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ASBMBTODAY

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

A matter of degree

We ask experts what steers so many black scientists toward earning a master's before a Ph.D.

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ASBMB 20 **ANNUAL MEETING**

ASBMBTODAY
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Picking up the slack

By Comfort Dorn

Marion Sewer

I came to work at the American Society for Biochemistry and Molecular Biology about 16 months after Marion Sewer died. When I first heard her name, in connection with an undergraduate scholarship program, I assumed she was a long-gone figure in the society's history.

She came into focus when I was putting together an article about the winners of that scholarship and I first saw the photo of her smiling in front of a shelf of heavy books. The photo accompanied Squire Booker's remembrance of Sewer, which is where I learned that she died suddenly, so suddenly that her last article for this magazine was published days after her death, and that she was only 43 when she died. She remains forever that unlined face with the broad, arresting smile.

Sewer crammed more into her life than most of us can hope to do in twice the time. She was a professor at the Skaggs School of Pharmacy and Pharmaceutical Sciences at the University of California, San Diego. She published more than 44 papers and reviews, 30 of those as an independent investigator, on her work in lipid metabolism and steroid hormone biosynthesis.

Sewer worked hard at her science, but she found time to advocate for a diverse workforce, most notably (to us) as a leader of the ASBMB Minority Affairs Committee. She led research projects in increasing participation among underrepresented minorities and furthering student training. She was, as Booker wrote, "a mover and a shaker and a champion of those young scientists who are in desperate need of role models to affirm that their dreams and aspirations are indeed achievable."

Sewer was a black woman in science. In an essay about imposter syndrome, she wrote about teachers and mentors disparaging her accomplishments, causing her to doubt herself. I didn't know her, so I can't speak to her motivations, but I imagine her work on behalf of minority students was inspired by a desire to counter such experiences.

Members of underrepresented minority groups are often at the helm of efforts to level the playing field. Their experiences inspire them to this work, but these responsibilities are piled on top of the need to, as Sewer wrote, "work twice as hard" as their non-URM colleagues.

That's a heavy load. I'll leave it at that.

Comfort Dorn
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Acting to protect research integrity

By Benjamin Corb

The U.S. House of Representatives Science and Technology Committee approved the Scientific Research Integrity Act in October with an overwhelmingly bipartisan vote.

If you get most of your information from television news or newspapers, you might not have heard about this. You might think Congress did little in the final quarter of 2019 beyond debating the impeachment of President Donald Trump and passing federal spending bills. My job is monitoring Congress, and sometimes even those of us who do this for a living have trouble finding reporting — outside our science policy-focused news sources — about any activity unrelated to impeachment on Capitol Hill.

That said, here is an example of what Congress is doing. Introduced by Rep. Paul Tonko, D-N.Y., the Scientific Research Integrity Act, or H.R. 1709, aims to codify protections for federally funded science and federally funded scientific researchers and to put the brakes on policymakers' and administration officials' efforts to politicize science funding.

Specifically, the bill allows federal agencies and government-employed scientists to review data for technical accuracy and provides a mechanism for scientists to review and revise official statements about their findings. Further, it allows federal scientists to present findings at scientific conferences, sit on councils and participate in peer review (subject to conflict-of-interest review). Under the proposal, federal scientists would be authorized to talk to the news media about their science without prior approval from the administration or the agency they work for.

When Tonko introduced this legislation, he said of government scientists, "More and more, their research has become the subject of one political agenda or another. Not since the Scientific Revolution has there been a more important moment to stand for the basic ideas that inquiry must be free and facts and evidence matter."

My job is monitoring Congress, and sometimes even those of us who do this for a living have trouble finding reporting — outside our science policy-focused news sources — about any activity unrelated to impeachment on Capitol Hill.

The American Society for Biochemistry and Molecular Biology Public Affairs Advisory Committee applauds Tonko for this important legislation, which would create barriers to political pressure on federal scientists and the politicization of scientific findings. We are encouraged to see that the legislation has bipartisan support. The majority of ASBMB members are not federal scientists, but some are — and we think they should be trusted to serve as reliable and unbiased experts in the scientific enterprise.

This legislation is not likely to become federal law. Some of our analytical tools, supplied by the media company Politico, estimate a less than 5% chance of enactment. In the past 10 Congresses, or 20 years, an average of only 3.1% of bills introduced have been enacted into law. While passage of the bill may not be likely, it is not uncommon for popular, noncontroversial proposals in legislation to be included in other related bills that are on track for passage.

We will continue to support passage of this bill, and we will encourage our partners on Capitol Hill to view this legislation as an important way to support the scientific enterprise.

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

CREDIT: MARYMOUNT MANHATTAN COLLEGE STUDENT CHAPTER

Keeping abreast with student outreach

The Marymount Manhattan College ASBMB Student Chapter used an American Society for Biochemistry and Molecular Biology Student Chapters Outreach Grant to host its second annual "I Heart Boobies!" event in October for Breast Cancer Awareness Month. Chapter officers, from left, Simran Sahansra (campus coordinator), Elena Markovitz (treasurer), Jordan Barnett (vice president), Julia Furnari (president) and Elizabeth Scott (secretary) pose at their display table. Read more at asbmb.org/asbmbtoday.

Baharvand, Chen among new TWAS fellows

Baharvand

Chen

Hossein Baharvand and Ye-Guang Chen are among the 36 fellows newly elected to the World Academy of Science.

Baharvand is the director of the Royan Institute for Cell Biology and Technology in Tehran. Throughout his career, he has contributed to the understanding of how mouse and human embryonic stem cells establish and maintain pluripotency and differentiation over generations. He was the first scientist to induce pluripotent stem cells in Iran.

Chen is a professor and Cheung Kong scholar at Tsinghua University in Beijing. There, he has researched cell-fate determination and tumorigenesis by investigating the mechanisms of TGF-beta signaling specificity, discovered the regulation of Wnt signaling by autophagy, and showed the essential role of bone morphogenetic protein signaling in intestinal stem cells.

Established in 1983 under the leadership of the Pakistani physicist and Nobel laureate Abdus Salam, TWAS recognizes, supports and promotes excellence in scientific research in the developing world.

Agarwal leads nephrology society

Agarwal

Anupam Agarwal, a physician–scientist who directs the division of nephrology and serves as the executive vice dean at the University of Alabama at Birmingham's medical school, took office in January as the president of the American Society of Nephrology.

Agarwal, who also directs the O'Brien Center for Acute Kidney Injury Research at UAB, is known for research into acute kidney injury and its transition to chronic kidney disease. His laboratory studies heme oxygenase-1, or HO-1, an enzyme involved in the breakdown of heme to biliverdin, carbon monoxide and ferrous iron. The conversion removes heme, a strong oxidant, from the kidney and replaces it with cytoprotective products. Agarwal's laboratory has provided important insights into the mechanisms for the protective effects of this enzyme system and is exploring this pathway as a promising therapeutic target in acute kidney injury.

The ASN is an organization of some 20,000 physicians in 131 countries. It publishes three journals, supports continuing medical education and advocates for kidney science.

Dahms honored for achievements in glycobiology


Dahms

Nancy Dahms, a professor of biochemistry at the Medical College of Wisconsin, received the 2019 Rosalind Kornfeld Award for Lifetime Achievement from the Society for Glycobiology.

Mannose-6-phosphate is a tag added in the Golgi during posttranslational processing to direct lysosomal enzymes to the lysosome. Dahms is best known for her work on this trafficking pathway; over her career, she has isolated and characterized several lectins that act as mannose-6-phosphate binding receptors. Her lab currently studies an endoplasmic enzyme called glucosidase II, which regulates glycoprotein folding in the ER, and a lysosomal storage disease called Fabry disease caused by mutations to another glycan-trimming enzyme, alpha-galactosidase A.

Dahms has served on the editorial board of the Journal of Biological Chemistry and other journals, is on the board of directors of the Society for Glycobiology, and has won numerous teaching and service awards at the Medical College of Wisconsin.

Bassler among first Genius of NJ awardees


Bassler

Bonnie Bassler, chair of the department of molecular biology at Princeton University and a Howard Hughes Medical Institute investigator, is among the first class of recipients of the Genius of New Jersey awards.

Bassler is a leader in the field of quorum sensing, the mechanism by which bacteria communicate with chemicals, detect the number of neighboring cells present and, as collectives, change their behaviors. Such intercellular signaling among single-celled organisms, once considered outlandish, is now known to govern behaviors from bioluminescence to virulence to biofilm formation.

Quorum-sensing bacteria release small molecules called autoinducers. When the molecules accumulate to a critical threshold level, they bind to receptors that drive the activation and transcription of quorum-sensing genes to effect changes in group behaviors. Autoinducers, many of which Bassler discovered or co-discovered, have exotic forms: cyclic oligopeptides, lactones, fatty acids and sugar derivatives containing boron. Researchers hope that interrupting quorum sensing could suppress infection and other pathogenic behaviors. Bassler holds 19 patents on various strategies to antagonize quorum sensing.

Bassler has received numerous awards, including a MacArthur "Genius Grant." This latest award was conferred in December during a gala fundraiser at the Liberty Science Center, a science museum in Jersey City.


CHRISTOPHER LEARY, NYC

Reyes–Soffer named Irving scholar

Gissette Reyes-–Soffer, an assistant professor of medicine at Columbia University Medical Center, has won recognition from the Herbert and Florence Irving Scholars Program.

As an Irving fellow, Reyes–Soffer will receive $60,000 a year for three years for her research project titled "Unraveling the complexities of lipoprotein (a) in humans through stable isotope metabolic studies, proteomics, and particle characterization." She also will hold a named professorship.

Reyes–Soffer is a junior associate editor for the American Society for Biochemistry and Molecular Biology's Journal of Lipid Research.

Agre joins Aeromics board


Agre

Peter Agre has joined the board of Aeromics Inc., a pharmaceutical company developing a drug candidate to reduce complications of stroke.

Agre, a distinguished professor at the Johns Hopkins Bloomberg School of Public Health and director of its Malaria Research Institute, is best known for his discovery of aquaporins, membrane channel proteins that allow water to cross the hydrophobic cell membrane. In 2003, Agre shared the Nobel Prize in chemistry with potassium channel biologist Roderick MacKinnon. He also served as president of the American Association for

IN MEMORIAM

Larry Rudel

Lawrence Lee Rudel, professor emeritus at Wake Forest University, died in Winston–Salem, North Carolina, on Aug. 29. He was 77.

Rudel was born in Salt Lake City in 1941. He attended Colorado State University, receiving a bachelor's degree in physical sciences in 1963, and then the University of Arkansas Medical Center, where he earned a Ph.D. in biochemistry in 1969. After completing his postdoctoral training at the Banting and Best Institute in Toronto and the University of California, San Francisco, he joined the faculty at the Wake Forest School of Medicine, then named the Bowman Gray School of Medicine, in 1973.

