Vol. 22 / No. 8 / September 2023

ASBMBTODAY

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

Next-gen biopsies take the sting out of diagnosis

American Society for Biochemistry and Molecular Biology

Discover BMB | 2024

SAN ANTONIO | MARCH 23–26

Get ready to submit your abstract.

When you present your research at #DiscoverBMB, you get the recognition and constructive feedback that you need to make your work even better.

#DiscoverBMB 2024's abstract submission site will open mid-September.

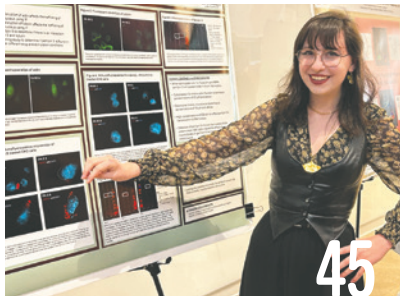
LEARN MORE: discoverbmb.asbmb.org

CONTENTS

NEWS

FEATURES

PERSPECTIVES



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

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

Wellness and trauma

By Comfort Dorn

Two days before my wedding, I was mugged.

A friend and I were walking home with groceries when four people pushed us down in an alley and started kicking us and demanding money.

I was more angry than afraid. My wallet was under me, in my back pocket, and I was determined not to give it up. Our attackers were all wearing shorts and sneakers, and I noticed that only one of them was kicking me, while three were kicking my friend. That seemed unfair. My friend was screaming. I was silent.

Most of our groceries were scattered on the ground, but the hamburger rolls were up in a bush. I wondered about the ice cream. It was a balmy evening, just around sunset, and I noticed people sitting and talking on nearby porches. After what seemed forever but was probably just a few minutes, one of those people yelled something and the four would-be thieves sprinted away down the alley empty-handed.

We picked up the groceries, thanked the man who had yelled and walked home. We called the police and filed a report, then ate our hamburgers accompanied by several stiff drinks.

Two days later, I had big bruises on my thighs, and my friend could barely walk. When I told my mother what had happened, she said, "Thank God they didn't get your face."

I got married, danced with my bruised friend at the reception and went on my honeymoon. Everything seemed fine. I told myself it could have been worse. I don't remember anyone ever asking me if I was OK once the bruises faded. But I felt different. I was afraid. Ever since then, I'm wary when I pass an alley.

In the great continuum of trauma, I think this is at the low end. But it had an impact. And my mother's appalling (but understandable) reaction was a wound.

In one way or another, we all experience trauma and its aftermath. It shapes who we are. A big part of wellness is our ability to recover and learn from trauma — and our ability to be supportive and empathetic when those around us experience trauma.

For that reason, we are making trauma and recovery the theme of our 2024 wellness issue, to be published in January.

Telling stories helps us heal. I just shared my trauma story. Now I want to read yours. Send it to asbmbtoday@asbmb.org. The deadline is Oct. 1.

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

Let's talk about Texas

By Ann Stock

Discover BMB, the annual meeting of the American Society for Biochemistry and Molecular Biology, will be held next year in San Antonio, a historic, culturally diverse city with many lovely attractions and affordable lodging. It's located in a state that is home to leading research and teaching institutions — and more than 500 ASBMB members.

And, yes, San Antonio is in Texas.

In my 30-plus years as an ASBMB member, I've come to appreciate how informed and politically astute members of our community are. You know that Texas politicians are making national headlines by stripping away abortion rights and targeting the LGBTQIA+ community. And then there are the guns.

You know that policies enacted at the state and local levels across the U.S. affect the lives and careers of our members. They also influence scientists' decision-making when it comes to attending conferences.

I'm writing to you today because I understand your concern about gathering in Texas next year.

In the early 1970s, the ASBMB founded committees focused on the advancement of women and marginalized scientists. For more than half a century, the society has spoken up and put its money where its mouth is by funding travel awards, scholarships, awards and mentoring. Pouring money into a state with leaders who are actively harming members of our community doesn't align with our values or our public statement on diversity, equity and inclusion.

The ASBMB Council selects meeting sites years in advance. As president, I am responsible for the good stewardship of the society's funds. I understand the many factors that go into picking a meeting site, and I understand the decision to stick it out.

In hindsight, what's happening in Texas and elsewhere today isn't all that surprising, but none of us can foretell the future.

Several years ago, as we prepared for Discover BMB 2023 in Seattle, we asked groups of members how we could better meet their needs in future meetings. They told us repeatedly that the cost of flights to and hotel rooms in coastal cities is prohibitive and that we need to be more open-minded about locations if we want entire labs to be able to attend, which of course we do.

Texas is known as the Lone Star State, but Texas is not alone when it

comes to laws reducing individual rights and freedoms. Almost every day, we hear another state or locality has enacted policies targeting women and marginalized people.

California now prohibits state-funded travel to states with discriminatory laws. As of today, that list includes 24 states, and Texas is among them. The way things are going, more than half of the states in the nation might be on the list by 2024. And that's not counting states where lawmakers are attacking academic freedom by eliminating tenure and diversity and education programming.

If we decide not to meet in any of these states, we cut ourselves off from much of the country. And we give up a chance to show up and show solidarity with members and colleagues whose work and study have brought them to live, day in and day out, under these laws.

For a long time, institutions in the southern and middle regions of America have received less federal research grant funding than those on the coasts. That's on top of the decades-long defunding of state institutions. In light of growing efforts to make voting more difficult and to gerrymander districts, the disparity and disinvestment are likely to deepen, even if it is unpopular with voters. Bioscientists who need to stay, for whatever reason, will be forced to do their best with even less.

The ASBMB provides resources for its members to engage with legislators at the state and local levels. I encourage all our members to take advantage of them. Elected officials need to hear from you about your experiences and concerns. They need to know how state and local policies affect your ability to recruit students and faculty, for example, or your family's ability to access needed health care. They need to know if you feel unsafe going about your life.

All of this is to say that I too am concerned about Texas. I worry about the safety and well-being of our members who live and work there. I worry about their family members, friends and neighbors. I worry about the future of science in Texas.

When we meet in San Antonio next year, all of us must show our solidarity with Texas scientists, women and members of the LGBTQIA+ community.

The ASBMB Meetings Committee is committed to making our gathering an inclusive space for all who attend. To this end, the Maximizing Access Committee, the Women in BMB Committee and the Public Affairs Advisory Committee are teaming up to create opportunities for us to demonstrate our commitment to scientific and social progress and to advocate for policies that protect academic freedom and the most vulnerable.

I look forward to sharing more details in a future column. And in the meantime, I invite you to share with me your suggestions for gestures of support.

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.

Protein Society recognizes Gardner, Gestwicki

American Society for Biochemistry and Molecular Biology members **Kevin Gardner** and **Jason Gestwicki** have received 2023 awards from the Protein Society.

Gardner won the Stein & Moore Award, which recognizes eminent leaders in protein science who have made sustained high-impact research contributions to the field. Gestwicki received the Emil Thomas Kaiser Award, which recognizes a recent and highly significant contribution or application of chemistry to the study of proteins.

Gardner is a professor of chemistry and biochemistry at the City College of New York and City University of New York Graduate Center as well as director of the Structural Biology Initiative at the CUNY Advanced Science Research Center. He studies the structure, dynamics and function of ligand-regulated protein interaction domains from bacteria, plants and humans to develop innovative optogenetic tools and cancer therapies. Gardner has won many honors for his research and mentoring including the Biophysical Society Biophysics of Health and Disease Award. He is a member of the ASBMB Public Affairs Advisory Committee.

GARDNER

Gestwicki is a professor of pharmaceutical chemistry and associate director of the Institute for Neurodegenerative Diseases at the University of California, San Francisco. His research focuses on molecular chaperones and developing innovative tools and approaches to target diseases of protein misfolding. The group recently published a research article on the structure–activity relationships of the human 20S proteasome activators.

GESTWICKI

Gardner, Gestwicki and other Protein Society award recipients will be honored in July at the society's annual symposium in Boston.

Bridwell–Rabb, Jimah win Sloan fellowships

Two members of the American Society for Biochemistry and Molecular Biology, **Jennifer Bridwell–Rabb** and **John Jimah**, are among this year's 125 recipients of Sloan Research Fellowships, which are awarded to early-career, tenure-track faculty members in the U.S. and Canada.

Jimah, an assistant professor of molecular biology at Princeton University, studies the molecular mechanism of membrane remodeling in human cells and malaria parasites. His research relies on cryo-electron microscopy and tomography, as well as cell biology, biochemical and biophysical approaches. Jimah earned a Ph.D. in biology and biomedical sciences at Washington University in St. Louis.

JIMAH

Bridwell–Rabb, an assistant professor of chemistry at the University of Michigan, studies how organisms use metalloenzymes to power chemical reactions, with and without molecular oxygen. Specifically, her lab studies how plants modify chlorophyll and bacteriochlorophyll to absorb different colors of light, how enzymes use metallocenters to conduct hydroxylation and how light affects gene regulation. Bridwell–Rabb earned a Ph.D. in chemistry at Texas A&M University.

BRIDWELL–RABB

The Sloan fellowships recognize distinguished performance and a unique potential to make substantial contributions to a scientist or scholar's field. Fellows receive $75,000 over two years for research-related expenses.

Doudna receives first Kimberly Prize

Jennifer Doudna was awarded the inaugural Kimberly Prize in Biochemistry and Molecular Genetics by the Simpson Querrey Institute for Epigenetics for her research contributions to the development of CRISPR/Cas9 technology. The prize will be awarded annually to a scientist who has made "outstanding research contributions into the molecular basis of life with a direct demonstrated link of their discovery into the clinic for the betterment of humankind." Doudna will receive $250,000.

DOUDNA

Doudna is a professor of biomedical science at the University of California, Berkeley. She received the 2020 Nobel Prize in Chemistry with Emmanuelle Charpentier, a professor of the science of pathogens

at the Max Planck Institute, for her work on CRISPR/ Cas9 genome editing. Her lab continues to investigate the CRISPR bacterial adaptive immune system as well as ways to target and engineer CRISPR/Cas systems.

Doudna is a member of the National Academy of Sciences, the American Academy of Arts and Sciences, the National Academy of Medicine, the National Academy of Inventors, the American Academy of Microbiology, the Royal Academy and the Pontifical Academy of Sciences. Her numerous honors include the Golden Plate Award from the American Academy of Achievement, a Guggenheim Fellowship and the Award for Excellence in Molecular Diagnostics from the Association for Molecular Pathology. She received the first American Society for Biochemistry and Molecular Biology Mildred Cohn Award in 2013.

Matthews wins Rice award

Kathleen Shive Matthews received a 2023 Gold Medal Award from Rice University. This award, Rice's highest honor, is given to faculty members who demonstrate extraordinary service to the university. The award was presented in May at the Association of Rice Alumni's 2023 Laureates Awards ceremony.

MATTHEWS

Matthews is a professor of biosciences at Rice. Her research has focused on the structure and function of genetic regulatory proteins such as the lactose repressor in E. coli. Her lab recently published an article showing that the lactose repressor's hinge domain binds independently to DNA.

A fellow of the American Association for the Advancement of Science, Matthews won the American Society for Biochemistry and Molecular Biology William C. Rose Award in 2015 for excellence in research and mentoring young scientists.

Matthews served on the editorial board of the Journal of Biological Chemistry from 1989 to 1994 and as an associate editor from 1994 to 1999. She was on the ASBMB Nominating Committee 1993–1994 and 1996–1997 as well as the Finance Committee 1997–1999 and 2001–2004.

AHA honors Pandey

Kailash N. Pandey received the 2022 Lewis K. Dahl Memorial Lecture Award from the American Heart Association Council on Hypertension. This award honors researchers who have made outstanding research contributions to the field of hypertension. Pandey gave the award lecture during the AHA's Hypertension Scientific Sessions in September and received a $1,000 honorarium.

PANDEY

Pandey is a professor and vice chair of medical research in the Department of Physiology at Tulane University Health Sciences Center, School of Medicine. His lab focuses on determining the genetic and epigenetic basis of hypertension and other cardiovascular disorders.

Pandey has received several other awards from the AHA, including an Established Investigator Award. He has a publication record of more than 140 original peer-reviewed research articles, reviews and book chapters. He has trained more than 40 postdoctoral fellows and graduate students and has presented invited lectures at 98 universities and research institutions.

Garg wins AAAS public engagement award

Neil Garg has been awarded the Bhaumik Award for Public Engagement with Science by the American Association for the Advancement of Science. This award recognizes scientists and engineers who promote meaningful exchanges between science and society via dialogue with the public. His public engagement initiatives include a coloring book to teach students of all ages the wonders of organic chemistry. Garg received a monetary prize of $5,000, a commemorative plaque and recognition at the AAAS annual meeting.

Garg is a professor of chemistry and biochemistry at the University of California, Los Angeles. His lab focuses on developing synthetic strategies and methods to create bioactive molecules to treat various diseases. Garg and his lab recently published an article describing a new, efficient method for synthesizing lissodendoric acid A, a compound that might be useful for treating Parkinson's disease. He has also published articles about the importance of mentoring and education in science.

GARG

In 2019, Garg won the American

Society for Biochemistry and Molecular Biology Award for Exemplary Contributions to Education. More recently, he was awarded the Royal Society of Chemistry's Horizon Prize and became a fellow of the American Institute of Chemists.

Chandel receives innovation award

Navdeep Chandel has won an IDP Research Innovation Challenge Award. With his co-principal investigator, Seth Pollack, a professor at Northwestern University, Chandel will receive funding for his project on selecting antigen-specific T cells for cancer therapy using mitochondrial membrane potential. The IDP Foundation gives these five-year awards to innovative, team-driven, cancer research projects that are translational, cross-disciplinary and collaborative.

CHANDEL

Chandel is a professor of medicine and biochemistry and molecular genetics at Northwestern. His lab studies mitochondrial metabolism and how it impacts cancer cells as well as immune cell differentiation and function. In 2015, he published an introductory book titled "Navigating Metabolism."

Chandel has published hundreds of research articles and has been named to the Global "Highly Cited" list by Clarivate Analytics in 2020, 2021 and 2022. He received the National Cancer Institute Outstanding Investigator Award in 2016. He has also been awarded the Clarence Ver Steeg Faculty Mentor Award, which recognizes outstanding faculty from Northwestern in supporting and encouraging the academic and professional development of graduate students.

Cancer research grant for Post's team

Steven Post belongs to one of five teams of cancer researchers that received the 2023 Team Science Awards from the Winthrop P. Rockefeller Cancer Institute at the University of Arkansas for Medical Sciences. This award program provides support to unite teams of cancer researchers in a multidisciplinary effort to uncover new approaches to treat cancer.

Post is a professor of pathology, and his coinvestigator, Marjan Boerma, is a professor of pharmaceutical sciences, both at UAMS. Their project is titled "Synergistic effects of SR-A blockade and radiation therapy."

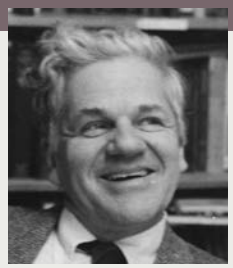
Post's lab studies how macrophages sense and respond to their environment via scavenger receptors such as SR-A. Post is interested in the molecular basis underlying the contribution of macrophages in chronic inflammatory diseases, including cancer.

POST

The project funded by the award will determine whether targeting SR-A sensitizes breast tumors to targeted radiation therapy. This work may lead to future novel therapeutic approaches targeting macrophages in cancer and other diseases.

Post and Boerma received a $100,000 pilot grant and a commemorative plaque.

Melvin Simpson



Melvin Simpson, founder of the biochemistry department at Stony Brook University and a member of the American Society for Biochemistry and Molecular Biology since 1955, died on Jan. 31, 2022, the society learned recently. He was 100 years old.

Simpson was born on July 15, 1921. He earned his Ph.D. in 1949 from the University of California at Berkeley for studies of protein biosynthesis in the laboratory of Harold Tarver and began his independent career as a professor at Yale before moving to Dartmouth where he was an American Cancer Society Professor.

In 1967, Simpson joined the faculty of Stony Brook University to start a section in biochemistry within the biology department. Two years later, biochemistry became a separate department with Simpson as the founding chair. He worked to recruit faculty as well as establish a positive, inspiring environment. "He always had a smile on his face … he wanted everyone to be happy," Norm Arnheim recalled in a Stony Brook memorial article.

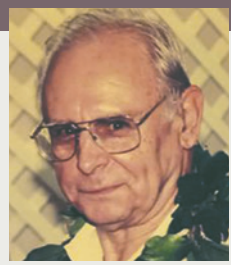
Protein synthesis was the focus of Simpson's early scientific career; he pioneered a method to track synthesis using radioactive methionine. Later, his interests expanded to include DNA, in particular mitochondrial DNA synthesis and metabolism. His studies included work on a mitochondrial topoisomerase and mitochondrial DNA evolution. He also studied the mechanism of nucleoside analog AZT, which was being tested as an AIDS antiviral at the time.

Simpson served in the U.S. Navy during World War II. He maintained a love of boats and sailing his whole life, often sharing stories of places he visited. His wide-ranging interests beyond scientific research included archeology, a subject in which he took classes at Stony Brook while a professor.

Simpson's colleagues and former students remember him as someone who treated everyone with respect and kindness; they write that he was a good mentor who asked critical questions while also supporting his mentees and colleagues with a helping hand both within and outside of the lab.

— Elizabeth Stivison

Robert H. McKay Jr.



