- What if the alleged effects of coffee berries are not felt until 31 minutes postconsumption?
- Findings will have low impact: It is unlikely that most people would go to this sort of trouble when they could easily take a nap.

Bill Sullivan (wjsulliv@iu.edu) is a professor at Indiana University School of Medicine and the author of several books. He is also chair of the ASBMB Today editorial advisory board.

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