During his decades at Wake Forest, Rudel, who served on the editorial board for the Journal of Lipid Research for 36 years, focused on cholesterol metabolism and cardiovascular disease. He trained and mentored graduate students and postdoctoral fellows and published the results of his research extensively. His many awards included the Established Investigator Award in basic sciences in 2001 for his outstanding research achievements. He retired in 2018.

He is survived by his wife, Katherine Bouwman Rudel; three sons, Brian (Sheri) Rudel, John (Cindee) Rudel and David Rudel; five grandchildren; and a niece.

Jane Park

Jane Park, who served as treasurer for the American Society for Biochemistry and Molecular Biology in the 1970s, died Aug. 19 in Nashville, Tennessee. She was 94.

Park was a professor and researcher at Vanderbilt University for six decades. She used nuclear magnetic resonance spectroscopy and magnetic resonance imaging to study muscle function in a variety of muscle diseases, including muscular dystrophy.

Born in St. Louis in 1925, Park did her undergraduate and Ph.D. studies at Washington University in St. Louis, where she worked with the noted embryologist Victor Hamburger. She did postdoctoral work at New York University with Severo Ochoa, who won a Nobel Prize a few years later. In 1953, she married Charles "Rollo" Park, then the newly appointed chair of the department of physiology at Vanderbilt.

As a professor of molecular physiology and biophysics at Vanderbilt, Park initially focused her research on glyceraldehyde-3-phosphate dehydrogenase and became nationally known for her mechanistic studies of this enzyme. She began studying muscular dystrophy in the mid-1970s, using a hereditary model of the disease in chickens. She became professor emerita in 2014.

In addition to serving as the ASBMB treasurer from 1976 to 1979, she chaired the Board of Scientific Counselors of the National Institute on Aging.

the Advancement of Science from 2009 to 2010.

The lead compound in development by Aeromics, which was founded by physiologists Marc Pelletier and Walter Boron, is an aquaporin-4 inhibitor. Aquaporin-4 is expressed in the blood–brain barrier, and the company hopes that blocking its water permeability may be a successful drug target for edema, or swelling, of the brain, which is often a complication of stroke. The company expects to begin phase 2 clinical studies of the drug this year.

New members

The American Society for Biochemistry and Molecular Biology welcomed more than 1,300 new members in November from all over the United States and beyond. To find out who they are, go to asbmb.org/asbmbtoday.

Honoring undergrads who promote diversity

By Stephanie Paxson

The American Society for Biochemistry and Molecular Biology's Minority Affairs Committee created the Marion B. Sewer Distinguished Scholarship for Undergraduates in 2016 to support students who excel academically and are dedicated to enhancing diversity in science. The award was named to honor Marion B. Sewer, who was an ASBMB member and past chair of the Minority Affairs Committee when she died in January 2016 at age 43.

As well as being an international authority on the regulation of cytochrome P450 enzymes and on the biosynthesis of steroid hormones, Sewer was a principal investigator on projects devoted to increasing participation among underrepresented minorities and furthering student training. Within the ASBMB, she organized the MAC's Interactive Mentoring Activities for Grantsmanship Enhancement workshop program for postdoctoral fellows and early-career scientists, known as IMAGE, which addresses the disparity in underrepresented minority scientists' ability to secure federal research grants. She also wrote about issues that URM scientists face, such as impostor syndrome. Sewer's work reflected her commitment to diversity and inclusivity of underrepresented minorities in science, technology, engineering and math.

Each year, the MAC and the Student Chapters Steering Committee select up to five undergraduate students to receive up to $2,000 toward tuition. The 2019 Sewer scholarship recipients are Diego Rodriguez, Oregon State University; Ifechukwu Okeke, University of California, Berkeley; Olivia Drake, Juniata College; Selena Vanapruks, Colgate University; and Shellaina Gordon, Northeastern University. Read more about them at asbmb.org/asbmbtoday.

Stephanie Paxson (spaxson@asbmb.org) is the ASBMB's diversity and undergraduate coordinator. Follow her on Twitter @stephaniepaxson.

Pictured above: Diego Rodriguez, Ifechukwu Okeke, Olivia Drake, Selena Vanapruks and Shellaina Gordon.

ABOUT THE SEWER SCHOLARSHIP

The Marion B. Sewer Distinguished Scholarship for Undergraduates provides up to $2,000 toward tuition to students who demonstrate an interest in the fields of biochemistry and molecular biology and who enhance the diversity of science.

All undergraduate members of the American Society for Biochemistry and Molecular Biology are eligible to apply for the scholarship, which aims to support students whose social, educational or economic background adds to the diversity of the biomedical workforce or who show commitment to enhancing academic success of underrepresented students.

Applicants must describe how they uphold diversity on their campus or in the science community, how the scholarship will help their career goals, and any hardships they have experienced while pursuing their own educations.

Apply at asbmb.org/diversity by June 1.

JBC

Kensal E. van Holde (1928 – 2019)

By Christopher K. Mathews

Kensal van Holde, one of the world's premier physical biochemists and a longtime associate editor of the Journal of Biological Chemistry, died peacefully at home on Nov. 11 following a brief illness. He was 91.

Perhaps the best way to appreciate Ken's scientific career is to read his own words. In a 2008 Reflections article in JBC, he describes a scientific odyssey that began in the 1950s with a focus on the ultracentrifuge. Together with Robert "Buzz" Baldwin at the University of Wisconsin, he developed a method for rapid approach to sedimentation equilibrium and its use to analyze the size and shape of protein molecules. This led to a faculty position in the department of chemistry at the University of Illinois, where he designed improvements in light scattering and circular dichroism, as well as ultracentrifugation. He continued to explore protein structure and function, with emphasis on invertebrate respiratory proteins.

As Ken's interests evolved, he sought an environment where he could focus his biophysical strengths on problems in biology. In 1967, he moved his laboratory to Oregon State University, joining the newly formed department of biochemistry and biophysics. There he met Irvin Isenberg, who introduced him to chromatin.

Irv and Ken noted that four of the five histones in chromatin were present in equimolar quantities. The prevailing view was that histones somehow coated fibers of supercoiled DNA. Measurements of electric dichroism of calf thymus chromatin carried out in Ken's lab by Randy Rill ruled that out but didn't solve the structure.

Randy and Ken turned to the ultracentrifuge. Limited digestion of chromatin with micrococcal nuclease yielded a preparation containing both DNA and the core histones, which displayed a ladder when analyzed in the ultracentrifuge or by gel electrophoresis. Analysis by precipitation and resolubilization suggested that the DNA in chromatin was present in two forms, one of which was particulate. Physical analysis of the particulate fraction indicated that DNA was on the outside of the particle, in disagreement with the prevailing model. Chintamin Sahasrabuddhe and others analyzed these particles, showing them to be spherical, with the DNA wrapped around the outside.

Ken's laboratory had described the nucleosome core particle. Others took notice, and Ken's group was then in a race to define chromatin that continued until 1997, when X-ray crystallography confirmed the van Holde model.

I met Ken in 1977, when I was a candidate for the chairmanship of his department at OSU. Ken had recently been awarded an American Cancer Society research professorship, and this relieved him of all departmental duties. I asked how he wanted to contribute, and he said he would maintain a full teaching load (three courses per year) so long as I promised not to put him on any committees. To say that I was delighted would be an understatement. I didn't realize at that embryonic stage of our relationship that Ken was as devoted to teaching as to research. In the summers, he regularly decamped to Massachusetts, where he taught and served as instructor-in-chief of the famed physiology course of the Marine Biological Laboratory at Woods Hole.

I learned more about Ken's devotion to teaching when he suggested that we teach a course together. We called the course DNA-Protein Interactions and graded each student not by exams but by preparation of an original research proposal — just like the National Institutes of Health, but we assigned grades, not priority scores. Ken was a spellbinding lecturer, and I learned a great deal during the several times that we taught the course together.

Members of Ken's research group were devoted to him to a greater extent than I have seen with other professors. They worshipped him. Their unusual esprit de corps was evident on Friday afternoons. Ken's laboratory included a small room in the building's inner core dubbed the Cave. There, members of his group and others gathered to drink beer and talk science. As department chair, I had to tell them liquor was forbidden on campus and that the Cave would close if anyone complained. Eventually, someone complained, and the OSU president

This photo portrait accompanied a 2010 article, "Chromatin Structure and the Nucleus: The Work of Kensal E. van Holde," in the Journal of Biological Chemistry.

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visited my office to admonish me for permitting Cave parties even though they were the occasions for some excellent science.

Ken was a gifted writer as was shown in his two research monographs, "Chromatin" and "Oxygen and the Evolution of Life" as well as in "Principles of Physical Biochemistry," co-authored in the second edition with Shing Ho and Curtis Johnson. I should not have been surprised at Ken's excitement when I approached him about co-authoring a general biochemistry textbook. By the time we had written a prospectus, outline and two sample chapters (one each), I feared this was a bigger job than we could handle. However, in a phone call between Corvallis and Stockholm, where I was on sabbatical, Ken's enthusiasm was palpable. We pushed ahead, and "Biochemistry" was published in four editions, sometimes with co-authors, in a competitive market.

After his formal retirement in 1993, Ken continued to write books—now with his former associate, Jordanka Zlatanova. In 2015, they published "Molecular Biology," a textbook, and in 2018, barely a year before Ken's death, "The Evolution of Molecular Biology," a historical account. Both books display Ken's biophysical expertise and his gift for clear writing.

Ken enjoyed a rich family life. With his wife Barbara and their four children, he shuttled between Corvallis, Woods Hole and their mountain retreat in the Oregon Cascades. Some years after Barb's death in 2010, Ken reconnected with a widowed OSU faculty wife, Myrna Shepper, and they were married in 2015.

In recognition of his work, Ken was elected to the National Academy of Science in 1989 and to the American Academy of Arts and Sciences in 1996.

Christopher K. Mathews (Christopher.Mathews@oregonstate.edu) is a distinguished professor emeritus in the department of biochemistry and biophysics at Oregon State University.

Understanding how arsenic changes chromatin and causes cancer

By Kerri Beth Boggs

Yvonne Fondufe–Mittendorf took a winding path from the Republic of Cameroon to the bluegrass of Kentucky.

"I call myself an academic tourist," she said.

Inspired by her older sisters who studied science, Fondufe–Mittendorf moved from Cameroon to Nigeria to earn bachelor's and master's degrees from the University of Ibadan.

While she was at the university, a visiting researcher from Germany told the students about his university's doctorate program. Eager to continue her academic journey, Fondufe–Mittendorf applied to the program at the Georg-August Universitaet in Göttingen. She was accepted and moved to Germany to pursue a doctorate in molecular genetics.

Her time in Germany was a learning experience. She had never seen a micropipette before. Neither had she experienced a snowy winter.