Robert Harvey McKay Jr., a longtime professor at the University of Hawaii, died on October 17, 2022, in Hawaii at age 95. He had been a member of the American Society for Biochemistry and Molecular Biology since 1968.

McKay was born on June 12, 1927, to Orpha Vivian Ellis and Robert Harvey McKay Sr. in Cordova, in what was then the U.S. Territory of Alaska. He attended high school in Bremerton, Washington, and completed his undergraduate studies at the University of Washington in 1953. He received his Ph.D. in biochemistry in 1959 under the mentorship of Richard Fineberg at the University of California, Berkeley, where he was able to isolate an insoluble iron-rich microscopic granule, hemosiderin, from horse spleen. He did his postdoctoral work at Harvard and Brandeis universities.

McKay married Monica McTigue in 1958. The couple and their three children moved to Hawaii in 1963, and McKay started his independent research career as an associate professor of biochemistry and biophysics at the University of Hawaii. During his 34-year career, his research work focused on hematology, specifically iron metabolism in humans.

In a tribute posted to his obituary, a former student remembered being part of McKay's cancer research and wrote that he was a "wonderful mentor" as well as a very "kind and patient" person. He was president and founder of the Shhh Hawaii Charter Chapter of Ohana Kokua, an organization to help people with hearing impairments.

McKay loved to spend long weekends fishing, hiking or playing tennis or poker with his friends and colleagues. He married Anne Winifred Walker in 1998 and enjoyed traveling around the world with her.

Anne McKay died in July 2022. Robert McKay is survived by his children, Karen Fothergill, Jon McKay, Kevin McKay and their families; and three stepchildren and their families.

From failing to acing chemistry

By Kanika Khanna

Early in high school, Carolyn J. Karns loved attending chemistry fairs and wearing her "periodic table T-shirt." But during her junior year, she began to feel like she didn't fit in. She wanted a different environment, so she enrolled in a community college.

Karns' journey took an unexpected turn, however, when she failed her first chemistry class. "It was a reality check," she said. "I had underestimated the amount of work that was needed for college studies."

After this setback, she almost abandoned college.

While feeling uncertain about her academic future, Karns stumbled on an ad for undergraduate admissions at Eastern Illinois University. Drawn in by the campus's beauty and friendly atmosphere, she decided to give it a try.

At the university, Diane Burns, chair of the geology and geography department, noticed Karns' curiosity and encouraged her to take science classes.

"She helped me believe in myself again," Karns said.

With renewed confidence, Karns decided to give chemistry another shot. She later joined Michael Beck's lab as an undergraduate researcher. Beck is the faculty adviser of the ASBMB Student Chapter at Eastern Illinois. Karns became involved in the chapter's activities in 2020 and served as its president from 2021 to 2022.

The chapter community supports students in their quest for research careers. "It has been invaluable to surround myself with like-minded individuals who share similar goals and have the ability to bounce ideas off one another," Karns said. "I found some of my best friends here."

Karns was an organizer for what she called a "Rapid Research" event for students who were interested in research but uncertain where to begin. Professors from the biological sciences and chemistry departments gave five-minute presentations on their labs' work. Chapter members then helped students connect with the professors for further guidance.

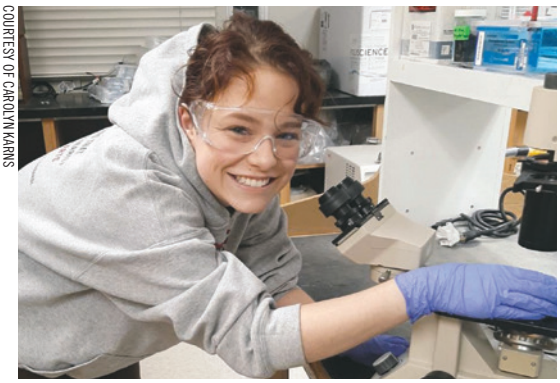
The chapter collaborates to organize workshops on résumé building and reviewing graduate applications. Karns has invited professionals from diverse backgrounds, including academia and industry, to share their experiences with students on campus.

"Engaging with students and conducting outreach initiatives has been instrumental in cultivating and sustaining interest in the field of sciences," she said.

Karns received an ASBMB Student Chapter travel award to share her research at the 2022 Experimental Biology conference. She was still exploring potential career paths and valued the networking opportunities in the ASBMB lounge.

"I found the interactions during the sessions to be immensely beneficial," she said. "They helped shift my perspective from what I 'could' do in my career to what I truly 'want' to do."

Karns graduated in 2022. Now a first-year student in the master's in biological sciences program at Eastern Illinois, she's focusing on chemical biology. In Beck's lab, she is developing novel fluorescent chemical tools to study carboxylesterases — enzymes that play a crucial role in the metabolism of organic compounds found in drugs such as aspirin as well as narcotics like cocaine and heroin. Beck has helped Karns realize her scientific potential.



COURTESY OF CAROLYN KARNS

Carolyn Karns is now a first-year student in the master's in biological sciences program at Eastern Illinois University.

"He encouraged and nurtured my inquisitiveness," she said, "(and) kept me going on in science."

Upon completing her master's degree, Karns is considering pivoting her focus to pursue a Ph.D. in marine biology. The ocean provides her with great solace, she said, and she also wants a new adventure. "I yearn to engage in hands-on fieldwork," she said.

Karns believes in the power of perseverance. "If you want it, you can do it all," she said. "Have the confidence and don't give up."

Kanika Khanna is a postdoctoral fellow at the University of California, Berkeley. She earned her Ph.D. at University of California, San Diego. She is passionate about science outreach and communication and likes to crochet and hike in her free time.

What do ASBMB members work on?

Results from the member interests survey

By Joanna Kotloski

In late April, the American Society for Biochemistry put out a survey asking its members what they work on. Biochemistry and molecular biology cover a lot of ground, and the responses reflected that: The members who responded work on a wide range of topics.

The most common primary area of research was protein structure and folding, followed by molecular bases of disease, gene regulation, metabolism and enzymology.

Of those who focus primarily on protein structure and folding, 20.4% study the role of proteins in disease, 16.7% are interested in protein folding from a biophysical perspective, 11.1% work on enzymes and another 11.1% are interested in signal transduction.

As for those whose work falls primarily under the "molecular bases of disease" category, 20.4% said they are interested in signal transduction, 13% in protein structure and folding, 13% in gene regulation, 9.3% in metabolism and 7.4% in immunology.

Importantly, the options provided to respondents didn't neatly describe everyone's work. In fact, the top choice of primary area of interest was "other."

Some of the interests of those who marked "other" include protein engineering, biofuels, medicinal chemistry, oncology, drug design, chemical biology and developmental biology.

Respondents also offered a lot of helpful comments. For example, some people suggested the society do more events and annual meeting sessions on the topics of DNA replication and chromosome biology, on instruction in new research techniques and educational best practices, and on extracellular vesicles, nutritional biochemistry and cancer biology.

The society also will use these data to develop future opportunities for members to connect with other researchers working in the same field to exchange knowledge, expertise and resources. If you'd like to host a networking event at your home institution, the ASBMB will help you promote it.

And while networking with researchers in the same field is invaluable, sometimes discovery stems from less obvious connections.

After all, linking microbiology and neurology has helped elucidate the gut-brain axis and how our gut microbiomes interact with our brains; combining structural biology and genetics has helped the field of epigenetics evolve into what it is today; viewing cancer biology through the lens of immunology resulted in the development of CAR-T cell therapies. The ASBMB annual meeting, Discover BMB, brings together researchers from every field in biochemistry and molecular biology and is an ideal venue for the conversations that spark innovation.

Joanna Kotloski (jkotloski@asbmb.org) is the ASBMB membership director.

PRIMARY AREA OF INTEREST

ASBMB members selected the following as their primary areas of research interest:

13.7%	Other
10.6%	Protein structure and folding
10.6%	Molecular bases of disease
9%	Gene regulation
8%	Metabolism
7.5%	Enzymology
7.1%	Microbiology
4.9%	Immunology
4.3%	Molecular biophysics
4.3%	Lipids
4.1%	Neurobiology
3.7%	Signal transduction
3.3%	Membrane biology
2.5%	Computational biology
2.7%	BMB education
2%	Protein synthesis and degradation
1.4%	Glycobiology

SECONDARY AREA OF INTEREST

ASBMB members selected the following as their secondary areas of research interest:

16.9%	Molecular bases of disease
11%	Other
10.2%	Protein structure and folding
8.2%	Gene regulation
9.4%	Signal transduction
6.5%	Metabolism
5.3%	Molecular biophysics
4.7%	Microbiology
4.1%	Immunology
3.9%	BMB education
3.7%	Enzymology
2.7%	Protein synthesis and degradation
2.7%	Neurobiology
2.5%	Lipids
2.5%	Computational biology
2.4%	Membrane biology
1.6%	Methods

Probing for a ketone body's link to age-related inflammation

By Meric Ozturk

Glucose levels in the blood and cells are regulated by the pancreatic hormones insulin and glucagon. While insulin helps cells to take in glucose and reduces blood glucose levels, glucagon initiates the conversion of stored glycogen to glucose.

When glucose is depleted, insulin levels decrease but glucagon levels remain stable. In cells, this triggers the release of fats, which are converted into different types of ketone bodies by the enzyme 3-Hydroxy-3-methylglutaryl-CoA, or HMGCL, in the liver. One of these ketone bodies, beta-hydroxybutyrate, or BHB, can be an energy source for the brain and skeletal muscle when blood glucose is low. Several studies have also shown that BHB also plays a role in the signaling pathways of lipolysis and aging.

Emily Goldberg, a researcher at the University of California, San Francisco, studies NOD-, LRR- and pyrin domain-containing protein 3, known as NLRP3, and how this protein interacts with BHB. NLRP3 helps to regulate the innate immune system and inflammatory signaling as well as age-related inflammation.

"We had previously shown that the NLRP3 drives age-related inflammation and that the ketone body BHB inhibits NLRP3 activation in macrophages and neutrophils, so we hypothesized that BHB might inhibit age-related inflammation," Goldberg said.

Although most ketone bodies are produced in liver cells, researchers hypothesize that they also can be synthesized by cells from other tissues, including macrophages and neutrophils.

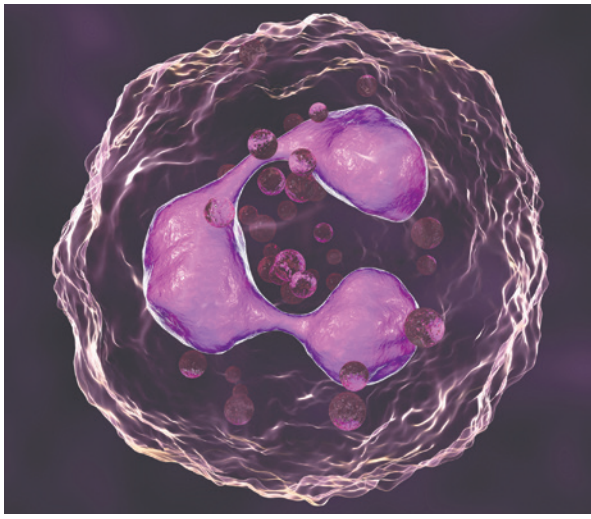
To test their hypothesis about BHB, Goldberg and a team of researchers from UCSF and the Yale School of Medicine used mice from which they deleted the gene that encodes the HMGCL enzyme. This helped them prevent ketone body synthesis in specific cell types, namely macrophages and neutrophils.

"Making the mice to test this hypothesis and planning the experiments to have enough aged mice was the most difficult part of the study," Goldberg said.

The team compared the role of liver-based ketone body formation with that of cell-specific ketone body formation in age-related inflammation.

In their recent paper published in the **Journal of Biological Chemistry**, the researchers point out that the liver is the only organ that can produce enough ketone bodies to maintain blood glucose levels, and neutrophil-based ketogenesis does not regulate age-related metabolic health.

"Exogenous ketones are likely responsible for controlling innate immune inflammation in aging," Goldberg said, "Macrophages can metabolize acetoacetate, but not BHB and this is important for their function. But why innate immune cells take up BHB remains unclear."

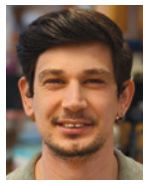


Neutrophils are the most abundant type of white blood cells in the human body and play an important role in inflammation.

The group only used a single mouse strain; using other strains and different mutations in different enzymes in the ketone body formation pathway could show different results. Goldberg said that next they will consider all these limitations and aim to determine why innate immune cells take up BHB.

DOI: 10.1016/j.jbc.2023.103005

Meric Ozturk (ozturk@iastate.edu) is a first-year Ph.D. student in biochemistry at Iowa State University.



Peering into ocular waste removal

Discovery of a mechanism that causes blindness could lead to targeted therapies

By Marissa Locke Rottinghaus

Similar to a garbage removal service, a biological process transports potentially toxic compounds out of the eye. Like the food we eat (and the waste it generates), these compounds are essential for the eye to function properly — until they build up.

A study published recently in the **Journal of Biological Chemistry** revealed the key to a protein that is essential to this process and that, when mutated, can cause blindness indirectly.

The authors of the paper study a protein transporter called ABCA4 that lines the edges of specialized photoreceptor cells in the retina and normally is poised to remove toxic, fatty byproducts of retinal called N-Ret-PE. Retinal is a derivative of vitamin A, which is found in foods such as leafy green vegetables.

"Retinal is critical for vision," said Robert Molday, a professor of biochemistry and molecular biology at the University of British Columbia who oversaw the work. "But it's also potentially very toxic because it has a very reactive element. So, cells have to be able to balance between using retinal for sustained vision and managing its toxicity."

Mutations in ABCA4 can cause N-Ret-PE buildup, which leads to vision loss in diseases such as Stargardt disease. Stargardt disease is the most common inherited form of macular degeneration and affects approximately 30,000 people nationwide. There is currently no therapy or cure for the disease.

The researchers were interested in finding out how the ABCA4 transporter malfunctions to cause vision loss. They found that a portion of the protein that interacts with N-Ret-PE, known as the binding pocket, is inert in some patients with Stargardt disease. Therefore, the toxic compounds slip out of the ABCA4 transporter and cannot be removed from the retina.

Next, by changing the makeup of ABCA4, the researchers showed they could mimic the effect of the Stargardt mutations.

"We were able to elucidate the mechanism of binding, which paves the way for treatments for Stargardt disease," said Tongzhou Xu, a postdoctoral fellow at UBC and lead author of the study.

The team is optimistic that one day gene therapy and specialized particles for delivery to the eye may offer a targeted therapeutic for patients with Stargardt disease. Gene therapy approaches already have been used successfully to correct mutations in a similar transporter that causes cystic fibrosis.

"We are now applying two types of technologies to alter ABCA4," Molday said. "One which was developed to specifically correct the DNA with gene-editing approaches. We are coupling that with lipid nanoparticles, which have been used in the COVID-19 vaccine to encapsulate mRNA. So, by combining these two technologies, we envision being able to potentially correct the defects in individuals with Stargardt's disease that have specific point mutations."

DOI:10.1016/j.jbc.2023.104614

Marissa Locke Rottinghaus (mlocke@asbmb.org) is the science and policy communications specialist for the ASBMB.

A second chance for a healthy heart

Researchers use cellular reprogramming to make damaged organs almost good as new

By Marissa Locke Rottinghaus

Cardiovascular disease is the leading cause of death worldwide — so what if you could turn back the clock after a heart attack? In a recent study, researchers used RNAs to instruct cells in a mouse's injured heart to eliminate scar tissue and recreate cardiac muscle, allowing the heart to function like new again.

Conrad Hodgkinson, an associate professor of medicine and pathology at Duke University School of Medicine, oversaw the study. The results were published in the **Journal of Biological Chemistry**.

"Adult human hearts are not very good at repairing themselves," Hodgkinson said. "Once they have a heart attack or any type of damage, there's no capacity to replace the heart muscle that dies. So, what the heart does to stop itself from basically blowing up is it activates fibroblasts to come in and form a scar."

"Like the scars on skin from injury or surgery, scar tissue generated in the heart after a heart attack is nonflexible and can prevent the organ from functioning at its full potential," Hodgkinson said.

The researchers wanted to find an efficient way to convert the scar tissue back into functioning cardiac muscle to essentially reverse the effects of a heart attack. To do this, they set out to transform fibroblasts into heart muscle cells via a process called cellular reprogramming. Hodgkinson's lab delivers reprogramming instructions to cells in the form of RNAs. However, they noticed that adult fibroblasts are not very good at following instructions and are resistant to reprogramming.

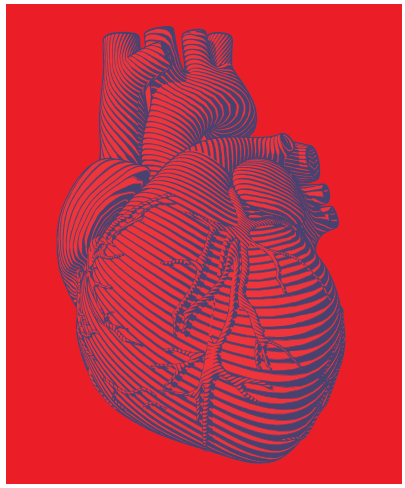
"We found that if you take cardiac fibroblasts from juveniles, they reprogram very nicely," Hodgkinson said. "But, if you take cardiac fibroblasts from adults, they don't, in fact, respond at all. So, we tried to understand whether the aging process was actually interfering with fibroblast reprogramming."

Hodgkinson and his team discovered that a protein oxygen sensor, Epas1, prevents adult fibroblasts from reprogramming themselves. The researchers were able to harness the regenerative capacity of young cells by blocking Epas1 in adult fibroblasts.