"I remember the first winter I came outside, and everything was white," she said.

She excitedly put on her new winter boots and hurried to the bus stop to catch a ride to the university. However, her excitement turned to surprise when her boots lost traction in the wintery mix. Her dash to the bus stop came to a crashing halt as she slipped and fell.

That first snowfall in Germany reflected her experience as a young scientist stepping into unknown territory.

"I had never done that much molecular biology," she said, "and I was always hesitant to trust my results."

UNIVERSITY OF KENTUCKY

On her winding journey from Cameroon to the U.S., Yvonne Fondufe–Mittendorf learned the importance of asking for help in science. "When I face roadblocks in my research," she said, "I reach out to fellow colleagues and other scientists in my field for help. I'm not afraid to say 'I don't know.'"

During her doctoral training, Fondufe–Mittendorf attended a seminar on epigenetics. "Scientists had just started understanding that not every disease is caused by mutations and how chromatin packaging could be dysregulated," she said, "and that actually intrigued me."

Her interest in epigenetics led her to a postdoc at Northwestern University, where her mentor, the late Jonathan Widom, dramatically influenced the course of her career.

"I didn't think I could be a PI, and I wasn't sure of myself," she said.

Widom helped her overcome this self-doubt by convincing her that she was already asking the right questions to pursue an academic research career.

"He said, 'I think you can do it,' so he pushed me towards that," she said. "He believed in me."

Finding a niche

After completing her postdoc, Fondufe–Mittendorf took a position at the University of Kentucky in the department of molecular and cellular biochemistry to study the epigenetics of cancer. With her transition from postdoc to principal investigator, she faced a new set of challenges.

ABOUT THE RESEARCH SPOTLIGHT

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

UNIVERSITY OF KENTUCKY

Yvonne Fondufe–Mittendorf, pictured with Meredith Eckstein in the lab at the University of Kentucky, analyzes the effects of toxicants on chromatin biology.

"I wrote two or three grants and they were all triaged," she said. "I realized that names count, and I was playing with the big guys. Fortunately, I kept searching and found a different perspective that I could bring to the competition."

Although Fondufe–Mittendorf never had studied toxicology, she found her niche analyzing the effects of toxicants on chromatin biology.

The impact of arsenic exposure on gene regulation became one focus of her research. Arsenic is a naturally occurring element and a known carcinogen that poses a significant risk to human health when it contaminates drinking water sources. Residents of Eastern Kentucky and other coal-mining areas face a greater risk of arsenic contamination, and these regions often have higher cancer rates.

Fondufe–Mittendorf's research suggests that arsenic may displace zinc in proteins that regulate chromatin structure for gene expression, leading to changes in protein-DNA binding that alter the wiring of the genome. Work from her lab also focuses on the effects of arsenic exposure on the incorporation of histone variants into the chromatin since the variants are upregulated in cancer. By studying these effects on chromatin regulation, she aims to understand the connection between arsenic exposure and disease pathology.

The lab also studies chromatin to understand how it is involved in basic cellular processes such as transcription, DNA repair and alternative splicing.

Along her journey from Cameroon to the U.S., Fondufe–Mittendorf learned the importance of asking for help in science.

"When I face roadblocks in my research," she said, "I reach out to fellow colleagues and other scientists

COURTESY OF YVONNE FONDUFE–MITTENDORF

Yvonne Fondufe–Mittendorf, second from right, poses with members of her lab at the University of Kentucky during an outing in summer 2019.

in my field for help. I'm not afraid to say 'I don't know.'"

Just be yourself

Fondufe–Mittendorf encourages her students to talk about their research struggles, and she offers them wisdom from her own story. "If I could do it despite my long journey from a different place where I hadn't done molecular biology, then I think you can do it too," she said.

Wesley Saitilnord, an international Ph.D. student from Haiti, reflected on why he chose to join Fondufe–Mittendorf's lab at the University of Kentucky.

"Choosing a lab for graduate school is an important decision that can define your career," he said. "I joined Dr. Fondufe-Mittendorf's lab because she's built a welcoming and supportive lab environment. She makes sure I feel that I belong, and she makes herself readily available to discuss science and life in general."

Fondufe–Mittendorf knows that emotional and mental health play a key role in student success. She sets an example for her students by maintaining a balance among her work, family and hobbies. Outside of work, she enjoys watching movies with her two daughters, exploring different parts of the world and shopping.

Although fashion and science don't usually go together, Fondufe–Mittendorf embraces both. Her interest in fashion started at a young age when her older sisters dressed her in different outfits. Though unwilling at first, she grew to love trying on clothes. Today, fashion helps her deal with the stress of grant writing.

"If I'm stressed while writing a grant, I go to the mall. I just walk around," she said. "It's like I'm not really thinking, I'm just walking. By doing that, I think I'm at peace."

Fondufe–Mittendorf also expresses herself with fashion. Instead of conforming to norms among science faculty, she proudly wears clothing, shoes and jewelry that complement her personality.

"Work is hard enough without trying to be like someone else," she said, "so you should do whatever makes you comfortable and happy. Just be yourself."

Fondufe–Mittendorf said her late father always let his girls know that nothing could stand in their path to success. She gratefully relies on the support of her daughters, husband, mother, brothers and sisters to achieve her goals.

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

Nan-Shan Chang has made WWOX his life's work

By Nuala Del Piccolo

The National Institute on Aging announced last year that a study of more than 94,000 people had identified five new risk genes for Alzheimer's disease. One of the five was the WW domain-containing oxidoreductase, or WWOX, gene, which codes for the cytoplasmic WWOX protein, a tumor suppressor involved in apoptosis.

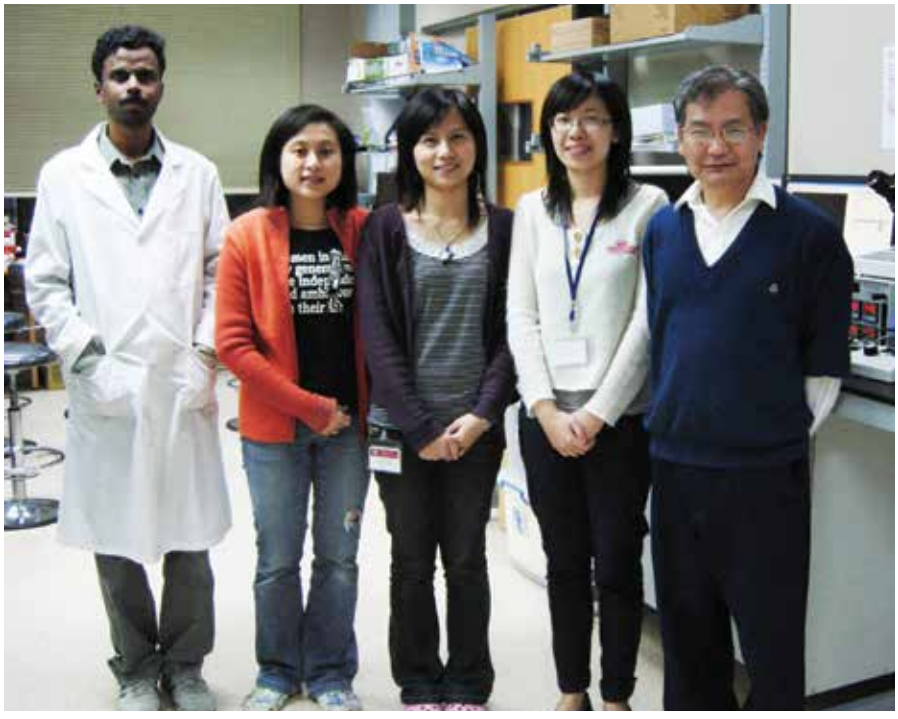
The importance of WWOX to Alzheimer's disease wasn't news to Nan-Shan Chang, a biochemist and immunologist at the National Cheng Kung University in Taiwan. Chang was involved in the initial cloning of the WWOX gene in the 1990s and since then has been studying the role of WWOX in both cancer and neurodegeneration. Chang is thrilled about the publicity around WWOX and neurodegeneration and said he hopes the "announcement encourages momentum, competition, collaborations, and new directions in WWOX research."

When Chang was ready to start college, his older brother told him that he'd make more money with a degree in food science, but Chang chose to follow his interests and study biology at the National Taiwan Normal University. He then earned a Ph.D. in immunology at the Medical University of South Carolina and completed his postdoctoral work in immunobiology at the Samuel Roberts Noble Foundation in Oklahoma.

While working as associate scientist and lab director at the Guthrie Research Institute in Pennsylvania, Chang became interested in the sensitivity of cancer cells to tumor necrosis factor, or TNF. At the time, scientists around the world were in what Chang described as a "crazy hot race to understand how WWOX works in cancer suppression," which was fueled by the WWOX gene's localization on a common chromosomal fragile site.

Though Chang's lab frequently numbered fewer than five people, his team was one of three to report independently the cloning of WWOX in the Journal of Biological Chemistry in 2001. He described his research journey in a recent interview: "I was

COURTESY OF NAN-SHAN CHANG



Nan-Shan Chang, an American Society for Biochemistry and Molecular Biology member for almost 20 years, has mentored many students and postdocs. Pictured in this 2009 photo are, from left, postdoc Dudekula Subhan, technicians Ming-Hui Esti Lee and Sing-Ru Lin, master student Jean-Yun Chang and Nan-Shan Chang. Chang's mentees Li-Jin Hsu, Jean-Yun Chang, Annie Su, Yongda Sie and Charlene Kuo won travel awards to the 2005, 2009, 2012, 2015 and 2017 ASBMB annual meetings, respectively; Kuo also gave an invited talk at an ASBMB mini-symposium in 2017. Another mentee, Tsung-Yun Tom Liu, will give an invited talk at Experimental Biology 2020.

COURTESY OF NAN-SHAN CHANG

Nan-Shan Chang (center) discovered the connection between WWOX and neurodegeneration through collaboration with two college classmates, neuroscientists Shur-Tzu (Su) Chen (not pictured), who died in 2015, and Chun-I Sze (left). Yu-Min Kuo (right) collaborates with Chang on a project studying the role of Zfra in Alzheimer's disease.

interested in understanding why certain cancer cells resist TNF cytotoxicity. I noticed that cancer cells secrete large amounts of hyaluronan and hyaluronidase in order to metastasize. Hyaluronidase increases the expression of tumor suppressor WWOX in cancer cells, thereby rendering them sensitive to TNF toxicity. By functional cloning, we caught the fish — WWOX. It took us five years."

Chang's paper explored how hyaluronidase contributes to the cytotoxicity of TNF; it linked hyaluronidase exposure to increased expression of a small protein dubbed WWOX. The paper reported the isolation of WWOX and established that the protein mediates the cytotoxicity of TNF by upregulating the tumor protein p53 and downregulating mitochondrial proteins that block apoptosis.

Chang discovered the connection between WWOX and neurodegeneration through collaboration with two classmates and friends from his undergraduate days in Taiwan, neuroscientists Chun-I Sze and Shur-Tzu (Su) Chen. They had heard the hype about WWOX and wondered whether the small but potent protein might play a role in neurons. The team looked for WWOX in developing and adult mice and found that the protein was expressed. They characterized WWOX expression in postmortem healthy and diseased human brain tissue and found that it was significantly downregulated in Alzheimer's. To follow up on this observation, the research team used siRNA technology to knock down WWOX expression in cells; to their amazement, this treatment led to the phosphorylation of the tau protein, a state implicated in the formation of Alzheimer's signature neurofibrillary tangles. These studies produced another Journal of Biological Chemistry article in 2004. This early work on the role of WWOX in Alzheimer's was cited in the Nature Genetics paper highlighted in the National Institute on Aging's announcement about the five new Alzheimer's risk factors.

In November 2006, Chang moved his laboratory to National Chang Kung University in Tainan, Taiwan, so he could care for his ailing father. His move prompted new collaborations with groups studying WWOX in immunology, dermatology and cancer, and Chang remains committed to his craft, frequently logging 16-hour days in the lab.

The Chang lab now studies WWOX and Zfra, another small protein involved in the TNF signaling pathway. The team examines how WWOX and Zfra expression, trafficking and phosphorylation influence cancer and neurodegeneration. Both proteins have proven particularly challenging to isolate, clone and characterize, but Chang hopes that hard work and time will overcome these obstacles to elucidating a more complete understanding of the role of WWOX in cancer and neurodegeneration.

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A cyclooxygenase inhibition hotspot

By Michael Malkowski

Prostaglandins, or PGs, are critical for such physiological functions as the regulation of renal water and sodium metabolism, blood clotting, parturition and stomach acid secretion. These lipid signaling molecules derive from the oxygenation of arachidonic acid by prostaglandin endoperoxide H synthases 1 and 2, commonly called cyclooxygenase-1 and -2, or COX-1 and COX-2.

Abnormal changes in PG production contribute to disease pathologies including inflammation and cancer, so researchers view COX-1 and COX-2 as pharmacological targets. Indeed, nonselective nonsteroidal anti-inflammatory drugs, or NSAIDs, such as ibuprofen, inhibit both isoforms, while coxibs such as Celebrex selectively inhibit COX-2.

COX enzymes are sequence homodimers; each subunit consists of physically distinct cyclooxygenase and peroxidase active sites linked by a bridging heme moiety. In solution, the enzymes function as heterodimers, such that only one subunit is catalytically active at a time.

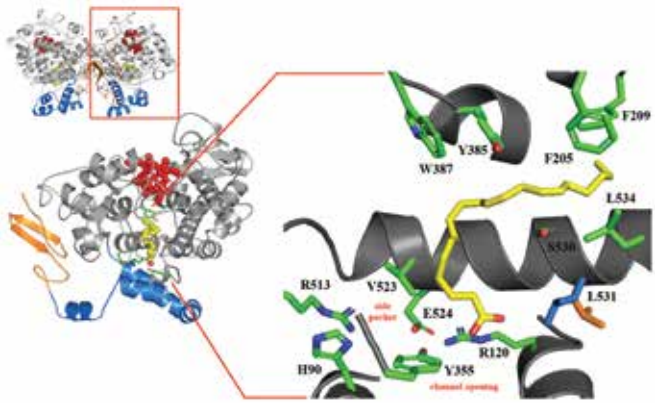
Structurally, COX-1 and COX-2 are virtually identical. However, subtle differences drive isoform-specific substrate specificity and inhibition. Among these are the substitutions of cyclooxygenase channel residues Ile-434, His-513 and Ile-523 in COX-1 for Val-434, Arg-513 and Val-523 in COX-2, which result in the formation of a unique side pocket and increased volume of the cyclooxygenase active site in COX-2. This side pocket, with Arg-513 at its base, has been exploited in the design of coxibs aimed at reducing the gastrointestinal side effects caused by conventional NSAIDs.

Researchers work to to identify the changes in COX-2 that drive the transitions between the kinetically observable inhibitor binding states. These studies originally focused on the COX-2 side pocket, but recent molecular dynamics simulations identified a different region of the active site critical for aspirin and Celebrex to inhibit COX-2. They showed rotation of the side chain of the residue Leu-531, opposite the side pocket, as a way to expand the volume of the cyclooxygenase channel. Crystal structures of COX-2 have provided evidence for the existence of alternate rotamer conformations for this side chain when different ligands are bound.

To evaluate the importance of the conformational flexibility of the side chain of Leu-531, our research group generated L531F and L531N mutations and showed that these substitutions reduced aspirin and Celebrex's inhibition of COX-2. Thus, expansion of the active site volume via the flexibility associated with the side chain of Leu-531 allows Celebrex to achieve a high-affinity binding state and facilitates formation of the initial noncovalent complex in the case of aspirin acetylation.

Deciphering the protein conformational motions associated with COX catalysis and inhibition is the next frontier in studying this enzyme. If we understand how the binding of substrates, allosteric activators and inhibitors induce conformational motions to modulate COX activity, we will be closer to developing and repurposing drugs for maximum efficacy with minimal risks.

MICHAEL MALKOWSKI

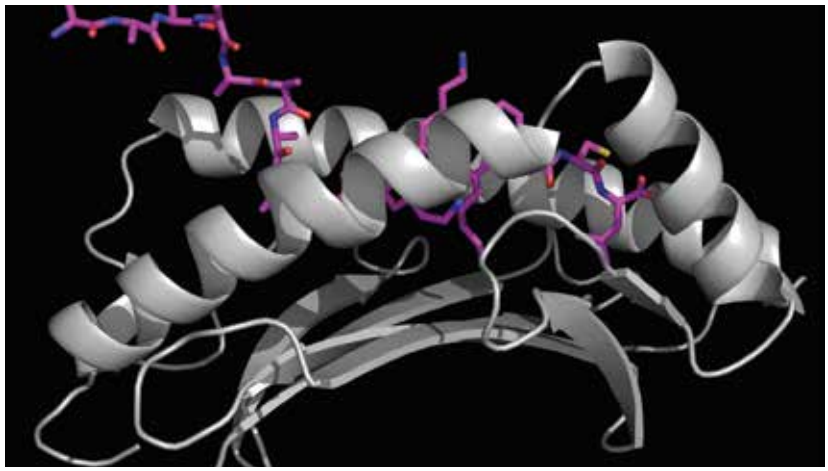


Each COX monomer comprises three domains and is bound by heme (red). Arachidonic acid (yellow) binds within the cyclooxygenase active site in an L-shaped conformation. The side chain of Leu-531 rotates from a closed conformation (blue) to an open conformation (gold) and in conjunction with Arg-513 serves as a critical determinant for the inhibition of COX-2 by aspirin and Celebrex.

Michael G. Malkowski (mgm22@buffalo.edu) is a professor and chair of the department of structural biology in the Jacobs School of Medicine and Biomedical Sciences at the State University of New York at Buffalo.

Early immune response may improve cancer immunotherapies

By Natasha Wadlington



CREDIT: BOUVIER LAB

An X-ray crystallography-generated image of a long foreign peptide (purple) being partially held inside MHC I protein's surface groove (gray).

Viruses, bacteria and cancer have many ways to replicate and survive in our bodies. Viruses and bacteria invade a cell directly to avoid detection. Cancer cells have the advantage of being native in the body. However, the body has safeguards against such sneaky tactics.

In a paper published in the **Journal of Biological Chemistry**, University of Illinois at Chicago researchers and colleagues report a new mechanism for detecting foreign material during early immune responses.

"There are proteins in the cell that await the presence of foreign material," said Marlene Bouvier, senior author and UIC professor of microbiology and immunology at the college of medicine. "One protein, called endoplasmic reticulum aminopeptidase 1, or ERAP1, is programmed to find foreign material, like viral and bacterial proteins, and break it into smaller parts, also known as peptides. Another protein — major histocompatibility complex class I, or MHC I — is programmed to attach itself to a foreign peptide and move it to the cell's surface. With the foreign peptide outside the cell, immune cells can recognize and destroy the infected cell."

This is an example of a normal process, Bouvier said, but sometimes a foreign peptide, once bound to MHC I, remains in the cell. This happens when the foreign material is not broken down to a small enough size or is too long.

Bouvier and colleagues used X-ray crystallography (a method to see structures on an atomic level) and mass spectrometry (used to identify peptide length by mass) to show that ERAP1 can cut extra-long peptides even after they have bound to MHC I.

"X-ray crystallography allowed us to determine three-dimensional structures to see how these longer peptides bound to the MHC I groove with high resolution," Bouvier said. "Using an ERAP1 enzymatic assay with mass spectrometry gave us the ability to show, for the first time, that ERAP1 can trim peptides bound to MHC I. These tools allowed us to develop a model of this new immune response mechanism."

Bouvier said this new information may help researchers leverage ERAP1 to fight infections and cancer.

"This research can have major implications for immunotherapies," she said. "For example, cancer cells do not always present enough peptides to be labeled as 'foreign' — allowing the cancer cells to replicate and grow. But if you have a way to manipulate how ERAP1 generates cancer peptides, then you can hopefully skew the peptide repertoire that is presented on the cell surface in our favor. This is the most translational application of our research."

Lenong Li and Mansoor Batliwala from the department of microbiology and immunology in the UIC College of Medicine are co-authors on the paper.

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The proteome of the cave bear

New metric helps researchers unlock strange samples

By Laurel Oldach

Among the exotic samples used in Richard Johnson's study was glacial meltwater.

As a rule, it takes a genome to interpret a proteome.

A genome database gives the range of possible proteins that a sample is expected to contain, allowing a computer program to match short peptide fragments from the raw data to the full-length proteins they came from. The genome is like a picture showing how a jigsaw puzzle will look when it's finished — and each peptide is a single tiny piece of the puzzle.

Richard Johnson, a staff scientist at the University of Washington's department of genome sciences, has spent nearly three decades working with no picture. Before genomes were assembled and available, he became an expert in de novo peptide sequencing, piecing together the overlapping puzzle pieces from mass spectra to determine the amino acid sequence of proteins.

That ability has been coming in handy recently since Johnson started seeing more requests for environmental proteomics and other exotic analyses.

"I sit next to an oceanographer, and she does these proteomics analyses on strange samples, like glacial meltwater and seawater," he said. "Those are cases where it's really difficult to decide what database to even search."

To annotate a sample from a human, a researcher can use a human genome database. But a tablespoon of ocean water or glacial runoff is likely to contain a complex community of microbes. So which genome databases should the researcher survey? Usually, researchers solve this problem by sequencing as much DNA as they can from a sample and using the result, a metagenome, to guide protein identification.