"When we reversed the fibroblast aging process, essentially making the fibroblasts think they were young again, we converted more fibroblasts into cardiac muscle," Hodgkinson said.

The researchers formulated a cocktail of RNAs and packaged them into exosomes. This technology allowed them to deliver the exosomes without surgical interventions.

"Exosomes are kind of like shopping bags," Hodgkinson said. "The cell sticks a lot of stuff into a big fat ball to send out and signal to other cells. They are a way cells can talk to each other."



When the researchers used the RNA-filled exosomes to instruct the fibroblasts to reprogram themselves in a mouse that had just experienced a heart attack, the results were, according to Hodgkinson, "impressive."

"We were able to recover almost all of the cardiac function that was lost after a heart attack by reversing the aging of the fibroblasts in the heart," Hodgkinson said.

DOI:10.1016/j.jbc.2023.104694

Marissa Locke Rottinghaus (mlocke@asbmb.org) is the science and policy communications specialist for the ASBMB.

Not all fat cells are created equal

By Sneha Das

Obesity can have adverse effects on physical and mental health and increases the risk of conditions such as heart disease, stroke, Type 2 diabetes and certain cancers. Since 1975, a combination of genetic, biological, environmental and socioeconomic factors has tripled worldwide obesity rates.

But fat is not always bad. Adipose tissues formed from fat cells make up 20% to 25% of body weight in healthy adults. These tissues store energy, help maintain body temperature, cushion vital organs and participate in a variety of biological processes.

Søren Madsen is a postdoctoral research associate in David James' group at the University of Sydney, Australia. "I've been interested in fat tissue since my Ph.D. work," Madsen said, "and I would argue that it is the most adaptable tissue in the body."

In mammals, when caloric intake exceeds the body's energy requirements, white adipose tissues can expand to make up 70% of total body mass. Our ancestors needed this expandability to survive.

When humans weren't able to eat at regular intervals, they consumed large amounts of food when it was available and the excess calories were stored as fat. When food was scarce, the stored fat provided energy for survival.

The body stores most excess energy as white adipose tissue, which accumulates mainly in two places or depots: Subcutaneous fat is under the skin, and visceral fat surrounds the internal organs in the abdominal cavity. Madsen and his team set out to understand the molecular basis for the health risks associated with the latter.

"It is an established dogma that the abdominal fat is bad fat," he said. "Our aim with this project was to systematically compare fat cells from the two fat depots and understand the difference between them during obesity."

In a study recently reported in the journal **Molecular & Cellular Proteomics**, Madsen and colleagues switched mice from what they described as a "lean control diet" to an "obesogenic Western diet," and the mice gained weight over nine months. The researchers then compared subcutaneous and visceral fat samples from the lean and obese states.

Fat cells are "quite brittle," Madsen said, and require meticulous collection. The team used proteomics to analyze the samples.

"Proteomics is a very powerful way to get a holistic view of a biological sample, and proteins can tell the story of what is happening," Madsen said. "We uncovered that the fat cells from different depots adapt quite differently to the obesogenic cue."

In the lean mice, subcutaneous and visceral fat cells were similar, and only 3% of the proteomes differed. Proteins in visceral fat made the cells bigger and favored fat storage, while subcutaneous fat cells were smaller and showed signs of higher metabolism.

Fat cells from obese mice differed widely, however, depending on what depot they came from. The researchers found that visceral fat cells had increased signatures for stress during obesity, explaining why abdominal fat can be more detrimental to health. They think these differences may result from the microenvironment surrounding these two fat depots.

"It will be interesting to understand why certain people store fat predominantly as abdominal fat or subcutaneous fat, and we want to follow this up," Madsen said.

The research group hopes this work will contribute to public health education efforts and highlight the role of fat cells from different depots in overall health.

DOI: 10.1016/j.mcpro.2023.100508

Sneha Das is a Ph.D. candidate in microbiology at the University of Illinois at Urbana–Champaign. Follow her on LinkedIn: Sneha Das. https://www.linkedin.com/in/sneha-das-6b5a46a1/

Finding a way to combat long COVID

Neurodegenerative biomarkers offer clues for monitoring and potential treatment

By Marissa Locke Rottinghaus

A recent study has identified potential neurological biomarkers of long COVID-19 in nonhuman primates that may help physicians diagnose, monitor and treat this condition.

Over 65 million people worldwide have developed long COVID after being infected with SARS-CoV-2, and cases are only becoming more common. Long COVID symptoms can last weeks, months or years. Even more perplexing is the fact that symptoms can vary widely among individuals and consist of any combination of fatigue, fever, chest pain, trouble breathing, neurological symptoms such as "brain fog" and many more. Long COVID puts a gigantic burden on the U.S. healthcare system, and some doctors doubt the condition exists, leaving patients unable to find care.

A team of researchers at Tulane University is trying to shed light on this condition and find tools to manage it. They published their work in the journal **Molecular & Cellular Proteomics**.

"Our primary goal was to better understand the inside of the brain after COVID infection," said Jia Fan, an assistant professor of biochemistry and molecular biology who oversaw the study. "This understanding could provide a potential target to use in the clinic for long COVID evaluation and monitoring. We also thought this study may give us some clues to find a potential treatment strategy for long COVID in patients."

However, because long COVID can vary drastically among individuals, studying this disorder has been difficult for scientists and clinicians alike.

"There's a very limited understanding of the neuropathogenesis of long COVID," Fan said. "It is almost impossible to get any brain tissue or samples of any kind from patients that have mild symptoms or no long COVID symptoms because there is no reason for invasive procedures."

Therefore, the group turned to a nonhuman primate model of the condition.

The team found that certain proteins associated with neurodegenerative disorders, such as Parkinson's disease, were elevated in the brain, cerebrospinal fluid and blood after SARS-CoV-2 infection even in nonhuman primates that showed mild or no symptoms.

According to Sudipa Maity, first author on the study, these elevated proteins indicate that the immune systems of the monkeys remained activated even after infection.

"Our findings suggest that the major neurological complications are arising due to the body's natural immune defenses," Maity said. "The immune system has a very important and significant impact on the neurological complications of COVID."

The next steps of the project involve validating the biomarkers the team identified in human samples such as blood, Fan said.

"It is currently hard to score the severity of (long COVID) patient symptoms because they are based on self-reports," Fan said. "If we can find a group of proteins in the blood associated with long COVID, this is a less invasive way to easily evaluate the severity of the long COVID patients. We hope what we started can provide a clue to find a potential treatment to better the long COVID patient experience."

DOI: 10.1016/j.mcpro.2023.100523

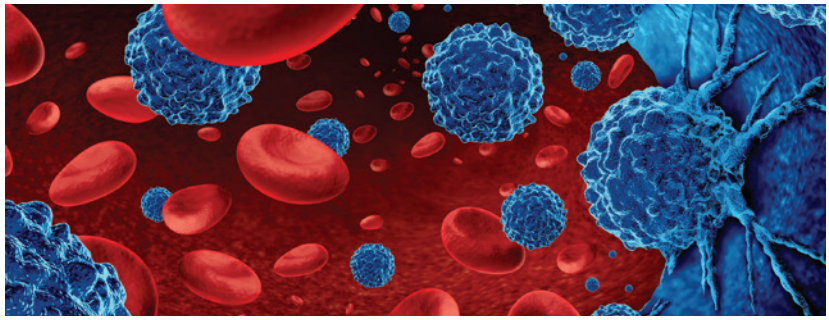
Marissa Locke Rottinghaus (mlocke@asbmb.org) is the science and policy communications specialist for the ASBMB.

Seeking leukemia's Achilles heel

Researchers identify potential therapeutic that targets a DNA repair protein

By Marissa Locke Rottinghaus

A team of researchers has discovered a potential therapeutic that can synergize with existing drugs to kill certain leukemia cells more effectively. The authors published their results in **Molecular & Cellular Proteomics**.



Acute myeloid leukemia is a cancer of developing immune cells that can manifest in all individuals. According to the National Cancer Institute, only about 30% of adult patients survive beyond five years after diagnosis.

Unlike most cancers, AML is found in bodily fluids like blood. Like passengers traveling to places all over the world on a high-speed train, AML cancer cells have access to every corner of the body via the blood.

To make things more difficult, "No two leukemias are alike," Heather Murray, a postdoctoral researcher at the University of Newcastle and lead author of the study, said.

A patient's prognosis can vary depending on genetic mutations in their AML cells. "Gene mutations present in a patient's cancer have been used to predict aggressiveness of the disease and inform which treatment the patient should receive," Murray said.

Since the breakthroughs of the Human Genome Project, many cancer researchers have been focused on finding the cause of cancer inside patients' DNA. However, because a cure for cancer remains elusive, Murray and her colleagues are diving deeper into tumor cell abnormalities beyond DNA.

"Our team has been working to develop precision therapies," Murray said. "This involves identifying the specific features of different AML cells that drive them to grow and spread. We use this information to try and tailor therapies that target these specific features."

A growing number of studies show that "analyzing the makeup of the cancer cells and how they communicate, such as proteomic and phosphoproteomic analyses, combined with the study of gene mutations, reveals much more," she said.

Phosphoproteomics is a technique that allows researchers to look at the modifications of proteins inside a cell. Specifically, this technique examines the phosphorylation status of a protein. Phosphorylation is known as a cellular on/off switch. Combined with other methods, phosphoproteomics takes cancer research to the next level, according to Nicole Verrills, an associate professor at University of Newcastle who oversaw the study.

The researchers used mouse cells that were engineered to have a mutation in a gene called KIT, which is found in about 1 in 20 AML patients.

The team observed that a protein called DNA-dependent protein kinase, DNA-PK for short, always is turned on in leukemia cells with the KIT mutation. So they decided to try inhibiting both mutant KIT and DNA-PK to stop leukemia cell growth.

They found that a combination of the standard-of-care drugs and a DNA-PK inhibitor significantly reduced the survival of the leukemia cells with minimal impact on healthy cells.

Verrills and Murray have a vision of future precision therapy efforts that incorporates rapid genomic and phosphoproteomic studies as well as a large drug screen on an AML patient's cancer cells before they receive any treatment. Verrills said this kind of testing would allow clinicians to predict the therapeutics to which an individual patient will or will not respond.

DOI: 10.1016/j.mcpro.2023.100503

Marissa Locke Rottinghaus (mlocke@asbmb.org) is the science and policy communications specialist for the ASBMB.

An unexpected component in retinal survival

By Jessica Desamero

At the back of the eyeball, in the retina, photoreceptor cells convert light into electrical signals that are sent to the brain for processing. When these photoreceptors degenerate, vision can become impaired, and conditions such as macular degeneration and retinitis pigmentosa sometimes develop. Blindness may result.

In a recent study published in the **Journal of Lipid Research**, researchers at the National Eye Institute describe how they discovered the importance of a membrane-linked receptor protein called pigment epithelium-derived factor receptor, or PEDF-R, in photoreceptor structure and function and, ultimately, in retinal survival.

Alexandra Bernardo Colón, a biologist at the National Eye Institute, works in Patricia Becerra's lab, where they focus on retinal degeneration. They aim to understand factors that can play a role in preventing photoreceptor cell death, including PEDF, a protein that helps protect the retina by interacting with PEDF-R to spur its phospholipase activity.

Bernardo Colón became interested in PEDF-R due to this phospholipase activity. Photoreceptors, which are rich in phospholipids, produce PEDF-R, and, upon binding of PEDF, PEDF-R catalyzes the hydrolysis of phospholipids and triglycerides.

"Phospholipid metabolism is really critical for the homeostasis of photoreceptors and health of the retina," Bernardo Colón said. "What is unclear is whether PEDF-R, as a phospholipase, is a molecular link between phospholipids and the photoreceptor survival, so that's why this is intriguing."

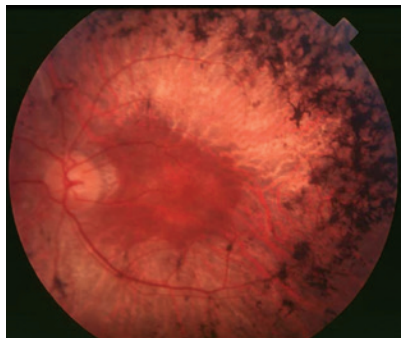
This receptor is usually called adipose triglyceride lipase, or ATGL, but Bernardo Colón believes her term is more accurate in the field of eye health. "We are calling it PEDF-R because it's not just found in the adipose tissue," she said. "We found that we can see it in the entire retina."

To investigate the role of PEDF-R in photoreceptor structure, the team used CRISPR technology to knock out Pnpla2, the gene encoding for PEDF-R, in mice. They also ensured that known mutations causing retinal degeneration were not present. They found that mice deficient in PEDF-R had photoreceptor deformities, such as smaller thickness of multiple retinal layers and unevenly arranged outer segments, and accumulation of two main retinal phospholipids.

"We're suggesting a causal link to photoreceptor dysfunction," Bernardo Colón said.

PEDF-R deficiency caused decreases in both mRNA and immunofluorescence levels of rhodopsin and opsin, which are the photoreceptor cells that help detect light.

The team then performed an electroretinogram to measure how different cells in the retina, including photoreceptors, responded to light. They found that missing just one copy of the Pnpla2 gene compromised photoreceptor function and missing both was even more detrimental.



CHRISTIAN HAMEL

Degenerating photoreceptors contribute to conditions such as retinitis pigmentosa.

Overall, the researchers noted that PEDF-R plays a crucial role in photoreceptor structure and function as well as phospholipid metabolism. They also underlined the fact that all layers of the retina are interconnected.

"When one layer malfunctions, all of the other layers will follow," Bernardo Colón said, "so if PEDF-R is not functioning, eventually all of the other layers of the retina will not function as well."

Ultimately, this research team hopes to develop drugs to ensure retinal survival and combat blindness, with phospholipid metabolism as a potential therapeutic target.

DOI: 10.1016/j.jlr.2023.100358

Jessica Desamero (jdesamero@gradcenter.cuny.edu) is a graduate student in the City University of New York's biochemistry Ph.D. program and volunteers with science outreach organizations. Follow her on Twitter: @JessicaDesamero.

From the journals

By Ken Farabaugh, Laura McCormick & Swarnali Roy

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

How CBD works to treat neuropathic pain

Almost 1 in 10 people experience neuropathic pain, or NP, which can significantly affect their quality of life. Peripheral nerve injuries can sometimes trigger related changes in the spinal cord and dorsal root ganglion, leading to altered expression of neurotransmitters such as glutamate, glycine and GABA. Treatment options are limited, and some patients feel no pain relief after treatments. However, scientists have found several compensatory mechanisms to suppress pain via endogenous processes. These include modulating inflammatory cytokines and synaptic receptors or ion channels.

In a recent paper in the **Journal of Biological Chemistry**, Jing Xia, Dan Xiao and colleagues at the University of Science and Technology in Hefei, China investigated the role of a glycine receptor subunit GlyRα1 in NP and the potential effects of cannabinoids in treating the pain. Using mice in which nerves were cut and ligated to induce chronic pain, the authors observed that spinal GlyRα1 levels are increased in NP via a calcium-dependent mechanism. They also found that the synthetic cannabinoid DH-CBD interacted with a specific amino acid, serine 296 in GlyRα1, to block glycinergic neurotransmission and suppress neuronal hyperactivity.

This study shows that DH-CBD in part relieves pain by enhancing the function of the inhibitory neurotransmission of glycine receptors. Although further testing is needed, these findings present a potential mechanism behind the efficacy of using cannabinoids to treat NP.

DOI: 10.1016/j.jbc.2023.104769

Mathematical models of membrane binding

Cholesterol — a sterol lipid — is essential for moderating the properties of phospholipid membranes. Cholesterol also interacts with a multitude of membrane proteins and participates in numerous cellular processes.

Researchers often seek to quantify the affinity of proteins for cholesterol. Yet, these measurements usually disregard the fact that most membrane cholesterol is associated with membrane phospholipids, creating competition between proteins and phospholipids for cholesterol. In turn, this complicates the analysis of protein–sterol interactions.

To address this problem, Yvonne Lange of Rush University and a team of researchers created a mathematical model to examine protein and cholesterol binding in phospholipid membranes. Their results were recently published in the **Journal of Lipid Research**. This model postulates that cholesterol not bound to phospholipids can readily bind proteins. In addition, the model shows that cholesterol bound to phospholipids can be extracted by the protein.

The team validated their model by simulating the binding of the bacterially-derived Perfringolysin O protein to membrane cholesterol. Their results matched previously published experimental data using both artificially created liposomes and cellular membranes.

With this new approach, the authors hope to improve understanding of protein–cholesterol interactions and guide new experiments. In particular, this model may benefit researchers working on ligands with a weak affinity for cholesterol, where competition with phospholipids complicates the interpretation of measurements.

DOI: 10.1016/j.jlr.2023.100344

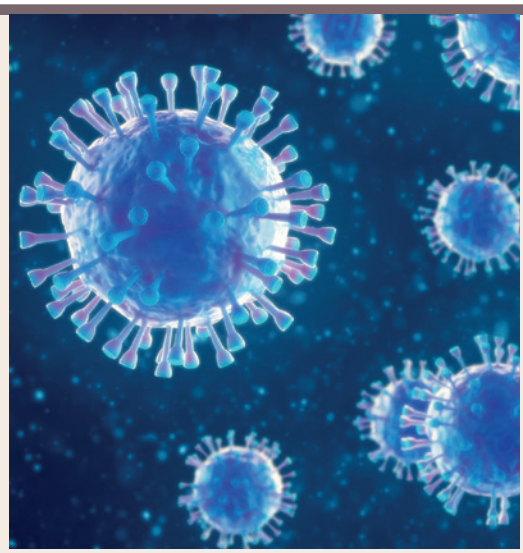
Slowing age-dependent liver inflammation

Chronic liver diseases are prevalent in elderly people and are the 12th leading cause of death in the United States. Developing new therapeutics requires an in-depth understanding of the mechanism of liver inflammation.