But even with a metagenome, sometimes the proteins observed in a proteomics experiment just don't match the given reference database. "I came up with a metric that can tell you whether the protein sequence database is any good for interpreting your mass spectrometry data," Johnson said.

The technique, which Johnson and colleagues recently published in **Molecular & Cellular Proteomics**, can be used to solve related problems, such as proteomic analysis of an animal whose genome has not been sequenced. "You typically use a sequence database from a closely related species and hope that the sequences did not diverge too much," Johnson said. "Sometimes that hope is warranted, and other times it's not."

Johnson has used this approach to study the makeup of electrosensory organs in electric fish.

A third potential application is for analysis of very old but not fossilized tissues — those that come from extinct species, such as a vial of powdered cave bear bone that Johnson's team obtained. Extinct species very rarely have a genome assembled, and the close-cousin conundrum is compounded by slow biochemical changes to proteins that happen over thousands of years.

But the approach doesn't solve every problem. Johnson said, "Using this quality metric tells you how good or bad a sequence database is. But it won't tell you what to do about it if it's bad."

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Quantifying bacteria-borne bile

By John Arnst

Beyond breaking down food, the steroid bile acids produced both by our livers and by our intestinal inhabitants have a range of functions, from helping absorb lipids and fat-soluble vitamins to acting as signaling molecules for myriad pathways.

When gut microbes use amino acids to conjugate metabolites or primary bile acids created by the liver, secondary bile acids are formed. These secondary acids are linked to an increased risk of metabolic diseases, but their physiochemical properties make it difficult to puzzle out which bile acids are being produced by which gut bacteria. To rectify this, researchers in Stanley L. Hazen's laboratory at the Cleveland Clinic's Center for Microbiome and Human Health have developed a new stable isotope dilution liquid chromatography-tandem mass spectrometry method to quantify bile acids in mice and humans. They described their method in the **Journal of Lipid Research**.

Ima Nemet is a senior scientist in Hazen's lab and the corresponding author on the paper. "We know that so many bile acids have been known and studied for a long time, but we wanted to have some very robust methods that can be very easily used for large clinical studies," Nemet said. "When we run these large cohorts, we use multiple instruments that are sometimes even from different vendors. So we wanted to have something that's 'clickable' on all different types of machines."

Eating foods containing high amounts of choline, notably red meat, spurs gut bacteria to produce the bile acid trimethylamine N-oxide, or TMAO, Hazen and colleagues reported in 2018. TMAO can cause plaque to accumulate in arteries and is a predictor of heart attacks. They reported in 2015 that TMAO derived from dietary sources of choline was elevated in cases of chronic kidney diseases.

WELLCOME COLLECTION

The liver, pictured here in a Chinese woodcut from the Ming period, is responsible for the production of primary bile acids.

To validate their new analytical method, a bile acid panel, the researchers examined circulating levels of more than 50 primary and secondary bile acids in serum and fecal samples from mice and humans. They used the panel to identify a handful of circulating bile acids associated with diabetes in samples obtained from a study of people with Type 2 diabetes.

Nemet was intrigued to find that bacteria played a role in regulating the production of a number of primary bile acids that were thought to be produced exclusively by the liver.

"The circulating levels of three primary bile acids are completely dependent on microbial activity," she said. "That's really interesting for me, because usually people say primary bile acids are host-derived, but … if we put humans or mice on antibiotics, these levels go down. That means the majority of these bile acids are coming from microbial contribution, even though we're calling them primary."

Nemet and Hazen plan to use the bile panel to test samples from larger clinical studies before homing in on the specific mechanisms by which bile acids increase the risk of Type 2 diabetes, which potentially could be disrupted by small-molecule drugs.

"This is our start in looking into the contribution of bile acids in developing metabolic diseases," Nemet said. "There are now a plethora of experiments where we can look and see whether these metabolites are just associations or whether they are driving Type 2 diabetes."

DOI: 10.1194/jlr.RA119000311

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From the journals

By Isha Dey, Anand Rao & Tori Zirul

Trimming peptides down to size

An important step for activating the immune system in response to potential threats is the processing and presentation of peptides by major histocompatibility complex, or MHC, molecules. To accomplish this, a mechanism for handling peptides of various lengths is necessary. The processes underpinning these alterations are not fully understood.

Answers might lie in studying endoplasmic reticulum aminopeptidases, or ERAPs, enzymes essential for the presentation of peptides by MHC I molecules. In a paper published in the **Journal of Biological Chemistry**, Lenong Li and colleagues at the University of Illinois shed new light on how peptide trimming by ERAP1 shapes the MHC I immunopeptidome and provide detailed structural and biochemical evidence demonstrating how peptides of noncanonical lengths interact with MHC I. Their results provide new fundamental knowledge about the processing and presentation of unconventional peptides by MHC I.
DOI: 10.1074/jbc.RA119.010102

Profiling autologous body fluid exosomes

The saying goes, it's what's on the inside that counts, but some studies require researchers to look at a cell's surroundings as well as its internal processes. In tissue, where cells are in close contact, exosomes — bioactive RNA and proteins encased in a fatty bilayer — are released into the body to communicate with other cells and mirror the function of the producer cells. Exosomes of varying tissue types look and behave differently, and these distinctions can be used as biomarkers for diseases. Fluids such as blood and semen are conduits for infection of many viruses, but little is known about the function and composition of their exosomes.

Hussein Kaddour and a team of researchers led by Chioma Okeoma at Stony Brook University were the first to compare the proteomes of autologous blood and semen exosomes from HIV-infected and non-HIV-infected individuals. Their findings were published in the journal **Molecular & Cellular Proteomics**. They identified discrepancies within and between exosome samples from blood and semen of infected and noninfected individuals using systematic multifactorial proteomic profiling detection methods. Proteins unique to blood or semen were identified along with their role in reproduction and HIV pathogenesis.
DOI: 10.1074/mcp.RA119.001594

A novel method to detect brain DHA turnover

Docosahexaenoic acid, or DHA, is essential for brain development in infants and normal functioning of adult brain. The brain can produce only a limited quantity of this polyunsaturated fatty acid, so it depends on a supply from circulating blood to replenish the metabolized DHA. Decreased DHA levels in the brain are associated with the onset of Alzheimer's disease, making DHA metabolism in the brain an important topic of research. However, the existing method to study DHA turnover requires infusing stable isotope tracer-labeled fatty acid followed by tracing its metabolism kinetics. Not only is this approach expensive and complicated, but its limitations include inaccurate measurement of steady-state kinetics.

R. J. Scott Lacombe and a team at the University of Toronto devised a tracer-free way to study DHA turnover by measuring the ratio of natural 13C to 12C of DHA with high-precision gas chromatography combustion isotope ratio mass spectrometry. They fed mice with either alpha-linolenic acid or DHA for six weeks and then switched the fatty acids in their diets, followed by analyzing 13C to 12C DHA for six months. Their results, published in the **Journal of Lipid Research**, correlate to findings using isotope tracers.
DOI: 10.1194/jlr.D119000518

Synthesis versus salvage in parasite species

The large phylum of apicomplexans includes parasites such as Toxoplasma gondii, which causes the infectious disease toxoplasmosis, and the malaria-causing Plasmodium falciparum. These parasitic intruders can acquire metabolites from their hosts in addition to using their own metabolic reactions to thrive in the hosts they've hijacked.

In a review published in the **Journal of Biological Chemistry**, Dominique Soldati–Favre, recipient of the ASBMB's 2019 Alice and C.

Gut feeling: the endocannabinoidome and intestinal microbe connection

The endocannabinoidome is a complex signaling pathway consisting of several G protein–coupled receptors, metabolic enzymes and 20-plus lipid mediators. Recent research links this pathway to intestinal health. With the discovery of endocannabinoid receptors in the gut, mechanisms underlying crosstalk between such receptors and the gut microbiota are being investigated. Scientists have speculated that a dysregulated endocannabinoid system may lead to inflammatory bowel disease and colon cancer.

To take a deep dive into the interactions of the endocannabinoid pathway with the gut microbiome, Claudia Manca and researchers from Canada, Belgium and Italy investigated alterations in the endocannabinoidome in germ-free and conventionally housed mice, both juveniles and adults. Using transcriptomic analysis, they found that expression of several endocannabinoid receptors was reduced in the germ-free mice compared to conventionally housed ones. However, when fecal matter containing natural bacteria from healthy mice was transferred to the germ-free mice, this receptor expression was restored. Endocannabinoidome signaling tone can also be affected by the basal endocannabinoidome lipid mediator levels as well as receptor expression, so the authors used liquid chromatography–mass spectrometry lipidomics to analyze the different endocannabinoidome lipid mediators and found that their levels were altered substantially in the intestines of both kinds of mice. The levels of some of these molecules were significantly different under germ-free conditions and sensitive to the introduction of fecal matter from conventionally raised mice. Thus, germ-free and conventionally housed mice had differing global gene expression of endocannabinoidome.

The research shows that lack of gut microbiota significantly altered the levels of endocannabinoid receptors as well their effector molecules at the transcriptome level in the small and large intestines of mice. Published in the **Journal of Lipid Research**, this study provides evidence of direct interaction of the endocannabinoidome with gut microbiota and opens new avenues to investigate the pathophysiological role of endocannabinoid signaling.
DOI: 10.1194/jlr.RA119000424

—Isha Dey

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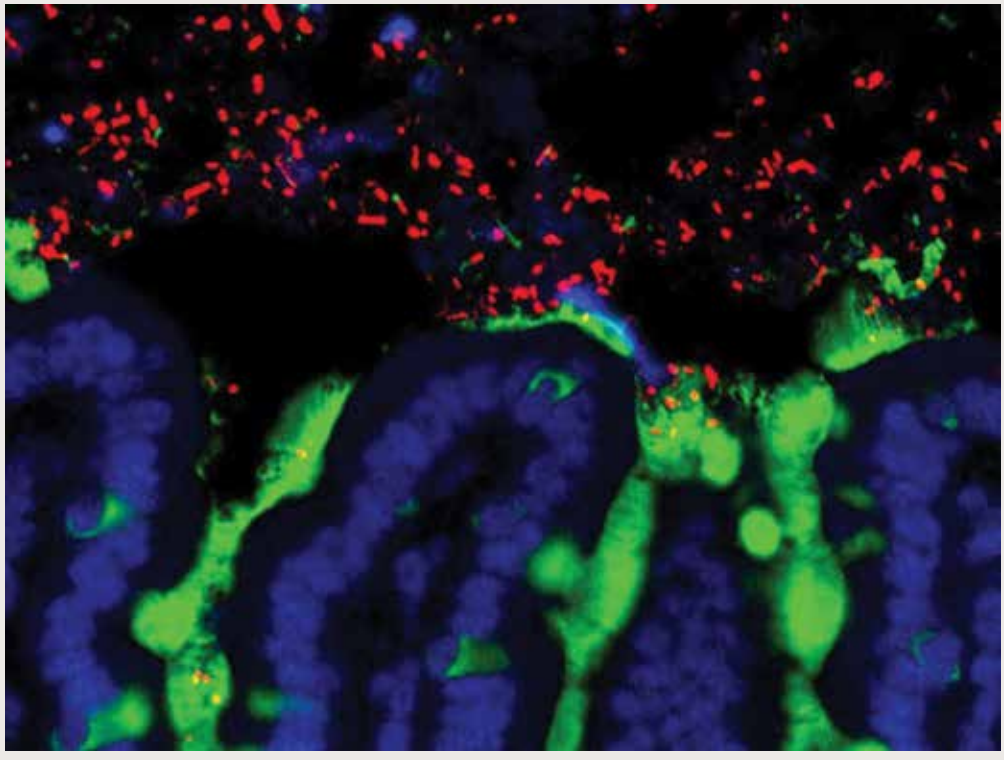

Commensal bacteria (red) reside among the mucus (green) and epithelial cells (blue) of a mouse small intestine.

C. Wang Award in Molecular Parasitology, and colleagues at the University of Geneva discuss the salvage and synthesis pathways that provide vitamins to these species, with an eye toward new therapeutic targets.
DOI: 10.1074/jbc.AW119.008150

Treating insulin resistance: To err on the side of caution

In the pathological condition known as insulin resistance, cells fail to respond to insulin, resulting in increased blood glucose levels. This can result in increased risk of Type 2 diabetes, heart attacks, strokes and cancer. An underlying cause of this condition is an excess of circulating fatty acids, which promotes the oxidation of fat over glucose. Thus, inhibition of fatty acid oxidation, or FAOX, has been suggested as a treatment for insulin resistance.

Anne-Marie Lundsgaard and a team from Germany and Denmark did a collaborative study to understand the consequences of inhibiting FAOX on overall metabolism. They used etomoxir to inhibit FAOX in mice, which in the short term resulted in increased glucose oxidation and lowered blood glucose as expected. However, within days, they saw triglyceride accumulation in the heart and liver. In fact, when etomoxir was administered to mice over a prolonged period, it resulted in hepatic steatosis or fatty liver disease and glucose intolerance. Their findings, published in the **Journal of Lipid Research**, shed light on the long-term consequences of FAOX inhibition for treating insulin resistance, which could move researchers to rethink such treatment strategies.
DOI: 10.1194/jlr.RA119000177

How mollusk proteins modulate the immune system

Hemocyanins are respiratory proteins responsible for transporting oxygen in a variety of arthropods and mollusks. Mollusk hemocyanins are used widely as carriers, adjuvants and nonspecific immunostimulants in cancer treatments due to their ability to promote Th1 immunity. In a collaborative study published in the **Journal of Biological Chemistry**, Michelle L. Salazar and researchers in Chile sought to reveal how mollusk hemocyanins — specifically from Concholepas concholepas, Fissurella latimarginata and Megathura crenulata — modulate the immune system. Using an enzyme to remove sugar entities from hemocyanins, they found that sugar residues are important for their structure and immunogenic effects. The changes to glycan content altered the interaction of hemocyanins with immune cells. Their findings elucidate aspects of hemocyanin immunological activities and have significant implications for the biomedical application of these proteins.
DOI: 10.1074/jbc.RA119.009525

Finding the RSK in melanoma protein interactions

According to the Centers for Disease Control and Prevention, skin cancer is the most common form of cancer in the U.S., and, of the various skin cancer types, melanoma is the most aggressive. Historically, deregulation of the Ras/mitogen-activated protein kinase, or MAPK, pathway has been known to result in cancer. The MAPK pathway activates a protein enzyme known as ribosomal s6 kinase, or RSK, a necessary component for growth and proliferation of melanoma. Little is known about behavior and cellular interactions in the relationship between RSK activity and melanoma progression.

Antoine Méant and colleagues at the Université de Montréal studied the RSK interacting proteins and identified their important role in melanoma. The study was published in the journal **Molecular & Cellular Proteomics**. The research used a proximity-dependent biotinylation technique called BioID and mass spectrometry to identify RSK cellular partners and protein interactions. Of the identified proteins, p120-catenin, or p120ctn, is noteworthy, as it is essential to the cell adhesion characteristic of cancer formation. When RSK activity is inhibited, cellular adhesion is increased. The study also showed Ser320 as a novel active site of p120ctn for activity of the MAPK pathway. These results indicate that RSK might be used as a therapeutic target against cancer, and the work contributes to the overall understanding of RSK behavior.
DOI: 10.1074/mcp.RA119.001811

A link between enzyme mutation and cerebellar ataxia

Spinocerebellar autosomal recessive type 16, known as SCAR16, is a fatal neurodegenerative disease characterized by difficulties with swallowing, eye movement, speech and coordinated voluntary movements. SCAR16 is a monogenetic disorder dependent upon coding mutations in a single gene called STUB1, which encodes the versatile enzyme C terminus of HSC70-interacting protein, or CHIP. In a study published in the **Journal of Biological Chemistry**, Sabrina Madrigal and colleagues at the University of North Carolina School of Medicine examined the relationships between clinical phenotypes of SCAR16 patients and the biophysical, biochemical and functional properties of CHIP variants. The researchers provide linear models that suggest that inhibition of mutant CHIP lessens disease severity, a finding that may be useful for clinical therapies.
DOI: 10.1074/jbc.RA119.011173

Untangling Alzheimer's and the spread of misfolded proteins

In 1906, seeking to understand the symptoms of a deceased patient who had been plagued by confusion, mood swings and disturbed sleep, Alois Alzheimer arranged for a brain autopsy. He found alterations to proteins in her brain cells, later called amyloid plaques and tau tangles. These are the hallmarks of what we now call Alzheimer's disease, which affects more that 5 million Americans aged 65 years or older. It remains incurable, with only symptomatic relief available.

In the past decade, Alzheimer's drug development largely has focused on the elimination of amyloid plaques, with little success. Recently, tau, a protein that modulates cellular support elements called microtubules, has emerged as a therapeutic target. Researchers now believe the buildup and tangling of the protein tau may be at the heart of disease severity. Mounting evidence suggests that tau aggregates spread via prionlike propagation.

To understand how misfolded tau spreads across brain cells, researchers from the University of California, San Francisco, used CRISPR interference, a genetic tool that allows specific genes to be turned off, to identify cellular components involved in the spread of pathological tau.

In a paper published in the **Journal of Biological Chemistry**, John Chen and colleagues reported that knocking down components of the endosomal sorting complexes required for transport, or ESCRT, machinery using CRISPR interference accelerated the spread of tau buildup in cells. Specifically, the researchers discovered that the individual knockdown of charged multivesicular body protein 6, known as CHMP6, or co-knockdown of CHMP2A and CHMP2B (a gene associated with familial frontotemporal dementia) caused the ESCRT pathway to become leaky and accelerated tau buildup. These results increase our understanding of how pathological tau spreads across brain cells and identify potential therapeutic targets.

DOI: 10.1074/jbc.RA119.009432

— Anand Rao

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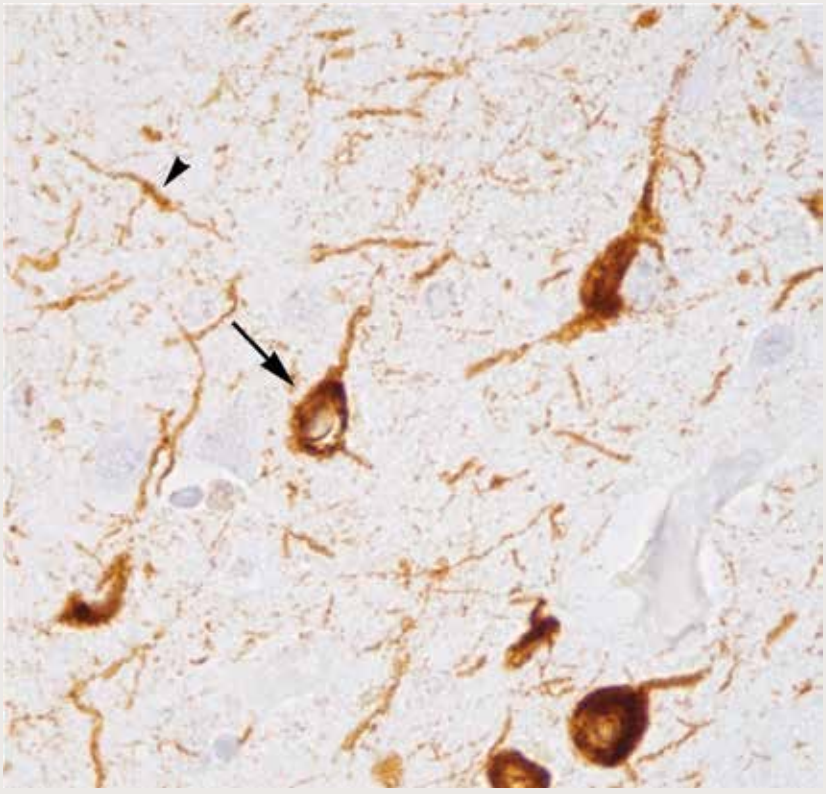

This photomicrograph shows nerve cell bodies (indicated by the arrow) and their processes (indicated by the arrowhead) in the neocortex of a patient who died with Alzheimer's disease. Tau protein is stained brown using immunohistochemistry.

PACAPturing a link between chronic migraines and opioid-induced sensitivity

Hundreds of millions of people suffer from debilitating migraines, and opioid-based medications regularly are prescribed to manage migraine pain. These treatments are effective at first but can lead to the progression of migraines from occasional to chronic, and continued use can lead to addiction and dependence on opioids. Regular opioid use also can lead to a lower pain threshold and higher opioid tolerance, a condition known as opioid-induced hyperalgesia, or OIH.

Researchers lack a complete mechanistic understanding of OIH and the exacerbating effect it has on migraines, making the development of alternative treatments a challenge. Krishna Anapindi and colleagues at the University of Illinois at Urbana–Champaign and the University of Illinois at Chicago studied neurological proteins to find mechanistic links between chronic migraines and OIH. The results of this study were published in the journal **Molecular & Cellular Proteomics**.

The team used liquid chromatography–mass spectrometry to identify and measure neuropeptide dysregulation similarities between the brains of mice engineered to have OIH and those engineered to have chronic migraines. Of the more than 1,500 neuropeptides they studied, the results showed 16 in common between the two disorders. Of those 16 peptides, pituitary adenylate cyclase-activating polypeptide, or PACAP, shows the most promise for further study, as it bridges the mechanistic gap between OIH and chronic migraines.