Activation of nuclear factor kappa-light-chain-enhancer of activated B cells, or NF-κB, is critical to the progress of liver inflammation. In humans, the multiprotein cellular scaffold p62, known as sequestosome 1, or SQSTM1, plays a pivotal role in controlling myriad cellular processes and promotes NFκB activation. The cellular protein NFκB inhibitor, alpha, or IκBα, on the other hand, inhibits NF-κB by masking its nuclear localization signals.

In a recently published article in the journal **Molecular & Cellular Proteomics**, Yi Liu and a team at the University of California, San Francisco showed that close association of p62/SQSTM1 with IκBα can extend the physiological half-life of IκBα by

Variability in flu virus subtypes



The influenza virus mutates rapidly, so host immune systems must constantly adapt to new strains. The most variable, rapidly evolving part of the virus is influenza hemagglutinin, or HA, a surface glycoprotein containing a head domain (part of the HA1 subunit), a connecting stem region and a fusion peptide (part of the HA2 subunit) responsible for mediating binding and membrane fusion. However, scientists know little about the roles of different HA subtypes, such as H1 and H3, in the fusion pathway.

Natalie Garcia, Sally Kephart and colleagues at the University of Washington in Seattle have now described in an article in the **Journal of Biological Chemistry** their findings on subtype-specific activation and inhibition of HA. The authors used hydrogen-deuterium exchange mass spectrometry to compare the fusion activation of H1N1 and H3N2 influenza subtypes.

They found that at acidic pH conditions that promote membrane fusion, different regions of these HA peptides displayed increased dynamic changes; in H1, the HA1/HA2 interface was more dynamic, while in H3 the fusion peptide was most altered. They also showed that a broadly neutralizing antibody that targets the stem region of HA led to decreased conformational dynamics in the fusion peptide of H3 but had no effect on dynamics in the H1 fusion peptide.

These findings show that sequence variation in HA impacts how the protein responds to pH, suggesting that there may be multiple mechanisms by which influenza viruses prime for membrane fusion. The authors also conclude that the entire HA complex does not behave as a cohesive unit and that local conformational dynamics play a considerable role in functional variation.

DOI: 10.1016/j.jbc.2023.104765

— Ken Farabaugh

saving it from proteasomal degradation and also terminates NF-κB activation. Before this study, scientists did not know how newly synthesized IκBα could survive to enter the nucleus, accelerate the termination of NF-κB transcriptional response and stop hepatic inflammation.

The researchers used in-cell chemical crosslinking mass spectrometry coupled with proteomic analysis to identify two subdomains of IκBα and basic residues in p62 that are important for their interaction and further stabilization. The researchers showed that liver-specific p62 deletion of the IκBα-interacting region in transgenic mice caused severe liver inflammation with aging. They hope continued study of p62-mediated NF-kB regulation will lead to new liver disease therapies.

DOI: 10.1016/j.mcpro.2023.100495

Why COVID-19 makes some patients sicker than others

After contracting COVID-19, some patients experience severe or extended respiratory symptoms, while others recover after only a brief infection. Scientists do not yet understand why this selective severity is experienced by some, in particular the elderly or patients with comorbidities such as high cholesterol.

The SARS-CoV-2 virus enters mammalian cells by binding to the angiotensin-converting enzyme 2, or ACE2, but the more infectious omicron variant also enters cells via endocytosis. In their recent paper published in the **Journal of Biological Chemistry**, Hao Wang and colleagues at the Herbert Wertheim UF Scripps Research Institute describe how they investigated SARS-CoV-2 infectivity.

Using direct stochastic optical reconstruction microscopy, the researchers showed that ACE2 was localized into nanoclusters containing the signaling lipid PIP2. However, after the uptake of cholesterol into

cell membranes, ACE2 moved from PIP2 lipid clusters to those containing endocytic ganglioside GM1 lipids. The team found that this movement of ACE2, as well as saturated lipids such as sphingomyelins, was an important contributor to SARS-CoV-2 entry into the endocytic pathway.

The researchers used these findings to propose a model for the role of cholesterol in age- and co-morbidity-dependent infection of SARS-CoV-2. Further research in this area could lead to new strategies to fight COVID-19, such as drugs that disrupt GM1 lipid nanoclusters in the plasma membrane and reduce viral uptake.

DOI: 10.1016/j.jbc.2023.104763

A 2D way to detangle complex data

Identifying and quantifying a protein sample to create a complete profile has always been a challenge in proteomics. Data-dependent acquisition and data-independent acquisition, or DDA and DIA, are techniques that are widely used to analyze proteomic data. DDA is biased to pick the strongest peptide signal whereas DIA analyzes the peptides within a defined mass-to-charge window. DIA has better reproducibility and is better able to overcome the limit of quantifying low-abundance peptides than DDA,

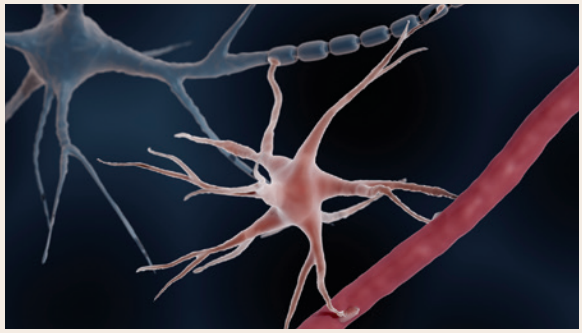
Linking lipid metabolism to microglia activation

Alzheimer's disease is characterized by neuronal death in response to the accumulation of protein plaques and tangles. However, nonneuronal cells — including microglia and astrocytes — also play a role in Alzheimer's risk factors and progression.

Microglia, the resident immune cells of the brain, modulate neuroinflammation often associated with Alzheimer's and other neurodegenerative diseases. Astrocytes provide metabolic support to neurons and secrete essential lipids in the form of lipoprotein particles. Lipoproteins also contain the apolipoprotein E, or ApoE, a protein with certain alleles linked to Alzheimer's disease.

Researchers have identified overexpression of the cholesterol-modifying enzyme cholesterol 25-hydroxylase, or CH25H, in the brains of Alzheimer's patients. In cell culture models, murine microglia also increase expression of the Ch25h gene following inflammatory stimuli and secrete CH25H's product, 25-hydroxycholesterol, or 25HC. This extracellular 25HC affects both immune cell signaling and neuronal function. However, although astrocytes play a role in lipid metabolism, scientists did not know if CH25H and 25HC regulate activity in this type of glia.

In new work published in the **Journal of Lipid Research**, Anil G. Cashikar and colleagues from the Washington University School of Medicine and the University of Texas Health Science Center identified a novel role for 25HC in astrocyte function. Although cultured astrocytes did not express detectable levels of the Ch25h gene, the team showed that these cells can take up extracellular



An astrocyte (pink) makes contact with a neuron (blue). In the brain, astrocytes support the function of neurons.

25HC. Also, astrocytes treated with 25HC showed increased secretion of ApoE-containing lipoproteins.

The authors also identified gene expression changes in astrocytes following 25HC treatment, including the upregulation of genes associated with the liver X receptor pathway and lipoprotein secretion and the downregulation of genes associated with sterol regulatory element-binding proteins and cholesterol synthesis.

Finally, the authors examined cholesterol esterification, a process cells typically use to store excess cholesterol. In 25HC-treated astrocytes, both cholesterol ester levels and the number of lipid droplets, a lipid storage organelle, increased.

Collectively, this work suggests 25HC — a lipid product released by microglia in response to inflammation — can modulate astrocytic gene expression and lipoprotein secretion. Although future research is needed in mouse models, the proposed pathway shows promise in the neurodegeneration field.

DOI: 10.1016/j.jlr.2023.100350

— Laura McCormick

which has made it an increasingly popular tool in proteomics.

In a recent paper in the journal **Molecular & Cellular Proteomics**, Patricia Skowronek of the Max Planck Institute of Biochemistry and an international group of researchers introduced a novel 2D technique they call "Synchro-PASEF" that precisely defines precursor–fragment relationships. The parallel accumulation-serial fragmentation, or PASEF, principle is built on the correlation of collisional cross sections and molecular weights of charged peptides. A synchro-PASEF scan, where a high-speed quadrupole is synchronized with the ion mobility release, can cover 19% of all precursors per isolation window and increases the detected fragment ion current severalfold at subsecond cycle times. The short cycling time gives threefold higher fragment intensities. Recombination of separated fragment parts with high specificity helped the research group to deconvolute complex tandem mass spectrometry spectra generated by DIA.
DOI: 10.1016/j.mcpro.2022.100489

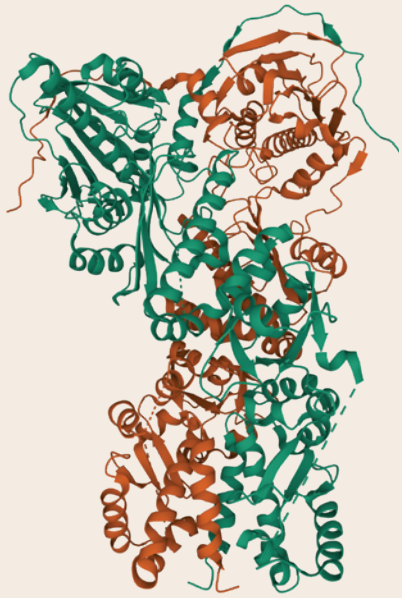
Ken Farabaugh (kfarabaugh@asbmb.org) is the ASBMB's science editor.

Laura McCormick (lemccorm@email.unc.edu) is a graduate student in cell biology and physiology at the University of North Carolina at Chapel Hill. Follow her on Twitter: @le_mccorm.

Swarnali Roy (swarnali.roy@nih.gov) is a postdoctoral fellow at the Laboratory of Bioorganic Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health.

A new approach to cancer proteome profiling

Protein synthesis, folding and degradation play a critical role in maintaining cell physiology. Molecular chaperones, a varied class of proteins, specialize in efficient folding of nascent polypeptides and maintaining the 3D conformation within the cell's concentrated environment. Heat shock protein 90, or HSP90, a key component of molecular chaperones, helps many oncoproteins mature and stabilize. Thus, understanding HSP90-based cellular machinery by profiling its cellular proteome is important in studying how cancer develops.



In a recent article in the journal **Molecular & Cellular Proteomics**, Rahul Samant and Silvia Batista of the Institute of Cancer Research and the Babraham Institute, with an international group of researchers, introduced a new size-exclusion chromatography–coupled mass spectrometry, or SEC–MS, technique to characterize how treatment with the HSP90 inhibitor tanespimycin changed the proteome profile.

After treating colon adenocarcinoma cells for eight hours with tanespimycin, the researchers used SEC–MS and identified 6,427 unique proteins. They saw no drastic differences between control and HSP90 inhibition across 4,645 proteins in biological replicates, identified by applying a quantitation algorithm. By analyzing differential protein fraction levels, they found that Anillin and mitochondrial isocitrate dehydrogenase 3 complex, or IDH3, were important HSP90 inhibitor–modulated proteins in the HSP90-dependent proteome. Anillin plays a critical role in tumor progression, and aberrant expression of an alpha subunit of IDH3 is related to malignancy.

This work used classical proteomics to shed light on the previously uncharacterized HSP90 inhibition response. The group is interested in using the SEC–MS method with other clinically approved HSP90 inhibitors and expanding its application for mechanistic pathway studies and the development of next-generation HSP90 family inhibitors. The SEC–MS data set is available online as a resource.
DOI: 10.1016/j.mcpro.2022.100485

—Swarnali Roy

Peer Review Week begins Sept. 25.

The theme this year is

Peer Review and the Future of Publishing

Visit ASBMB Today online to see how the society is recognizing the generous volunteers who do the heavy lifting at the Journal of Biological Chemistry, Journal of Lipid Research and Molecular & Cellular Proteomics.

JBC | JOURNAL OF BIOLOGICAL CHEMISTRY

JLR | JOURNAL OF LIPID RESEARCH

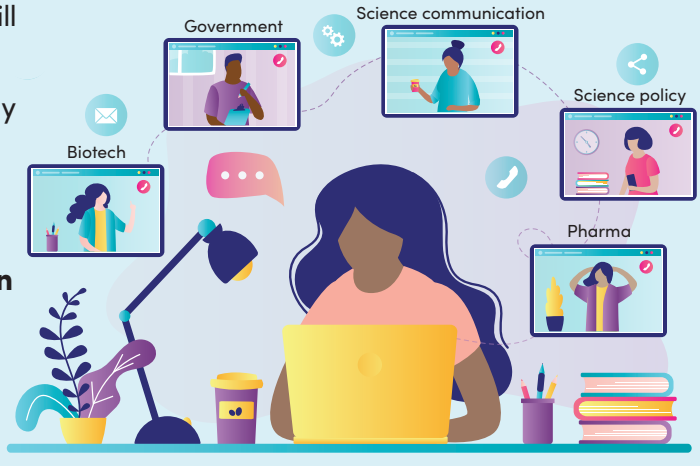
MCP | MOLECULAR & CELLULAR PROTEOMICS

The ASBMB Virtual Career Expo is back

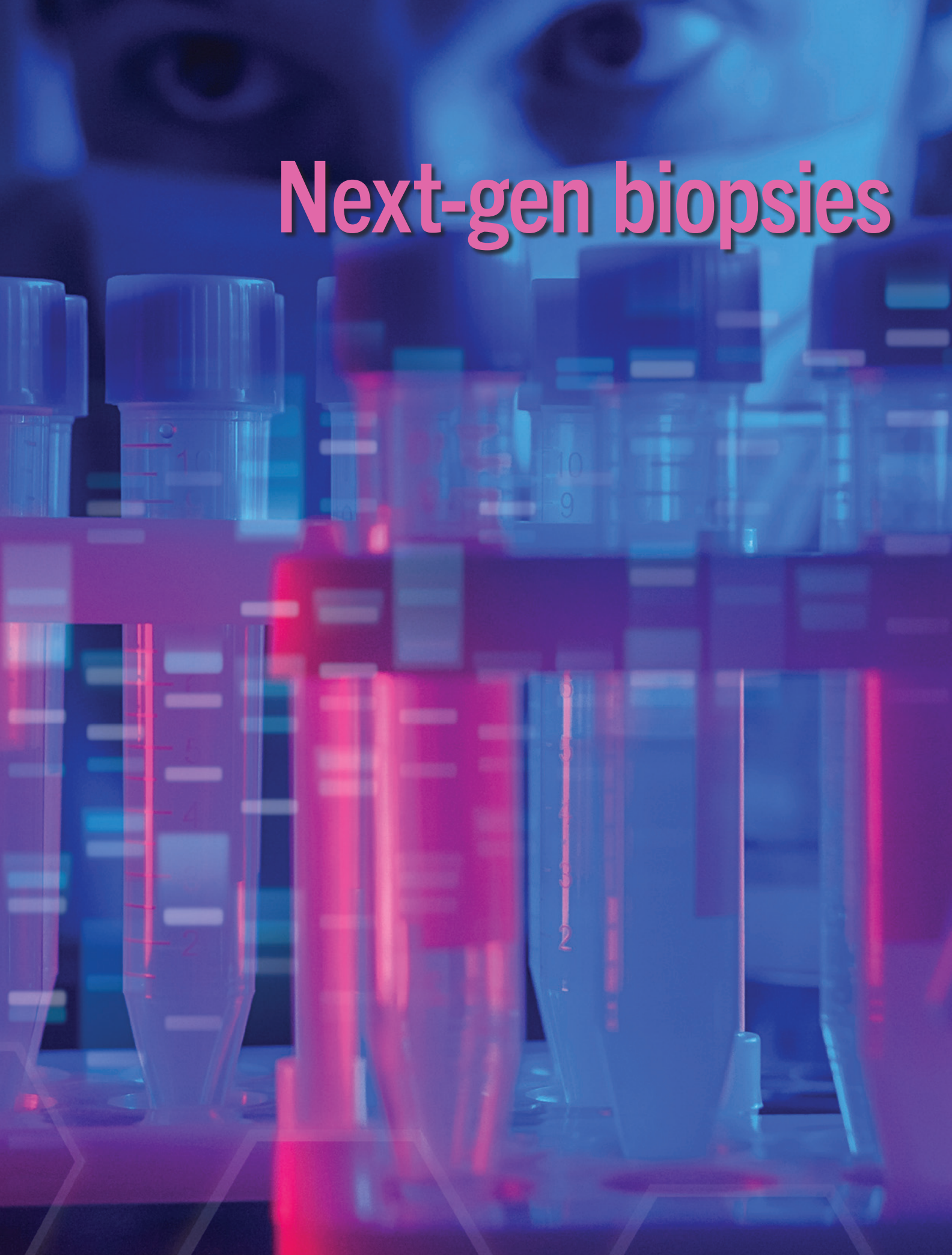
Join us Nov. 1

The ASBMB career expo aims to highlight the diversity of career choices available to modern biomedical scientists. No matter your career stage, this virtual event will provide a plethora of career options for you to explore while simultaneously connecting you with knowledgeable professionals in these careers.