PACAP, when working properly, dilates blood vessels, but if the signaling values increase, this vasodilation could lead to both disorders. When the researchers blocked the PACAP receptor, PAC1, for both groups of mice, the blocked receptor prevented hyperalgesia in both models.

This is the first study to identify PACAP as an aggravator of OIH and chronic migraines and blocking PAC1 as a possible solution. The results will be useful for developing treatment options with less risk of addiction and dependence than that associated with opioid-based therapeutics.
DOI: 10.1074/mcp.RA119.001767

— Tori Zirul

DOROTHY LOUDERMILK/UIUC SCHOOL OF CHEMICAL SCIENCES GRAPHIC SERVICES

Mouse models were used to examine changes in brain peptides associated with opioid-induced hyperalgesia and chronic migraines. A large-scale liquid chromatography–mass spectrometry screen of several brain regions revealed PACAP as a peptide that could bridge the mechanistic gap between chronic opioid use and chronic migraines.

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A matter of degree

What steers so many black scientists toward earning a master's before a Ph.D.?

By Laurel Oldach

Zerick Dunbar

Kenneth Gibbs

Growing up in Sicily Island, Louisiana, Zerick Dunbar loved his high school math and biology courses. He went to Tulane University, some 200 miles from home, to study biomedical engineering and landed a job after college that was in a lab — he worked in quality assurance at a petroleum company — but didn't fit his interest in biology. So he returned to Tulane after a few years to seek a master's degree, hoping to find work at a medical device company.

As he worked in the lab alongside Ph.D. students, Dunbar said, his ideas about what could be done with his degree changed. Now he's a third-year doctoral student at Meharry School of Medicine in Alabama studying variations between natural killer cells across tissues. He has become interested in entrepreneurship and hopes to pursue a career in biotechnology, eventually launching his own ventures after graduation.

About 30% of Americans who earned a Ph.D. in the biological and biomedical sciences in 2017 had, like Dunbar, earned a master's degree before they enrolled in their doctoral programs. Among students who identify as black or African American, that proportion is significantly higher: closer to 45%. A master's degree can be an important intermediate step for students who at first are not competitive for admission to doctoral programs. At the same time, it can be costly, and a bad experience could derail promising researchers at an early stage.

Knowledge of this disparity varied among experts on diversity and inclusion in science interviewed for this story. Some consider it common knowledge. Others expressed surprise and even skepticism.

Kenneth Gibbs, a program officer who directs training programs at the National Institute for General Medical Sciences, or NIGMS, said, "We need more research. That's not just a pat answer; we really need to understand better why individuals make the choices they do leading up to entering a Ph.D. program.

"A master's is not a bad degree. A master's en route to a Ph.D. is not a bad thing. It becomes a bad thing if there is some differential, systemic issue that is causing this

different outcome — that is, if admissions committees require more from black candidates than others."

Does such a systemic issue exist? Policymakers don't know for sure, but they point to several well-documented educational disparities that may make it likely for black Ph.D. recipients to enter graduate school with more education on their CVs than their peers.

First in the family

"Black scientists live as black people, and black people in America have different lived experiences than other groups," Gibbs said. One part of that mosaic is a legacy of limited access to education, meaning that many students of color are the first in their families to pursue college or postgraduate degrees.

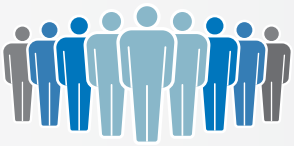
Zerick Dunbar is an example. "No one from where I'm from has ever gotten a Ph.D.," he said. "Maybe one guy back in the '50s or '60s." As a consequence, his path to graduate school was his to determine on his own.

Compared with many fields, including Dunbar's undergraduate major of engineering, biology is unusual in that students don't need to earn a master's degree before applying to doctoral programs. Students who don't have a family member or mentor with insider knowledge may not realize that.

Alyssa Cobbs, who finished her Ph.D. at Morehouse School of Medicine in 2019, started considering a research career as a senior in college, rethinking her original interest in pharmacy school. While attending the Annual Biomedical Research Conference for Minority Students, widely known as ABRCMS, she learned that she could apply for a funded Ph.D. program even without a master's degree in hand. The conference happened in November; Cobbs rushed to take the GRE graduate school entrance exam and wrote as many applications as she could finish before the December deadlines.

According to Cobbs, throughout graduate school, younger students would ask about

Alyssa Cobbs



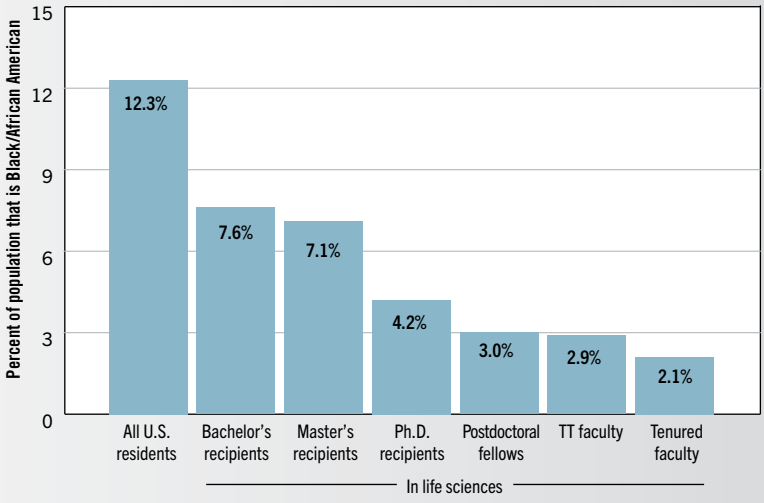
30%

of all U.S. biomedical Ph.D.s earned a master's degree first. Among black biomedical Ph.D.s, the proportion is significantly higher at

45%

Source: National Science Foundation/National Center for Science and Engineering Statistics (NSF/NCSES), Survey of Earned Doctorates (2017)

The proportion of life scientists who are black drops off over the stages of a traditional academic career path.



Source: NSF/NCSES, Women, Minorities and Persons with Disabilities in Science & Engineering (2019) and Science and Engineering Indicators (2018)

"A master's is not a bad degree. A master's en route to a Ph.D. is not a bad thing. It becomes a bad thing if there is some differential, systemic issue that is causing this different outcome."

— Kenneth Gibbs

Taylor Carmon

LINDSAY FRANCE/ CORNELL UNIVERSITY PHOTOGRAPHY

Avery August

where she earned her master's degree and were surprised when she said she didn't have one. Now her younger brothers and sisters are expressing interest in becoming scientists, and she looks forward to talking them through the process. "You know what you see," Cobbs said. "If you're never exposed to it, you don't know how to go about it."

Plenty of students are never exposed to the particulars of biomedical higher education. According to Avery August, a Howard Hughes Medical Institute professor of immunology and vice provost for academic affairs at Cornell University, some of the undergraduate students he counsels are "quite surprised that you can, so to speak, skip the master's degree. … The other really interesting thing is that many students still don't appreciate that during the process of getting a Ph.D., you are supported financially."

Paying out of pocket

The overwhelming majority of Ph.D. students in biological and biomedical sciences, some 95%, are supported by grants that cover both tuition and living expenses. In contrast, paying for a master's degree in the field most often falls on students. While about one-third of students join a funded program or land research or teaching assistantships, the majority of master's degrees in biomedical sciences are financed by loans or out of pocket.

Taylor Carmon took out student loans to finance his master's degree in food science at Alabama A&M University, a historically black university in Huntsville. He developed an interest in nutrition while reading up on diabetes and high cholesterol to help some relatives manage their diagnoses. That interest evolved into a college major and, eventually, a master's program.

Carmon said he chose Alabama A&M strategically. All of his prior education was in majority-white institutions.

"I decided that maybe I should look at HBCUs to get some diversity in my education. Just in case I didn't get tuition assistance, I decided to stay in Alabama." That narrowed the selection down to two programs, one of which he eventually joined.

The decision worked out for his scientific education. "My current adviser just picked me out of the crowd to start talking to me about molecular genetics," he said. "He got me interested in his research area by bringing me into the lab, talking to me about the different genes involved in lipid synthesis and how characterizing those genes could help people better understand certain diseases."

Almost three years later, Carmon has traveled to conferences to present research he did as a master's student and is building on that work as he pursues a Ph.D. in his adviser's lab.

But the master's, which was not funded, was costly; even for an Alabama resident, tuition for a year in the program is about $9,000, excluding living expenses. Across academic fields, according to the National Center for Education Statistics' Postsecondary Student Aid Survey, 81% of black M.S. graduates carry debt related to their master's degrees, compared with 56% of all M.S. graduates. Master's recipients who are black carry, on average, almost twice as much debt

as students in general.

Even now, neither Carmon's adviser nor his department is able to provide a stipend — or cover his tuition as a doctoral student researcher.

"That's the downfall of choosing an HBCU; they may not have the funding to pay for your education," Carmon said. "I know it's a disadvantage to me, because right now, I'm paying out of pocket. I chose to stay here over leaving … because I know the research in the lab, I know what's going on, I'm independent. I don't have to start over from scratch."

Carmon expects to graduate in three or four years. He said he and other students at Alabama A&M hope their department will land a grant sometime soon to cover tuition. In the meantime, he's racking up debt.

Time in the lab

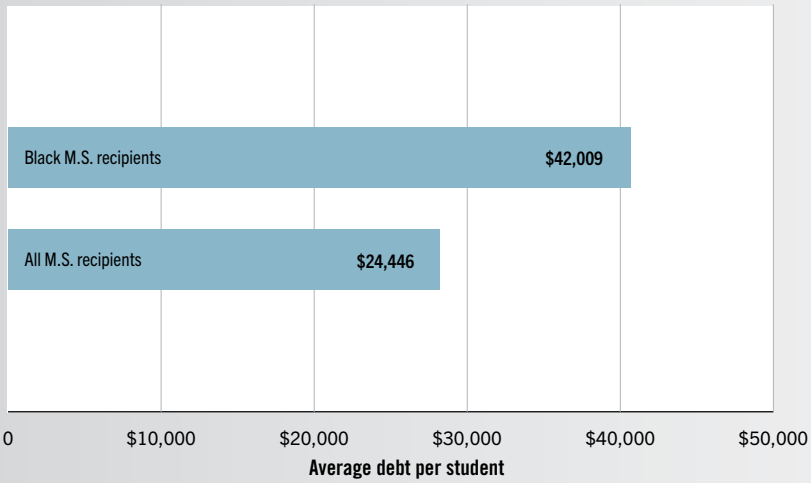
When Natasha Brooks was an undergraduate at Penn State with an interest in biochemistry in the early 2000s, she initially imagined a job in forensic science. A fan of the television show "CSI," she wanted to use her lab skills to solve crimes.

After her goal shifted to biomedical research, Brooks said, applying for a master's program seemed like the logical next step. She mentioned the plan to her research adviser, who told her, "'No, you need to just apply to Ph.D. programs.' He didn't feel that I needed to take the intermediate step."