More information will be posted on asbmb.org/meetings-events.



ASBMB
American Society for Biochemistry and Molecular Biology



Next-gen biopsies

take the sting out of diagnosis

Researchers develop noninvasive tests using exosomes, proteomics and bodily fluids

By Marissa Locke Rottinghaus

What if diagnosing anxiety was as easy as X-raying a broken bone and required little more than a trip to the doctor's office, a blood draw and time? That is the goal of Alexander Niculescu, a professor of psychiatry at the University of Indiana.

What if kidney cancer could be diagnosed and monitored with a simple urine sample, avoiding painful needle biopsies and unnecessary surgery? That's what researchers Ronald Boris and W. Andy Tao are working toward.

Traditional biopsies use needles to extract cells or tissues for testing. Painful and invasive, they are best known for their use in cancer diagnostics. And though useful for initial diagnosis, needle biopsies present significant health risks so physicians cannot use them to look at tumor heterogeneity, metastasis or behavior over time.

To take the sting out of biopsies and address their limitations, scientists have developed a new diagnostic and monitoring tool: the liquid biopsy. Instead of a needle painfully invading patient tissues, a liquid biopsy uses a small amount of blood, saliva or urine to test for disease-related materials such as DNA or proteins, sometimes called biomarkers, in the affected organ. With these biomarkers, physicians can easily determine the presence and severity of a disease.

NICHOLAS DAVIDSON

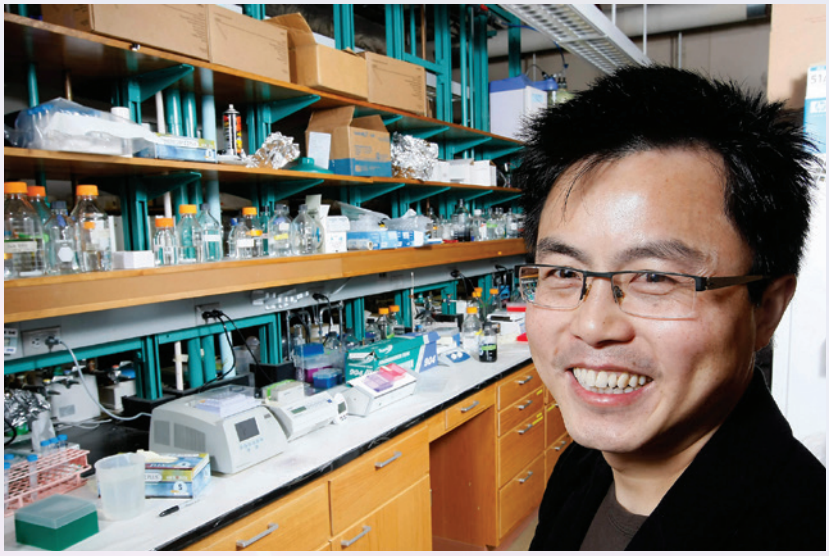
The US. Food and Drug Administration has approved several liquid biopsy tests that detect circulating tumor cells or DNA to help doctors identify the stage of a cancer and the most effective treatment.

Nick Davidson, division chief of gastroenterology at Washington University in St. Louis, Missouri, and co-editor-in-chief of the Journal of Lipid Research is on the front lines of liquid biopsy use in the clinic. Davidson uses liquid biopsy diagnostics to track disease recurrence in cancer patients who have undergone treatment.

"The emergence of (liquid biopsy) tests has been driven by increasing sophis-

A liquid biopsy uses a small amount of blood, saliva or urine to test for disease-related materials such as DNA or proteins, sometimes called biomarkers, in the affected organ.

PURDUE UNIVERSITY



W. Andy Tao (pictured), professor of chemical biology and analytical chemistry at Purdue University, and Marco Hadisurya, a graduate student at Purdue, are now working toward developing liquid biopsy tests for Parkinson's disease with the Michael J. Fox Foundation.

tication and decreased costs of DNA sequencing and other genetic profiling technologies," Davidson said. "As those costs have come down, their sensitivity has improved."

Not all tumors shed cells or DNA in the blood at detectable levels, and the scope of liquid biopsy technology in the clinic is limited. Therefore, researchers are working to expand the applications of this technology and exploring what other bodily fluids, such as urine, and molecules other than DNA can reveal about disease.

Researchers, including Davidson, say liquid biopsies will likely be a big part of the future of precision medicine. However, as with any burgeoning technology, the road has not always been smooth. And the bumps have included one of the biggest scandals in 21st-century medicine.

New-wave diagnosis and monitoring

If it's true that knowledge is power, therein lies a strength of liquid biopsies. The technology gives patients and physicians the knowledge and power to decide what constitutes the best individualized treatment plan.

Liquid biopsy tests exist for prostate and lung cancer but not for kidney cancer. This disease often goes undiagnosed for months after it develops because kidney tumors are slow to cause symptoms.

Boris, an associate professor of clinical urology at the Indiana University School of Medicine, and Tao, a professor of chemical biology and analytical chemistry at Purdue, teamed up to find a better way to diagnose and monitor kidney cancer patients.

"From the clinical standpoint, I think one of the things that we are lacking in renal cell cancer is a diagnostic technique to characterize masses before intervention," Boris said. "Historically, for renal cell tumors, we had this old adage, which is you see the tumor and you cut it out. There was not a whole lot of thought put into it from the surgical standpoint. … First and foremost, we now want to know if somebody has a threatening tumor or not."

RONALD BORIS

After doctors identify a potentially cancerous mass in a kidney, most patients choose surgery to remove the mass right away. However, this surgery is risky and may harm normal kidney functions. Noting the lack of noninvasive diagnostic tools, Tao and Boris wanted to find an easier way to diagnose and monitor kidney cancer.

"We asked the question: Is a 'liquid biopsy' for kidney cancer possible and potentially more reliable than a tissue biopsy?" Tao said.

The team focused on biomarkers called phosphoproteins. Marco

Hadisurya, a Purdue graduate student who works with Tao and Boris, described phosphoproteins as the workhorses of the tumor. Using phosphoproteins produced by a kidney tumor and excreted in urine, the researchers can interpret how aggressive the tumor may be. The team identified a unique set of these phosphoproteins that serve as a tumor's fingerprint and may help clinicians differentiate between low- and high-grade kidney cancer using only a urine sample. Their work was published in Molecular & Cellular Proteomics.

The phosphoproteins in urine are enveloped in extracellular vesicles, which Hadisurya described as "tiny packages." The team used a new method known as data-independent acquisition phosphoproteomics to tease apart the biomarkers found in these extracellular vesicles.

With this method, the researchers' data is highly reproducible, which addresses a challenge to the scientific research community of late, Tao said.

Unlike tissue biopsies, liquid biopsies can be taken repeatedly from one person, giving physicians a way to frequently and accurately monitor patients for recurrence.

'You cannot biopsy the brain'

Although liquid biopsies were first designed and implemented to detect cancer, psychiatry professor Niculescu at the University of Indiana is pushing the bounds of what can be surveyed using liquid biopsy technology.

In addition to being difficult to diagnose, mental health disorders such as depression and anxiety present a challenge to physicians because "you cannot biopsy the brain," Niculescu said.

When Niculescu began his clinical psychiatry residency 25 years ago, he dreamed of combining the skills in molecular cancer genetics he learned as a graduate student with his passion for treating patients with psychiatric disorders.

"I wanted to bring some of the insights, methodologies and precision from cancer over to mental health," he said.

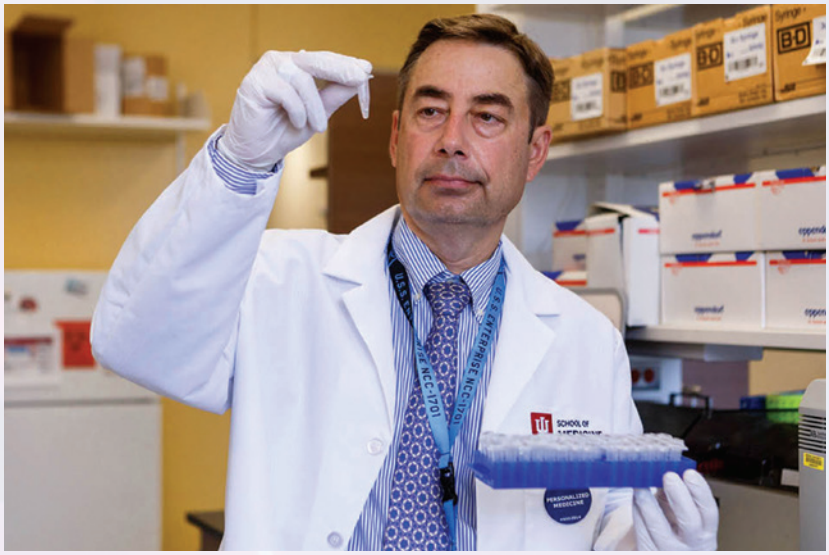
Niculescu's goal was a lofty one. Mental health and psychiatric disorders have long been misunderstood and misdiagnosed. He committed himself to reducing the "stigma and shame" so often associated with these disorders.

Over the past two decades, Niculescu has worked with patients, clinicians and scientists to collect and examine over 1,200 blood transcriptomic data sets from over 500 healthy and sick patients. Researchers examined the transcriptomic data to find patterns and biomarkers that correlate with disease. After completing correlation studies, they refined biomarker panels for a variety of disease profiles and published biomarker profiles for depression, anxiety, post-traumatic stress disorder, Alzheimer's disease and

W. ANDY TAO

Ronald Boris explains the dynamics of the robotic patient cart, which holds the camera and instruments that the surgeon controls from the robotic console used for kidney tumor removal, to Purdue graduate students Peipei Zhu and Marco Hadisurya in the surgical room.

> "We asked the question: Is a 'liquid biopsy' for kidney cancer possible and potentially more reliable than a tissue biopsy?"
>
> W. ANDY TAO



INDIANA UNIVERSITY SCHOOL OF MEDICINE

Alexander Niculescu, professor of psychiatry at the University of Indiana, founded MindX to bring liquid biopsy blood tests for mental disorders to the clinic. He is dedicated to transforming mental health care and has personally treated over 10,000 patients.

chronic pain in the journal Molecular Psychiatry.

After collecting this data, the team used convergent functional genomics to rank the association of certain biomarkers with each mental health disorder.

"(The method) reminds one of a Google page rank algorithm where the more relevant matches rise higher up in your search," Niculescu said, explaining that the more lines of evidence from different studies converge for a candidate biomarker, "the more it gets prioritized in the rank."

Because Niculescu's team followed the same individuals over time, it could weed out the genetic variation, or what he called "noise," from person to person.

As a part of their standard pipeline, once the researchers prioritize and validate the candidate biomarkers associated with each condition, they put the biomarkers through a final, rigorous test in patient cohorts.

"We look at additional independent clinical cohorts to see if our biomarkers accurately classify who's ill and who's not," Niculescu said. "We want to see if they can predict outcomes such as who will have future emergency room visits or hospitalizations for those disorders.

"It's a very comprehensive stepwise process to make sure that we discover the signal, and then prioritize, validate and test it in independent cohorts to show clinical validity of the signal. And at the end, we end up with that panel of biomarkers that went through all these hurdles, and that's what we put forward as useful clinically."

To diagnose a patient, along with behavioral questions and tests, Niculescu's team can use this data to see if an undiagnosed patient's transcriptomic profile overlaps with any of the biomarker panels they've established for conditions from previous studies.

Time and other hurdles

Liquid biopsy technology can detect many types of disease indicators, or biomarkers. These include tumor cells, DNA, RNA, genomic modifications, proteins and posttranslational modifications.

The human genome is made up of 22,000 genes. However, the proteins expressed in a cell can be modified with over 400 posttranslational modifications.

Therefore, the proteome — the entire complement of proteins with posttranslational modifications that is or can be expressed by a cell, tissue or organism — can consist of up to 1 million protein forms. Discovering an accurate, reproducible set of biomarkers by sifting through this data for multiple patients is like finding a needle in a very large haystack.

Mining for biomarkers to create a liquid biopsy test requires power and time, according to Jennifer Van Eyk, a professor of cardiology at Cedars–

Sinai Medical Center. In some cases, labs can take 10 years or more to move a biomarker through the pipeline and "many good biomarkers get lost along the way," she said.

"People often say, 'It's been so long that people have been doing discovery and proteomics … and not that many (tests) have hit the clinic,'" Van Eyk said. "Usually, people don't realize how hard it is to move a biomarker from discovery to clinical use. This is a very long process that requires time, money and equipment."

The process of taking a biomarker from discovery to clinical implementation as a liquid biopsy test requires the expertise of geneticists, pathologists, physicians and other experts, Van Eyk said.

JENNIFER VAN EYK

That's why Boris and Tao teamed up and combined their respective expertise in clinical urology and analytical chemistry to tackle the kidney cancer liquid biopsy.

"We were able to have conversations and learn from each other about science and medicine in the clinic and operating room," Tao said.

To streamline discovery and foster more such collaborations, Van Eyk and others founded the Precision Biomarker Laboratories at Cedars–Sinai. The center is designed to take biomarkers from the discovery phase through commercial development and finally to clinical use.

Liquid biopsy tests may seem simple, but they require expertise and equipment that cost hundreds of thousands of dollars. This cost is likely preventing them from being adopted widely, Niculescu said. However, he thinks this technology will eventually lessen the financial burden of diagnosis.

"Wide implementation of liquid biopsies would benefit the health care system," Niculescu said. "Even though liquid biopsy approaches are relatively expensive, the test is still cheaper than a day of hospitalization or an ER visit. They could also ease the distress of patients and their families by avoiding tragedies like suicide."

A liquid biopsy requires only a small sample to generate a huge data set; however, reduced access to healthcare in low-income and rural areas may stifle the implementation of this technology up front.

Van Eyk's lab has adopted an affordable solution.

The lab uses remote sampling devices to collect blood, which can then go through the biomarker discovery phase. These minimally invasive devices come with all the supplies a patient needs to perform a finger prick at home and collect a predetermined amount of blood in a plastic tube with little contamination. This sample is stable at room temperature and can be shipped anywhere around the world.

Van Eyk said these devices and mass spectrometry could help make healthcare and study participation more accessible.

"There are lots of conditions and situations where we use these sampling devices," she said.

Instead of going to a study site, a patient could perform their own blood draw, so the device reduces travel costs, Van Eyk said. "It also reduces barriers of who can participate in a study and moves us toward more equality of service. Right now, they are not so much being used clinically. But, we're hoping they will be pushing in that direction."

Liquid biopsies cannot completely replace tissue biopsies and haven't

> **"Wide implementation of liquid biopsies would benefit the health care system. Even though liquid biopsy approaches are relatively expensive, the test is still cheaper than a day of hospitalization or an ER visit."**
>
> ALEXANDER NICULESCU

Diamandis's interest in cutting-edge diagnostics landed him a role in one of the largest scientific scandals of the 21st century, which revolved around the blood diagnostic company Theranos and founder Elizabeth Holmes.

been extensively used in clinical settings outside of oncology. However, the technology is promising for many fields, Boris said, and may be able to guide individualized approaches to disease management.

Questions, scandal and promise

A few liquid biopsy diagnostic tests designed for home use are now commonly available, but results can be problematic. And patients may be wary after hearing news accounts of derailed attempts to commercialize liquid biopsy technology.

Davidson said some of his patients at WashU have become unnecessarily worried after using at-home tests such as Cologuard to detect colon cancer. Tests like these, in which patients mail stool samples to the manufacturer, do not differentiate between benign polyps and cancerous lesions. They can also produce false positives, according to Davidson.

"I have gotten calls from people with positive Cologuard tests who are convinced they have cancer, but they don't have any lesions in their colon," he said. "They continue to get scans and expensive tests, which reveal nothing, but the patient still has concern."

Cologuard has a false positive rate of 13%, which can cost patients thousands of dollars in unnecessary diagnostic tests.

Eventually, liquid biopsies may be able to help health care providers screen for and manage many different types of diseases. However, the technology is still new and must be honed and applied correctly to work well, Davidson said.

Like Davidson, Eleftherios Diamandis, senior scientist at the Lunenfeld-Tanenbaum Research Institute of Sinai Health System in Toronto, worries that liquid biopsies may not be sensitive and specific enough to be used for early detection screening and diagnostics. Specifically, liquid biopsies used for screening tend to produce many false positive results, about 1 in 10, he said.

ELEFTHERIOS DIAMANDIS

"A false positive in a screen can be very dangerous for the patient," Diamandis said. "They will worry and undergo unnecessary tests that may be harmful. This technology must be refined in order to make diagnoses.

"However, if we see more promising results in early detection, that could be revolutionary."

Diamandis's interest in cutting-edge diagnostics landed him a role in one of the largest scientific scandals of the 21st century, which revolved around the blood diagnostic company Theranos and founder Elizabeth Holmes.

Founded in 2003, Theranos claimed its technology could use a finger pinprick and a tiny amount of blood to rapidly diagnose hundreds of conditions such as high cholesterol and cancer. However, in 2018, the company was dissolved, and in 2022, Holmes was convicted of fraud after news reports revealed the technology the company boasted did not exist.

Diamandis was one of the first scientists to publicly criticize Theranos and Holmes. He learned about the company in about 2014 from his boss at Toronto.

"At the time, I had not heard of (Theranos)," Diamandis said. "So, I went to PubMed to search for their publications, and I found zero results. Then I turned to other information sources like what I heard through the

grapevine. … We had no idea how good their data was."

In 2015, he published an editorial questioning the cost, speed, methodology and results Theranos claimed. Some of his peers criticized him for voicing his skepticism, he said. However, after he, another scientist and a Wall Street Journal reporter all questioned the technology, the company's claims started to fall apart. Holmes is now serving an 11-year prison term.

David Wong, a professor and director of the Center for Oral/Head & Neck Oncology Research at the UCLA School of Dentistry and an expert on liquid biopsy, said the Theranos scandal emanated from the company's profound secrecy and lack of transparency.

DAVID WONG

"The scandal primarily revolved around Theranos' false claims and the lack of scientific evidence to support their technology, rather than being a reflection of the overall validity or potential of liquid biopsy as a diagnostic tool," Wong said. "Open communication about the limitations, potential risks and benefits of liquid biopsy is essential to manage public expectations and foster trust."

Though Holmes overpromised on the power of Theranos' technology and wounded public trust, Taichiro Nonaka, a professor of cellular biology and anatomy at Louisiana State University Health Sciences Center who studies saliva liquid biopsies, said the COVID-19 pandemic may have restored some public confidence in diagnostic technology.

At the beginning of the COVID-19 pandemic, saliva tests were widely used to quickly diagnose the disease. However, because not all individuals could produce enough saliva, these diagnostics were replaced by genetic testing of nasal swabs. Wong and Nonaka's current research focuses on using salivary liquid biopsies to diagnose breast, lung, esophageal cancers and more.

TAICHIRO NONAKA

"(Recent scientific) findings have created a favorable public view of saliva testing," Nonaka said. "I look forward to additional breakthroughs in this fast-moving field, and I see a bright future ahead for saliva diagnostics.

"Theranos may have been the worst-case scenario for the diagnostics industry, but their big picture is still true."

Next stop: precision medicine

Tao and colleagues said liquid biopsy technology has the potential to be a diagnostic and monitoring tool for kidney cancer patients' response to therapy and relapse. For Davidson, this is already a reality in the colon cancer clinic in St. Louis.

Boris and Tao's research now focuses on analyzing the phosphoproteins in urine samples from kidney cancer survivors over time to find out if they can detect signatures that correlate with cancer recurrence.

"All of the patients that come in to see me after surgery require imaging to determine whether or not they have a recurrence," Boris said.

"Open communication about the limitations, potential risks and benefits of liquid biopsy is essential to manage public expectations and foster trust."

DAVID WONG

> "I think the use of this technology is going to continue to increase. There is an appetite among patients for tools for convenient detection of disease."
>
> NICHOLAS DAVIDSON

"The vast majority of these patients do not have recurrences and are getting scanned over and over again for five to 10 years. So, just think about their cumulative exposure to radiation and the burden of having to get CT scans year in and year out.

"There could be limitless applications and benefits of having an easy biofluid test that could provide these answers."

Tao and Boris are optimistic that one day liquid biopsies will help urologists convince newly diagnosed patients with low-grade kidney cancer to be monitored instead of going straight to interventions that could result in unnecessary surgery and medical expenses.

Most liquid biopsy research and implementation is still confined to laboratories and clinical studies, Boris said.

However, Niculescu is forging ahead with clinical implementation of his novel liquid biopsy tests. He founded a company, MindX, to expand, market and distribute the tests to clinics everywhere. To date, the company has developed readily available liquid biopsy blood tests for mood disorders (depression/bipolar), anxiety, suicidality risk, stress (posttraumatic stress disorder), memory (Alzheimer's) and pain.

"Pain is very similar to other mental health disorders in the sense that it's subjective; patients perceive pain and report to the doctor," Niculescu said. "And the doctor has to rely on the patient's self-report for their clinical impression. (These tests) help the doctor in terms of not missing cases where people are in pain and the markers substantiate that."

Pain is difficult to treat, and Niculescu noted that attempts to treat pain caused the current opioid crisis. The U.S. Health and Resources and Services Administration reports that more than 130 people die per day from opioid-related drug overdoses. Niculescu said his liquid biopsy tests not only diagnose pain but can be used to suggest therapeutics based on the patient's biomarker profile.

"The pain biomarker panel can match people to nonaddictive, nonopioid medications," Niculescu said. "So, the doctor can use that information to avoid choices that might not work as well and can lead to addictions."

Niculescu and MindX are working on developing liquid biopsy tests for psychosis, to identify diseases such as schizophrenia, and for attention deficit disorder. He said ADHD must be addressed because the drug Adderall is so frequently prescribed and misused, especially in children.

Diamandis said the future of liquid biopsy screening and monitoring will likely use artificial intelligence to interpret test results due to the vast number of measurable biomarkers for each individual.

"Many companies and labs are doing multiparametric tests," Diamandis said. "Now the difficulty comes with the interpretation."

Diamandis and Davidson agree that liquid biopsies, despite their challenges, will play a large role in the future of medicine.

"I think the use of this technology is going to continue to increase," Davidson said. "There is an appetite among patients for tools for convenient detection of disease."

Marissa Locke Rottinghaus (mlocke@asbmb.org) is the science and policy communications specialist for the ASBMB.

Meet Sarah O'Connor

This JBC associate editor scouts the plant kingdom for intriguing pathways and hits the hiking trails in Germany

By Paula Amann

Sarah O'Connor was a postdoctoral fellow in an enzymology lab when she realized that most of the biochemists in her area were studying microbes and few were studying the complicated genomes of plants — so she decided to make plants her focus. She is now the director of the department of natural product biosynthesis at the Max Planck Institute of Chemical Ecology in Jena, Germany.

After receiving a bachelor's degree in chemistry at the University of Chicago, O'Connor earned a Ph.D. in organic chemistry at the Massachusetts Institute of Technology. Her postdoctoral research in biochemistry took her to Harvard Medical School, where, in the laboratory of the late Christopher T. Walsh, she discovered her research path.

O'Connor returned to MIT as an assistant and then associate professor of chemistry. She crossed the Atlantic to the John Innes Centre, an institution for the study of plant and microbial science in Norwich, U.K., where she quickly rose from lecturer to professor and then honorary professor. A call from a friend led her in 2019 to her current position.

O'Connor's science has won her multiple awards. Most recently, she took home the 2023 Gottfried Wilhelm Leibniz Prize for fundamental discoveries in plant natural product biosynthesis. In 2022, she received the Ernest Guenther Award in the Chemistry of Natural Products from the American Chemical Society. In 2019, she garnered the Perkin Prize for Organic Chemistry from the Royal Society of Chemistry for the discovery, enzymology and engineering of the biosynthetic pathways for complex natural products from plants.

In 2022, O'Connor began serving as an associate editor for the Journal of Biological Chemistry. This conversation has been edited.

COURTESY OF SARAH O'CONNOR

Sarah O'Connor, an associate editor for the Journal of Biological Chemistry, won the 2023 Leibniz Prize for fundamental discoveries in plant natural product biosynthesis.

Q: How did you come to venture into plant biochemistry?

When I was doing my postdoc with Chris Walsh, he was working on antibiotic synthesis, studying how microbes made complicated molecules. As I was reading the literature, I realized immediately that far fewer people were working in the area of plants. The genomes are more complicated; the biology is more complicated. I thought, "Let's keep the fundamental idea of being able to understand how nature does complicated chemistry but look and see how plants do it as opposed to bacteria or other microbes."

Bacteria are very good at organizing metabolic pathways into the segments of DNA we call operons. One stretch of the genome may have 10 genes all dedicated to the same pathway. In bacteria and even fungi, you can use a technique called genome mining to get a genome sequence, and then you can put those genome sequences into this beautiful software, and search the bacteria for so-called "gene clusters." Then you can identify the

> "I think the use of this technology is going to continue to increase. There is an appetite among patients for tools for convenient detection of disease."
>
> SARAH O'CONNOR

gene clusters very easily.

In plants, it's more complicated. Plants have much bigger genomes, so identifying individual genes is more difficult in a plant than for bacteria. Genes don't tend to be organized in operons, as they are in bacteria. Occasionally, they're proximal to each other, but there's a lot of distance between them, and sometimes they're just scattered randomly all over different chromosomes.

We know comparatively little about the noncoding regions of plant genomes. Now, with all the next-generation sequencing technology, we can start to look at chromatin structure and DNA structure. By better understanding the three-dimensional structure of the DNA, we can get a better idea about how these genes at distant points in the genome might actually be interacting with each other.

Q: So does genetic research on plants require special techniques?

One of the great things about working with plants is that all the people who are working on cancer and human biology pioneer wonderful techniques, and then we can turn around and try to apply them to plants. A lot of these techniques were pioneered in mammalian cell systems. One of these was single-cell sequencing. In the last couple of years, it has just been made feasible for plant systems.

When you're looking at these very complicated metabolites, they're typically only being produced in a very small subset of the different types of cells that you see. For example, a plant leaf has dozens of different cell types, and maybe just a couple of those cell types are producing a complicated molecule.

When you're trying to identify 10, 20 or 30 genes out of a plant that is expressing 40,000 or 50,000 genes, single-cell resolution, transcriptomic data make much more highly resolved data sets. It's fascinating because those leaves are also going to have pigment materials and structural materials to hold them together.

Q: What's involved in your study of medicinal plants?

It's difficult to get new drugs or new treatments into common use. A lot of regulatory hurdles need to be overcome. We focus on proof of concept: studies that show what can be possible.

The idea is to make analogs of plant compounds. We're getting closer and closer to coming up with things that are useful, using biosynthetic genes and production platforms. We can then collaborate with people who do more rigorous biological or pharmacological testing.

In medicinal chemistry, it's been shown over and over again that if you can do these structure-activity relationship studies, you can make very small changes around the structure of the molecule and then test those analogs. Tiny changes in the chemical structure of the molecule will have a big impact on its biological activity or its therapeutic value.

From a medicinal chemistry standpoint, putting atoms like fluorine or chlorine on the structure of a drug can change the pharmacokinetics of the compound. Medicinal chemists have found this often produces interesting changes in the biological activity of the compound.

Q: You recently co-authored a study of the medicinal plant, Catharanthus roseus (Madagascar periwinkle), with a team from the University of Georgia. How did you all connect and what are you trying to learn?

I collaborate with Robin Buell at the University of Georgia. We first got to know each other in 2009. We applied to the National Institutes of Health to study Catharanthus. We convinced the NIH that they should fund a large-scale plant transcriptomics initiative. This was the first federally funded medicinal plant omics initiative in the United States.

I was the biochemist in the consortium; Robin was the sequencing and genomics person. Everything that I know about genomics and transcriptomics, Robin taught me.

We've continued the collaboration since then, and it was Robin who, a couple of years ago, said to me, "Sarah, we need to be thinking about single-cell transcriptomics." And the paper you were referring to came out of that.

That was just a starting point. We have a number of other plants in the pipeline that we're looking at. The people in her lab are really trying to understand how the plant controls the production of some of these compounds.

In our lab, we're interested in using these data sets to find new biosynthetic pathways. And we're also interested in seeing how these data can help us engineer better production of these compounds using synthetic biology and metabolic engineering strategies.

Q: How did you get connected with the Journal of Biological Chemistry? What are your criteria for reviewing a paper?

MOKKIE/WIKIMEDIA COMMONS

Sarah O'Connor recently co-authored a study of the medicinal plant, Catharanthus roseus (Madagascar periwinkle), with a team from the University of Georgia.

If I have a nice piece of biochemistry, JBC is just the journal to send it to. I think this journal is an important place for research.

If we publish, we have to contribute to making the journals work, so being an associate editor is a service that I'm happy to do. It's also a good way to learn new things. Even by just skimming the abstract of a paper sent to me to handle, I usually learn something new.

First and foremost, the manuscript must contain a new biochemical discovery, such as the discovery of a new enzyme, a new mechanism or revision of an old mechanism. The data are held to the highest standard. Finally, presentation is important. Figures should be clear, and the manuscript must be well written.

Q: What's your advice for younger women in biochemistry?

I think all of us who are being honest and humble, including me, would say our careers are a work in

Sarah O'Connor enjoys hiking in the mountains around Jena, Germany, where she lives and works.

progress. You're still learning at every phase of your career.

There's definitely advice I give younger female scientists: Women scientists need to sell themselves better. I've been on review panels that require an interview. There is a trend for younger female scientists to be more self-deprecating or less forthcoming than men about their big scientific vision. I don't think it's because they don't have one; it's because they're reluctant to express it. I really encourage women scientists to express their scientific thoughts in a confident and logical, but not arrogant, way.

Q: What's the next research frontier you're interested in exploring?

It's amazing how a new environment prompts you to look at new systems. I now work at an institute with a lot of entomologists. We recently published a paper on aphids, and it turns out that aphids make the same molecule that the catnip plant does. It's called nepetalactone.

Female aphids produce it in their legs and use it to attract male aphids with sexual hormones. We were able to find the biosynthetic pathways in both the catnip plant and the female aphid hind leg and compare them. We couldn't have done it without the help of entomologists here.

Nepetalactone is not a pharmaceutical, but it has a lot of promise as an insect repellent.

Q: What do you do to recharge after a long week in the lab?

I like to go hiking anywhere from 10 to 30 km, depending on the kind of week I've had. During the summer here, it's really nice to get out in the sun. Jena is in the former East Germany, in a mountainous region, so there's a lot of beautiful scenery around.

Of course, I pay attention to the plants and try to pick out the ones I recognize. Given my colleagues here, I'm starting to pay more attention to the insects I see as well.

Paula Amann (pamann@asbmb.org) is the ASBMB's science writer.

Upcoming ASBMB events and deadlines

SEPTEMBER

6	Serine proteases conference early registration deadline
6	Serine proteases conference abstract submission deadline
12	Discover BMB deadline for interest group/workshop proposal
15	ASBMB accreditation applications due
18–22	*National Postdoc Appreciation Week*
25–29	*Peer Review Week*
27	**Lipid Research Division Seminar**

OCTOBER

1	Student Chapter Outreach Grant fall deadline
1	ASBMB Today wellness issue submission deadline
12	Discover BMB early-decision abstract submission deadline
31	Science Outreach and Communication Grant deadline
31	Serine proteases conference regular registration deadline

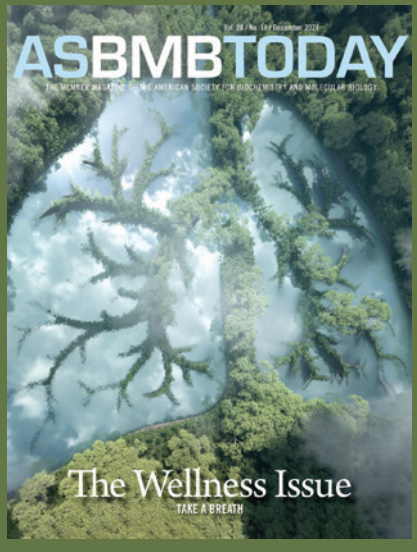
NOVEMBER

1	**ASBMB Virtual Career Expo**
2–3	**Serine proteases conference**
30	Discover BMB abstract and travel award submission deadline

ASBMB

CALL FOR SUBMISSIONS

The wellness issue — January 2024



Trauma and recovery

Have you

- experienced a traumatic event or illness?
- struggled with how to support survivors?
- received valuable assistance?

Or do you have a list of things well-meaning folks should absolutely avoid doing?

Whatever the case, we want to read about it.

For the January 2024 issue, we invite you to submit stories that tackle trauma and its aftermath.

Trauma comes in many forms. Telling stories helps us heal.

Send your idea (or questions) to the editors at asbmbtoday@asbmb.org.

DEADLINE: OCT. 1

ASBMBTODAY

Showcasing the future of BMB

By Marissa Locke Rottinghaus

The 10 thematic symposia at Discover BMB will focus on today's hottest topics in biochemistry and molecular biology. Each will feature thought leaders and experts discussing exciting findings. And new this year is a symposium on natural products and their role in bioengineering and biotechnology.

ZAREMBERG

TU

#DiscoverBMB 2024 co-chairs **Vanina Zaremberg**, a professor of biochemistry at the University of Calgary, and **Benjamin Tu**, a professor of biochemistry at the University of Texas Southwestern Medical Center, sat down recently with ASBMB Today writer Marissa Locke Rottinghaus to describe the cutting-edge thematic sessions they have selected, how to make your #DiscoverBMB experience worthwhile and why they look forward to this meeting being the best yet. Their conversation has been edited for clarity, length and style.

Can you talk about why you selected certain themes? I understand the one on natural products is new, for example.

Tu: In addition to the Education and Professional Development and Maximizing Access Committee sessions, Vanina and I chose these 10 scientific themes because we think they represent molecules and organelles that make life possible. In particular, we thought natural products would be great to include because biochemistry is required to figure out how these molecules are made and how they act on their targets.

I think there's also a growing interest in job opportunities in technology and bioengineering related to natural products. Some of the best biochemists and molecular biologists are those who work in this area. So, we wanted to get them involved in #DiscoverBMB.

Zaremberg: We think these themes reflect hot topics in biochemistry and molecular biology. Many of the themes have multiple different angles and reflect interdisciplinary approaches. We have a theme on membrane contact sites, which describes how organelles within the cell communicate and exchange metabolites, lipids, etc. We are bringing relegated organelles, like peroxisomes and chloroplasts, to the forefront as well.

How did you select the theme organizers? What qualities do you look for in these scientists?

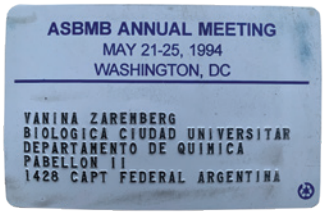
Tu: For the organizers, we wanted to choose people who are leaders in their respective fields, who have good taste in science and, most importantly, who will assemble a diverse panel of speakers who will share the latest developments in their research areas.

Zaremberg: We selected experts in all biochemistry fields who will uphold the standard of excellence at the ASBMB meeting. We tried to make sure the organizers were diverse, and the diversity came naturally with our selection of experts in each theme.

When did you attend your first scientific meeting, and what was that experience like?

Tu: I attended my first meeting as a graduate student. My mentor couldn't make it, and it was in Spain. So, I was a lonely graduate student traveling all by myself. I was selected to give a talk in my mentor's place. It was extremely nerve-racking, and I still remember all of my emotions. As a student, all I could think was, "Oh my gosh; I have to give a talk in front of the experts, and I better not embarrass my lab and my professor."

But, everyone was really friendly and welcoming. It turned out to be all



Vanina Zaremberg saved this ID card from her first ASBMB meeting in 1994, when she was a Ph.D. student from Argentina.

right, and it was definitely an experience that I'll never forget. It also made me realize how important meetings are and taught me to meet colleagues and key scientists in the field.

Zaremberg: I could talk for hours about my first ASBMB meeting — it was extremely exciting. Back in 1994 when I was a visiting Ph.D. student from Argentina in the U.S., I paid the meeting registration fee from my own pocket. I went to Washington, D.C., for the meeting, and I was in science heaven. I loved it. I thought it was so exciting that I could talk to and ask questions of the people who wrote papers I had read.

When I moved to Canada and started my own lab, I wanted my graduate students to have the same experience. So, I've been attending the ASBMB meetings for a long time. I look forward to it every year now. I've seen how the meetings have changed over the years, but the sense of community, the networking and the quality of the science has stayed the same.

What advice do you have for first-time attendees?

Tu: I would suggest taking a look at the schedule beforehand and making use of the app. Take advantage of the Meet the Experts sessions. There are various talks at the Career Hub that are quite helpful. Also, definitely attend the award lectures because many of them are quite inspiring.

Don't be afraid to approach senior scientists because we like it when random attendees come up to us to ask questions or seek advice.

Zaremberg: Participate, ask questions and engage in discussions. Go to the social events because they are fantastic for networking and meeting people. I agree with Ben; make a schedule of what you want to see and attend ahead of time.

Tell me about San Antonio. What are some of its appeals for prospective attendees?

Tu: San Antonio is centrally located. It's great that people from both coasts can easily access it. The meeting is going to be a great opportunity to experience culture and great Southern food. San Antonio is also home to the River Walk, which is fantastic, and the weather in late March should be great!

Zaremberg: I've never been to San Antonio, but I am really looking forward to it and have always wanted to visit. I think it is exciting that ASBMB is exploring new locations and venues for the annual meeting.

#DiscoverBMB 2024 scientific symposia and organizers

Microbial signaling, communication and metabolism — Peter Chien, University of Massachusetts Amherst, and Jade Wang, University of Wisconsin–Madison

Cool and novel enzymes — Shelley Copley, University of Colorado Boulder, and Hung-wen (Ben) Liu, University of Texas at Austin

RNA biology — Katrin Karbstein, UF Scripps Institute for Biomedical Innovation & Technology, and Jeremy Wilusz, Baylor College of Medicine

New frontiers in structural biology — Jose Rodriguez, UCLA, and Hosea Nelson, California Institute of Technology

Advances in natural product biochemistry and biotechnology — Yi Tang, UCLA, and Katherine Ryan, University of British Columbia

Redox and metals in biology — Siavash Kurdistani, UCLA, and Gina DeNicola, Moffitt Cancer Center

Membrane contact sites — Chris Beh, Simon Fraser University, and Jen Liou, University of Texas Southwestern Medical Center

Lipid metabolism — Maria Fedorova, Dresden University of Technology, and Neale Ridgway, Dalhousie University

Signaling mechanisms in the nucleus — Glen Liszczak, University of Texas Southwestern Medical Center, and Aaron Johnson, University of Colorado Anschutz Medical Campus

Mitochondria, peroxisomes and chloroplast metabolism — Pere Puigserver, Dana–Farber Cancer Institute; Harvard Medical School, and Greg Moorhead, University of Calgary

Look for details about these symposia as well as symposia organized by the Maximizing Access Committee and the Education and Professional Development Committee in the October issue of ASBMB Today.

Marissa Locke Rottinghaus (mlocke@asbmb.org) is the science and policy communications specialist for the ASBMB.

Workshops enhance the #DiscoverBMB experience

Submit your proposals by Sept. 12

By Kirsten F. Block

The school year peeks over the horizon, and not long after that we'll hit the end-of-year holiday rush. Before you know it, our calendars turn to 2024, at which point we at the American Society for Biochemistry and Molecular Biology become laser-focused on the final touches for what will surely be an impactful annual meeting March 23–26 in San Antonio.

Before we get to those final touches, though, we are — and have been for quite some time — full steam ahead with program planning. The meeting organizers and thematic session chairs already have the scientific content covered.

But there's more. Did you know that you, as an ASBMB member, also have an opportunity to shape the program and run sessions? That's right, it's our annual call for workshop proposals.

Lessons learned in Seattle

#DiscoverBMB 2023 attendees may have noticed that the schedule and the feel were a bit different from other meetings in recent memory. By moving away from Experimental Biology to host our own annual meeting, the ASBMB was able to reimagine how this meeting serves the needs of our community.

Many of these changes were successful, but rarely is an experiment flawless on the first try. What can we learn from the 2023 program to enhance what we do in 2024? Here are a few observations from our Seattle experience.

- **Can we get some lunch, please?** Workshops were held during the lunch hour in Seattle. While this opened up late afternoons for poster sessions and unstructured networking time, it posed a difficult question for attendees: When can I eat without feeling like I'm missing something?

- **So many programs, so little time.** We heard this frequently and across the entire program, not just the workshops. National meetings often pack as much as possible into a tight schedule, and ours was no different. That said, a packed schedule could mean not just sprinting from room to room but also a higher likelihood that concurrent sessions have overlapping target audiences.

- **Know your audience.** Our call for proposals last year asked members to think broadly and creatively about workshop submissions, as long as submissions were aligned with our mission. We weren't sure what we might receive. Turns out, strictly by audience numbers, some topics were hits, and others were not so much. The two bullets above contributed to these numbers (don't you love trying to make sense of messy data?), but a third element likely played a part as well: Just who are our meeting attendees in general, and who among these attendees are likely to participate in workshops?

Small tweaks, not a total overhaul

Looking ahead to San Antonio, we've made a few changes to the program schedule to address the challenges above, and the workshop proposal form reflects these changes.

We've moved workshops out of the midday hour to open up space in the schedule for a lunch break. Instead, workshops will be split between the morning and afternoon. We have reduced the total number of workshops as well, hoping to avoid some of the inevitable scheduling conflicts.

Finally, to help guide submissions and subsequent review, we've focused the workshop proposal form on specific categories:

- **Diversity, equity, access and inclusion**
- **BMB educational tools, resources and programs**
- **Career skills**

These categories recognize both the types of topics we saw frequently last year and the topics that drew crowds to the 2023 workshops. We

also included an "other" category, since some workshop topics don't neatly fit into one of these three categories. All ideas are welcome, and we'll do our best to balance the interests of attendees and submitters to provide a wide-ranging suite of workshops that complement the scientific sessions.

Proposal reviewers will have tough decisions to make in the coming months, but now it's in your hands. Start thinking about what you want to see on the schedule next spring in San Antonio, and submit your workshop proposals at discoverbmb.asbmb.org/workshops by Sept. 12. I can't wait to see what you come up with.

Kirsten F. Block (kblock@asbmb.org) is the ASBMB's director of education, professional development and outreach. Follow her on Twitter: @kfblock.

Call for #DiscoverBMB 2024 interest group organizers

The American Society for Biochemistry and Molecular Biology is seeking organizers for interest group sessions at Discover BMB, to be held March 23–26 in San Antonio.

Just as with workshops, ASBMB members have the opportunity to shape the meeting program by developing interest group sessions in the following areas:

- Artificial intelligence and structural prediction/drug design
- Biochemistry and climate change
- BMB education and training
- Cancer biology and metabolism
- CRISPR based gene editing
- Gene regulation
- Immunology
- Mass spectrometry-based omics and disease
- Metabolism and metabolic disease
- Protein structure, synthesis and folding
- Signal transduction
- Vaccine development and delivery systems

Interest group sessions are two-hour mini symposia held on the first day of the meeting, March 23.

Organizers will secure a lineup of diverse speakers and create ample time for Q&A, panel discussions and networking to facilitate community building.

Submit a proposal to lead an interest group at discoverbmb.asbmb.org/program/interest-groups.

Decisions will be sent by Oct. 26, at which time a final speaker list will be required. For more information, visit discoverbmb.asbmb.org/interest-groups.

SAN ANTONIO | MARCH 23–26
Discover BMB | 2024
American Society for Biochemistry and Molecular Biology

Small grants power outreach

By Debra Martin & Michael Wolyniak

Did you know that outreach programming is one of the most effective ways for scientists to build trust with nonscientists? And that K–12 students who participate in science outreach activities are more likely to identify themselves as scientists?

The COVID-19 pandemic, climate change and other global challenges have raised public awareness of science and motivated a growing number of people to engage with the scientific process. Through outreach programs, scientists can communicate and engage nonscientists in their communities.

The ASBMB Science Outreach and Communication Committee supports science education by teaching effective communication skills and providing financial assistance for outreach programs.

The committee now provides up to five $1,000 Science Outreach and Communication mini grants each year to help ASBMB members develop and implement engaging outreach programs, particularly for underresourced and historically marginalized communities. These projects use innovative strategies to engage aspiring scientists of all ages and backgrounds.

By sharing here the work that's been done by three mini grant recipients, we hope to inspire others to think about outreach in their communities.

A DNA summer camp

Joshua Sokoloski, an assistant professor of chemistry at Salisbury University on Maryland's Eastern Shore, is committed to developing educational outreach initiatives. The grant was a perfect match for his enthusiasm.

"I have a strong personal conviction that outreach is a core part of being a scientist," Sokoloski said, "and I am fortunate enough to have a department and a school who support me and my colleagues in outreach activities."

Starting an outreach program can be difficult even with financial support. One key to Sokoloski's success was taking advantage of existing infrastructure and programming. Salisbury's Summer Enrichment Academies, or SEA, is a summer day camp for local middle school students. Using the existing SEA structure as a starting point, Sokoloski designed a two-session outreach program to show middle school students "just how awesome nucleic acids are and all the possibilities nucleic acid biotechnology offers for society."

Most of the 36 middle school students in the program were from groups traditionally underrepresented in the STEM disciplines. In the first session, they learned all about DNA, from its history to base pairing to modern RNA therapies for COVID-19. The students used 3D printed models of nucleotides with magnets to replicate hydrogen bonding and performed DNA extraction activities on fruit while hypothesizing which type of fruit would yield the most DNA per gram; it turns out strawberries won, with blueberries a close second.

In the second session, students learned how DNA gives each person a unique marker, like a fingerprint, that can be used in crime scene investigations. They worked to identify the culprit who stole a top-secret slime recipe — using lab equipment to prepare samples and run an agarose gel electrophoresis.

To develop a successful outreach project, Sokoloski recommends recruiting volunteers from your institution or related organizations. In his case, help came from undergraduate members of the ASBMB Student Chapter at Salisbury who were eager to work with middle school students.

With the support of the Student Chapter and the SEA program, Sokoloski was able to design engaging, hands-on scientific experiences. And middle school students got to work and think like scientists as well as consider what a career in science might be like.

Workshops seed the future

Haley Albright, an assistant professor at Shepherd University in West Virginia, wants to show young students that science and chemistry are happening around them every day.

Albright used the SOC grant for what she called "Seeding your Future." She teamed up with four other faculty members at Shepherd to host

COURTESY OF HALEY ALBRIGHT

Students look through microscopes during the "Seeding your Future" workshop series at Shepherd University in West Virginia.

four workshops that exposed more than 50 middle and high school students to science. They extracted caffeine from soda and tea and DNA from food; they built a robotic arm and a water filter. Each workshop included both hands-on activities and take-home portions for continued exploration.

The faculty members collaborated with undergraduate volunteers to organize and run the sessions. Communication was critical, and Albright used email to coordinate the workshops and keep participants in the know.

"The most challenging part was the planning of the event," she said. "A lot of this planning was done in increments."

Looking ahead to future projects, she said that, with so many faculty involved, an initial meeting to sort out details and get supply lists earlier on could streamline the process. And it's important to be flexible, she added, "since normally 20 students sign up for a workshop, and we had 70 students sign up."

Albright chose middle and high school students because "studies have shown that, especially for girls, interest in STEM significantly drops in middle school. We wanted to offer opportunities for students to keep that interest. Having a tie to real-life applications seems really important."

In Albright's workshop on extracting caffeine from soda and tea, participants establish connections between the beverages they or their parents consume and the diverse array of molecules those beverages contain.

"I like Mountain Dew, but I didn't know that there was caffeine in it or that caffeine was a type of molecule," one student said.

Parents provided positive feedback, including this comment via Facebook: "My son has loved every single workshop! This has been a wonderful experience for him."

Engaging young biochemists in Nigeria

After Victor Nweze, a biochemistry research assistant at the University of Nigeria in Nsukka, noticed that young people in his community did not pursue careers in biochemistry because it's less lucrative than other fields, he decided his aim would be to raise a new generation of African molecular biologists for global impact.

Nweze's project presented basic science via a symposium and workshops to help build a passion for

Interested in applying?

Visit asbmb.org/outreach-grant for more information about mini grants and application procedures. Applications are being accepted through Oct. 31. Contact outreach@asbmb.org with any questions about this program or any aspect of the SOCC's work.

COURTESY OF VICTOR NWEZE

Victor Nweze (left) leads students through a hands-on workshop in the Nsukka community in Nigeria.

biochemistry among students aged 12–18. The symposium included keynote speeches, a spelling bee and debate competitions and virtual lab presentations. The workshops involved hands-on techniques such as viewing bacteria and plant cells using microscopes, DNA extraction from cheek cells, a comparative study of saliva on starch using iodine tests and a session on career paths in biochemistry and molecular biology.

Coworkers from the biochemistry department, members of the university's Ethnopharmacology, Food and Drug Delivery Research Group and teachers at the three host secondary schools all helped Nweze. The program was held at each school over two days, with the symposium and competitions on the first day followed by a day of hands-on workshops in a chemistry lab.

More than 500 students participated. One of them was Favour Oluchukwau of the Nsukka community, who said, "I can testify that the ASBMB outreach made a great impact in our lives. As an African child, this was the best outreach I have ever experienced."

Chibuzo Nanadiebube agreed: "The ASBMB outreach was very well organized, impactful and enlightening. I can attest that the outreach created a new mental construct in the lives of the younger generation to become global problem-solvers and national transformers."

After completing this outreach project, Nweze was inspired to consider starting up a nongovernmental scientific organization to champion the advancement of biological sciences in Africa.

So how do I get started?

Starting an outreach project can be a daunting task. Building a successful program involves a variety of logistical challenges, and the content must be engaging for a chosen target audience.

These three mini grant awardees lowered some logistical barriers by looking for established programs that could facilitate recruitment and provide an existing structure on which to build.

Albright linked into "Your Future Initiative," an active program on her campus, while Sokoloski built his program into an existing summer day camp.

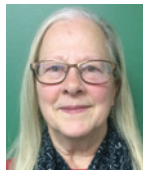
The awardees also suggest recruiting others who are passionate about outreach to help develop and implement ideas. Schools with ASBMB Student Chapters, like Salisbury, have an excellent source of prospective volunteers who may be eager to work with their community on scientific outreach. Nweze reached out to colleagues and students at the University of Nigeria to help implement his outreach ideas.

Seed-money success

No matter how exciting your ideas are and how many volunteers you recruit, a lack of funds can stand in the way of developing a successful outreach program. The SOC mini grant helps alleviate this barrier so awardees can focus on developing the programming and community connections that make their ideas succeed.

As awardees develop community connections, the committee hopes the mini grants will help seed long-term outreach programs around the world by forging bonds between ASBMB scientists and local organizations.

Debra Martin (dmartin@smumn.edu) is a professor at St. Mary's University of Minnesota and a member of the ASBMB Science Outreach and Communication Committee.



Michael Wolyniak (mwolyniak@hsc.edu) is a professor at Hampden–Sydney College and a member of the ASBMB Science Outreach and Communication Committee.

How to run an ASBMB Student Chapter

By Hailey Reiss

John Tansey is the faculty adviser of the American Society for Biochemistry and Molecular Biology Student Chapter at Otterbein University, a primarily undergraduate institution in Westerville, Ohio. As winner of the 2023 ASBMB Outstanding Chapter Award, Otterbein's chapter has developed to positively impact the community while providing opportunities for students to pursue compelling research and make strides toward future contributions to biochemistry and molecular biology.

Tansey sat down with Hailey Reiss, the ASBMB undergraduate education coordinator, to discuss his work with Otterbein's chapter. The interview has been edited for length, clarity and style.

How did you get involved with ASBMB, and what is your connection today?

A few years ago, I went to the ASBMB's "Transforming undergraduate education in the molecular life sciences" meeting. That's where I really found my community. I had gone to the ASBMB annual meeting and saw some of the people and heard some of the talks. But the education community is where I really started to find a home.

I got more involved with the society and began to work more with people in ASBMB. I got involved in the accreditation program, and then a few years ago, I was asked to join the Science Outreach and Communication Committee. Most recently, I was asked to join the Education and Professional Development Committee.

I can't say enough about the society. I have been really thrilled about my involvement.

How did you get involved with Student Chapters?

Before it was Student Chapters, it was the UAN, or Undergraduate Affiliate Network. We were trying to give our biochemistry majors at Otterbein their own student organization, so we got involved around 2011 or 2012. We've maintained the chapter since then because there are so many benefits, including travel awards and access to opportunities such as networking and exclusive awards.

> "I am in the business of creating people to create new knowledge of biochemistry and molecular biology. I produce graduate students."
>
> JOHN TANSEY

What makes your chapter outstanding?

We've had a very solid student chapter for quite a long time. Sometimes it comes and goes, such as during the pandemic. I think a lot of it comes down to people and who you have running the chapter. I've noticed that a lot of organizational success comes from the students.

This past year, Olivia Miller, an Honor Society inductee, has been fantastic. She shows up the first week of the semester with a list of ideas. We decide which initiatives we'll pursue, and from there, we design the budget.

ASBMB

John Tansey, left, and Otterbein Student Chapter members Savanna Glass, Kaitlin Dean, Olivia Miller, Mara Shields, Olivia Brickey, Ashni Patel and Mason Nolan were honored at Discover BMB, the ASBMB 2023 annual meeting in Seattle.

She has also brought other people in to help. Strong leadership like this is critical to our chapter's ongoing success.

What are some of your chapter's most memorable and successful activities?

For Valentine's Day, the chapter students made candy bags that people could pick up or that the students could deliver to different offices on campus. To add some science flair, they included little flyers about oxytocin or other biochemistry facts. This wasn't difficult to do, but it got our name out there.

On a related food note, we've made Cajun food to share with nonchapter students, and then we talk about spicy food and what, chemically, makes it spicy.

Off campus, we want to create a positive image around being a scientist. At a science festival in Columbus, we had a booth devoted to the science of gross things. We had tubes of gross-smelling substances and then built the structures of those molecules. We had a board to demonstrate how those molecules docked into different proteins. Little kids and adults loved it.

I think our outreach activities are generally very memorable.

As the adviser for your chapter, what challenges have you encountered?

The pandemic was definitely one of our biggest challenges to date. Our chapter does a lot of social activities, so it was hard when COVID-19 hit. At first, we tried to have weekly meetings online and just hang out. We sent silly emails to members of the chapter. We were trying to give people something to look forward to during lockdown.

When we came back to class in the fall of 2020, everything was distanced and often outdoors. We knew we wanted to host our coffee hours again, but we needed to figure out how to do it effectively. We'd always had Oreos in the past; now we had to eat them individually wrapped and six feet apart from each other.

We kept things going during the pandemic, but we had nowhere near the level of engagement that we were used to. We had enough student buy-in to keep everything afloat, and a permanent staff member on standby was really important during this time to maintain channels of communication and encourage student participation in virtual events.

Talk about the logistics of running your meetings and promoting awards.

We generally have two types of meetings. Our coffee hour is generally casual, without official business. And I'll meet with our leadership team early in the semester to organize our activities for that semester. We typically try to do one special activity each month. I think that really helps to get people involved.

When it comes to awards, we do different types of promotions

Senior and student chapter leader Olivia Miller was a member of the Science Outreach and Communication "Meet a Scientist" panel at #DiscoverBMB 2023.

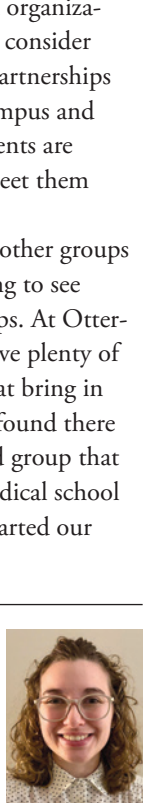
depending on which award we're looking at. With the travel award and Honor Society, the faculty and I typically decide who will receive the award or which students we nominate to the Honor Society. With the Undergraduate Research Award and Marion B. Sewer Scholarship for Distinguished Undergraduates, we tell the students about them and let them choose if they'd like to apply. With chapter-wide awards, such as the Outstanding Chapter Award, Regional Meeting Award, Science Fair Award or Outreach Grant, we encourage the students to put together an application. We will help them and review it with them, but I think it's a great experience for the students to do it themselves.

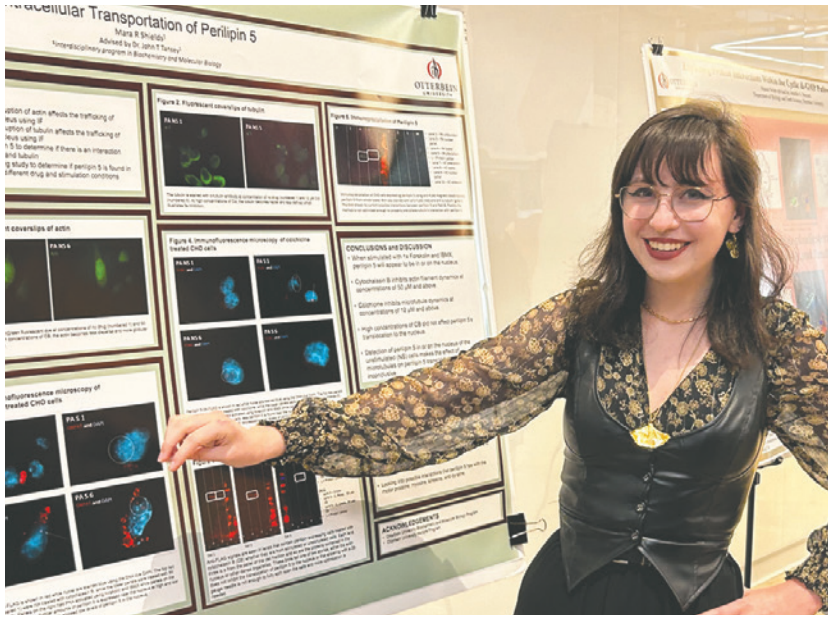
What advice would you give faculty members interested in starting a student chapter?

Be a little more hands-on to start. Make sure there's a good organizational structure in place, consider starting small, develop partnerships with other groups on campus and figure out what the students are interested in — try to meet them there.

You can look at what other groups on your campus are doing to see where there might be gaps. At Otterbein, for instance, we have plenty of great pre-med groups that bring in lots of speakers. But we found there was a need for a pre-med group that prepares students for medical school entrance exams, so we started our MCAT prep sessions.

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.





Senior Mara Shields discusses her research at Otterbein's Honors senior reporting day.

About Student Chapters

What is the ASBMB Student Chapters program?

ASBMB Student Chapters are a national community linking undergraduate students and faculty members with an interest in biochemistry and molecular biology. The chapters work to advance research, education and outreach in biochemistry and molecular biology.

How do I start a chapter?

Each chapter must have a faculty adviser who is a regular member of the ASBMB. This adviser must complete the application. Each chapter also needs a minimum of five students to receive full benefits. Chapter dues are $100 per year and cover up to 10 students. If you have more than 10, each additional student will be another $10.

The 2023–2024 renewal period for Student Chapters opens Sept. 1. To start a chapter, access the ASBMB student chapter registration system at asbmb.org/education.

What are the benefits of the program?

Both students and faculty members benefit.

Students have membership in the ASBMB and are eligible to apply for exclusive awards and grants such as travel awards, the ASBMB Honor Society and the Undergraduate Research Award. Students can also participate in professional development opportunities and network with each other on a national scale.

Faculty can receive funding to support their undergraduate research and science outreach efforts. They may also engage in education and professional development opportunities exclusive to chapter advisers, including a journal club and an online community of undergraduate educators.

Do you have questions about Student Chapters? Need guidance setting up a chapter? Email education@asbmb.org.

Scientific publishing, then and now

By Sudhansu K. Dey

When I was a graduate student at Calcutta University more than five decades ago, I submitted a paper on leucine amino peptidase localization in the guinea pig testis to a well-known journal in the U.K. The staff edited my English and shortened the paper without changing the theme or meaning of the study; the paper was then accepted. This paper helped me to obtain a postdoctoral fellowship in the U.S. and greatly helped my career advancement.

Back then, editors provided constructive feedback that improved our manuscripts. Editors and reviewers detailed the strengths and shortcomings of a study and how to address the deficiencies. Often, they suggested important additional experiments or constructive discussions to support the theme of the study. Once we addressed these comments, the paper would be accepted.

Like everything else, publishing has changed over the years.

My lab studies the uterine characteristics and circumstances necessary for successful embryo implantation, the implications of uterine aging and the origins of reproductive carcinomas. Recently, we worked for more than three years on a study using nine genetically engineered mouse lines with uterine-specific single and double mutations.

The study used molecular and cell biological techniques including 3D imaging of the implantation sites to show a unique discourse between heparin-binding EGF-like growth factor and the VANGL planar cell polarity protein 2 in implantation through VANGL2 tyrosine phosphorylation.

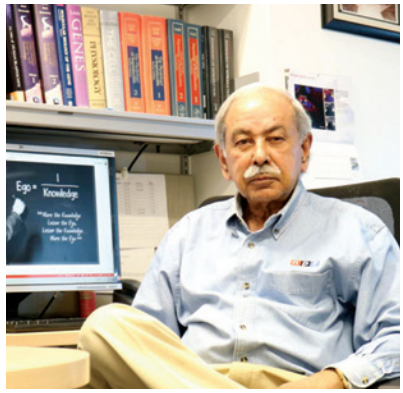
The experiments were time-consuming and tedious, but we felt satisfied with the study and our coauthors at other academic institutions gave us enthusiastic feedback. We had stumbled into a new area of investigation that may have implications for women's reproductive success.

My postdoc wrote the first draft of the paper about this work. We edited it more than 50 times with input from our coauthors and then submitted it to a journal with a high impact score.

Within days of submission, we received an email rejecting the manuscript without in-depth review. We tried two other journals and received similar rejection letters. Apparently, the journal editors did not like the study, but they wouldn't tell us why. My postdoc, who worked hard on the project even during the peak of the COVID-19 pandemic, was upset. This paper would be likely to help her in her career when she returned to her home country.

After revision and additional experiments, the paper was eventually published in a highly cited journal, but the process left me sad and irritated. In the past, we had worked with and published in the journals that had so quickly rejected this recent research. I thought about what had changed — and how we need to change for our survival. Or maybe the journals need structural changes.

I have been an author on 376 published studies, and I find that most papers submitted to certain



SUDHANSU K. DEY

high-impact journals are now rejected outright without commentary or directions on how to improve the study. This has an adverse impact on the career advancement of our graduate students, postdocs and early-career scientists. Those who can publish their papers in these influential journals are able to secure better positions.

More importantly, the editors adopting this approach miss an opportunity to improve authors' work and guide investigators as to what critical aspects of the study are missing. This is a loss to young investigators and a loss to science in general.

Do I have any major expectations to correct this course? No.

The large number of submissions may prevent editors or editorial staff from giving in-depth attention to every deserving manuscript. To remedy this, the journals should explicitly outline their scope and their expectations in detail so authors can avoid submitting manuscripts that are not suitable for those particular journals. However, most reputed journals shy away from laying out these details.

In addition, many editors appear

to lack broad expertise and tend to use shortcuts to evaluate manuscripts. They favor authors they've heard of from well-known universities or institutions. As a result, authors from less-known places are largely ignored.

Are all papers published in high-impact journals influential? No. And we don't expect all our studies will be exceptional. In this case, I thought we have an exceptional observation, so it's difficult to understand why we had so much trouble getting that study published in one of these journals.

I'd like to see the publishing industry restructured to maximize the benefits and joys of scientific discoveries. This restructuring for the better will require national debate.

Sudhansu K. Dey (sk.dey@cchmc.org) is a professor of pediatrics and co-director of the Center of Reproductive Sciences, Division of Developmental Biology, Cincinnati Children's Hospital Medical Center.

On our wall: A bird's eye view of metabolism

By Fatahiya Kashif

To understand the biochemical basis of life, disease and death, a student must first learn how the evanescent substances we call intermediates move and change through complex pathways and cycles. Vast amounts of scientific jargon make teaching about this metabolic map a challenge. When students look at versions of metabolic maps on a computer screen, they often feel lost in these mazes of complexity.

At Federal Medical College in Pakistan, we have constructed a map that gives students a big-picture view of metabolism at a glance. This can help them understand the complex pathways and their links as well as the applied aspects of biochemistry.

When I was a biochemistry student, I always found the concept of metabolism challenging. I struggled to understand the pathways and cycles presented in textbooks. Connecting the dots and establishing meaningful relationships between metabolic processes was even more daunting. The metabolic system functions as a harmonious ensemble, with no reaction occurring in isolation. However, textbooks often require us to study each metabolic process in isolation.

It took me years to integrate all the intricate pathways in my mind. Thinking about this, I became determined to make learning easier for my own students. I wanted to present the complexities of metabolism in a simplified format, providing them with a bird's-eye view so they could appreciate the entire system, rather than getting lost in individual components.

Early in the 2022 academic year, as I was updating study guides for my students, I had the idea of making a metabolic map on my office wall. To make it simple and attractive, I decided to avoid chemical formulas, highlight only the key concepts and preserve the essential content in a visually appealing and interactive format.

On the one hand, this map would help imprint the complex pathways and their links into the minds of my students, so they'd grasp it as one big picture. On the other hand, it would present the applied aspects of biochemistry, creating a mind shift from what students often think of as a "dreary biochemistry text" to a fascinating biochemistry expedition.

I set to work alone but was overjoyed when more and more students joined the effort. With 21 volunteers helping, we completed the project in one year. Even more volunteers, both students and faculty, helped with a celebration after the map was completed.

To create this masterpiece, we used plastic corrugated boards and felt sheets, foaming clay, wooden alphabet blocks and a variety of stationery supplies. Our map features blue metabolites, green coenzymes and a multicolor scheme for the enzymes. We used 3D casts to represent some components, such

COURTESY OF FATAHIYA KASHIF

Fatahiya Kashif (in white lab coat) shows visitors the metabolic pathways map she and her students created on the wall of her office at the Federal Medical College in Islamabad.

as yellow dots for membrane lipids and white dots for protons. Yellow-dotted membranes create cellular compartments such as mitochondria and cytosol. ATP and other nucleotides are sculpted to make them stand out.

We used chemical or structural formulae only for very small molecules such as water, oxygen, carbon dioxide and ammonia. Tiny space-filling models are mounted on the wall to show how these miniature entities enter and exit the pathways. Arrows drawn directly on the wall with permanent markers signify the movement of molecules across membranes and the conversion of substrates to products.

When we were ready to share our map, we wrote a 15-minute script showcasing the potential of integrating biochemistry with pharmacology, forensic medicine, community medicine, pathology and molecular medicine. The script is a dialogue among my 21 student volunteers who discuss the significance of metabolism.

We videotaped the script and added digital images of patients and medications. The video, "Vertical integration through a metabolic map," was uploaded on YouTube on our channel, "Dr Fatahiya Kashif's Students," in late 2022 — the first in a series. We added a second video, "Electron Transport Chain," in May 2023.

The college celebrated the map's completion in October 2022. We gave customized gifts and souvenirs with pictures of enzymes and metabolites to our volunteers and presenters.

To evaluate the effectiveness of our map, we solicited feedback from our students. Most responded positively.

Fatima Gulbahadur, a second-year student, wrote to me that the map "showed everyone that this is what biochemistry does for medicine, this is how important it actually is. All the disorders, enzymes with cute little models made it all so easy to get a picture of what's going on inside our body."

COURTESY OF FATAHIYA KASHIF

Fatahiya Kashif and students at the Federal Medical College in Islamabad gather in front of the metabolic pathways map.

Aimen Javed wrote that "the map gave us a very good idea about how each and every metabolic process in our body is interlinked."

"It was a fun activity which also helped us with our curriculum and helped us step out of our comfort zone and do something interesting," Alishba Moheeuddin wrote.

"This map made me switch my learning from ratta system (a rote method) to conceptual and integrated system," Faiqa Shabbir wrote.

"It motivated me to put all my heart into anything I'd attempt to do," Noor-ul-Ain Aziz wrote. "Topics that seem boring and difficult to me can be made easier if only I experiment with the ways of learning."

Before the map was created, "there was a rare interest of most students in biochemistry," Mujahid Mustafa wrote, "but throughout the event the interest for the subject and its importance was crystal clear."

This editable map is a dynamic resource. We used UHU patafix removable glue to mount the elements on the wall. While making the map, we kept on inserting, deleting and changing the locations of metabolites and related bits and pieces until we had the best possible positioning to fulfill the learning objective. And we can keep refining and improving it before each learning session with new batches of students.

Overall, our goal at Federal Medical College is to revisit how we teach and learn biochemistry. Better understanding is the key to new discoveries about novel therapies for disease diagnosis, monitoring and management. By creating a dynamic resource that students find engaging and exciting, we hope to inspire a deeper interest in biochemistry and its applications.

Fatahiya Kashif (fatahiyakashif@fmdc.edu.pk) is a biochemistry professor at Federal Medical College in Islamabad, Pakistan.

ASBMB
American Society for Biochemistry and Molecular Biology

Do you have a great idea for a scientific event?

You pick the topic, the sessions and the speakers, and we'll do the rest.

The ASBMB will manage registration, market the event to tens of thousands of scientists, and handle all logistics so that you can focus on the science.

Learn more about proposing an event:
asbmb.org/propose-event