Brooks had worked in the lab every summer since her freshman year, so the adviser was confident that she would be a strong graduate researcher. And he was right; Brooks was accepted to the University of Texas

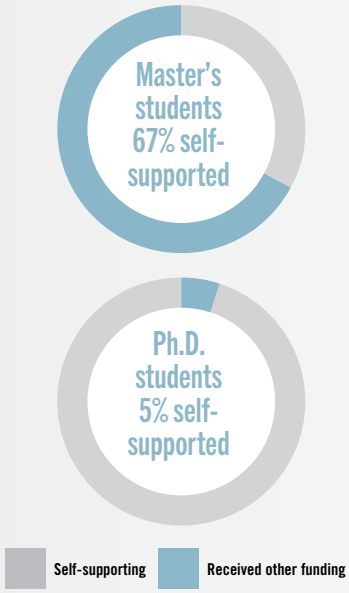
Natasha Brooks

The average debt burden is higher for black M.S. recipients in all fields than for their peers.



Source: U.S Department of Education, National Postsecondary Student Aid Survey (2016)

In biological sciences, master's students are more likely than Ph.D. students to pay out of pocket.



Source: NSF/NCSES, Graduate Students and Postdoctorates in Science and Engineering Survey (2018)

Kimberly Griffin

Medical Branch at Galveston for a Ph.D. in biochemistry and molecular biology, which she defended in 2012. She now works as a medical writer.

"The people who seemed to be more successful in the lab weren't the people who had the highest GPA and GRE scores," Brooks said about her fellow graduate students. "They were the people who actually had lab experience. I think that's a good predictor of the outcomes."

Kimberly Griffin, an associate professor of student affairs at the University of Maryland, confirmed this impression. Admissions committees, she said, "think quite critically about research experience and who you've had the opportunity to work with prior to entering your Ph.D. program."

All five of the top institutions where Ph.D. recipients earned their bachelor's degrees are classified as R1 universities by the Carnegie Commission on Higher Education, meaning that they have very high research activity. In contrast, the historically black colleges and universities that educated the most black students who later earned Ph.D.s have smaller research programs and graduate populations.

"HBCUs are wonderful institutions and are doing great work in terms of giving students the skills or the confidence they need to want to pursue graduate education," Griffin said. But "they may not have the lab facilities that would allow students to get the depth of experience doing lab-based science that other students might have."

For students whose degrees are from schools with less robust research activity, a master's degree may be a substitute for undergraduate research experience.

Kenneth Gibbs at the NIGMS thinks about it in terms of his own educational path. "If you're at Stanford, you have different levels of research available to you than at (the University of Maryland, Baltimore County). Those are two places that I went to school. I took advantage of what was available to me — but sometimes, at Stanford, Ph.D. applicants were judged by the Stanford standard."

Admissions committees, he said, would do well to consider how much access an applicant has had to research labs.

The NSF keeps track of where Ph.D. recipients first earn their undergraduate degrees. Whereas the top five alma maters of those who go on to earn Ph.D.s are all R1 universities, most of the top alma maters of black Ph.D. recipients are HBCUs, with lower research activity but stronger support systems.

Top five baccalaureate institutions of all Ph.D. recipients in science

Institution	Historically black college and university	Carnegie classification
University of California-Berkeley	No	Doctoral – very high research activity (VHRA)
Cornell University	No	Doctoral – VHRA
University of Wisconsin-Madison	No	Doctoral – VHRA
University of Michigan-Ann Arbor	No	Doctoral – VHRA
University of California-Los Angeles	No	Doctoral – VHRA

Source: NSF/NCSES, Women, Minorities and Persons with Disabilities in Science & Engineering (2019)

"Students have been figuring out on their own that where they initially can't get access to a Ph.D. program, a master's program can be a stepping stone." — Keivan Stassun

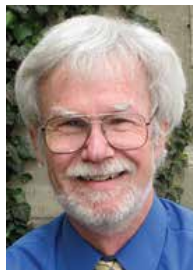
Gibbs often speaks to trainees — at various academic stages — whom he considers ready for a next career step by most metrics. Sometimes he finds that they don't feel ready. He suspects that the hypercompetitive culture of academia affects different groups to different degrees.

"As a professional black person, it's not uncommon to hear you have to be twice as good to get the same results as people from majority backgrounds," Gibbs said. That, he said, might motivate students to rack up extra credentials before applying to start a Ph.D.

In 1996, Richard McGee, a professor of medical education and associate dean of professional development at Northwestern University's medical school, started a postbaccalaureate program for students who want to spend more time in the lab before committing to a doctoral degree. The model has caught on and been adopted as the Postbaccalaureate Research Education Program at campuses across the country. McGee says he was motivated by having variations on the same conversation over and over at undergraduate research conferences for minority students.

"It wasn't an academic deficit," he emphasized. "It was 'I'm just not ready yet … I want to get more experience in research so I feel like I know what I'm getting myself in for.'"

For students he has worked with, McGee said, taking time to be sure of the decision to pursue a Ph.D. often has been positive. Whether the intermediate step is a master's degree or another training model, "Your confidence, your self-image, your self-efficacy; all this stuff is going to be bolstered at each step along the way (as) you get more data to counter the narrative that 'I don't belong here.'"



Richard McGee

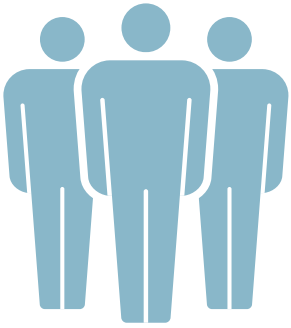
Keivan Stassun

The GRE

Along with research experience, recommendation letters and undergraduate grades, the GRE is an important factor in graduate admissions. According to Keivan Stassun, a physics professor at Vanderbilt University who has written extensively on equitable access to graduate education, "Doctoral programs have put and continue to put outsize

Top five baccalaureate institutions of black Ph.D. recipients in science

Institution	Historically black college and university	Carnegie classification
Howard University	Yes	Doctoral – higher research activity
Spelman College	Yes	Baccalaureate colleges – arts & science focus
Florida A&M University	Yes	Doctoral – higher research activity
University of Maryland Baltimore County	No	Doctoral – high research activity
Hampton University	Yes	Master's colleges & universities – medium programs



Critics say that the GRE is a biased test. Black test-takers interested in biology score lower on both halves of the test, on average, than their white peers. Their mean combined score is about

10

points lower on an

80

point total scale.

Source: Educational Testing Service, Snapshot of the individuals who took the GRE general test (2017).

influence on GRE scores. As soon as you realize that, all of these other patterns become understandable."

GRE scores have been known for decades to correlate with race and gender. The Educational Testing Service, which administers the GRE and other standardized tests, has taken steps to reduce that bias; though the gap is shrinking, it remains at greater than 10% of the possible score. That can be a problem at the triage stage of admissions, when committees decide which applications to review in depth and which are unlikely to be successful.

"If you sort your applicants by their GRE scores … because of the massive disparities in GRE scores that correlate with race and gender, your diverse applicants are going to end up being sorted to the bottom of the spreadsheet," Stassun said. Once those candidates are there, he added, even if diversity in admissions is a priority, the ranked list predisposes the committee to think of more diverse candidates as less qualified.

Qualitative research suggests that triage based on GRE score is common across scientific fields because the average committee must assess so many applications. But as research has begun to show that, while predictive of first-year grades, GRE scores are not correlated strongly with measures like publication rate and completion time in graduate school, an increasingly large movement, cheekily dubbed GRExit, is demanding that admissions committees drop their GRE requirement.

Another approach is to reduce the committee's focus on GRE scores while still gleaning some information from the test. That's the route Marenda Wilson–Pham took when she was assistant dean of diversity and alumni affairs at MD Anderson Cancer Center. In an article last year in the journal CBE-Life Sciences Education, Wilson-Pham and her team described an intervention to reduce the disproportionately high triage of applicants from underrepresented backgrounds. Once, a GRE score or GPA below a threshold got an application set aside right away, and only an intervention from interested faculty could rescue an applicant. In the redesigned admissions process, applications with weaker scores are reviewed by a second committee; if the reviewers think a student has potential, they forward the application to the main admission committee, which is blinded to applicants' triage status.

The safest bet

According to Wilson–Pham, now an associate dean at Rush University in Chicago, when admissions committees meet to discuss applicants who have cleared the triage hurdle, subtle bias may creep into their assessment of qualitative factors.

"People fall into this lull," Wilson–Pham said. "They like to see candidates who remind them of who they once were. … If I have to bet on which person is going to succeed, it's this person that looks just like me — because I succeeded."

This type of bias, known to social scientists as homophily, isn't only about race, ethnicity and gender. It can apply to any feature that a student and an admissions committee member shares, such as where they went to college or whether the applicant's recommendation letter comes from a professor whose reputation the admissions committee knows.

At MD Anderson, where she both earned her Ph.D. and got her start in academic administration, Wilson–Pham used the Socratic method when she sensed reviewers saw some applicants as safe bets and others as risky. "It's almost like a research seminar," she said. "The way I'd get people to reflect on their behavior was to ask a bunch of questions. 'Tell me why

you feel this way about this applicant. Well, then let's go back to this applicant that we reviewed an hour ago and this is what was said.' … My job was to make sure that, for every applicant, the criteria were equal."

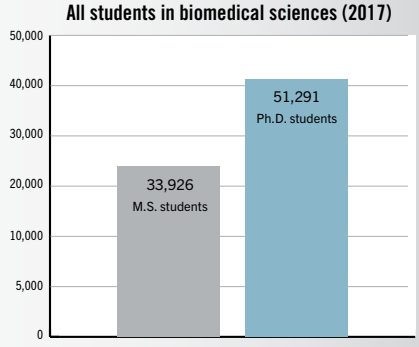
Aware that a program's future funding depends on student success, a committee with doubts about an applicant's ability to succeed may hedge its bets by suggesting that student consider a master's degree in the same department, generally with funding. Both Wilson–Pham and LaRuth McAfee, the senior assistant dean at the University of Delaware's graduate college, mentioned this when discussing the preponderance of master's degrees among black Ph.D. recipients.

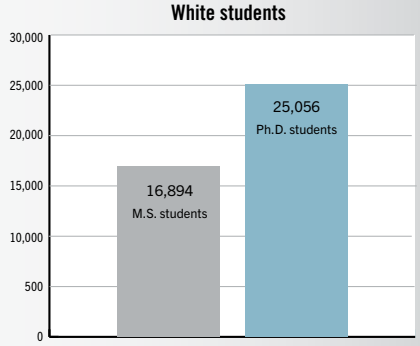
"Maybe the student knows they want a Ph.D., but the program wants them to prove themselves," McAfee said. "If they do well in the master's program, they can stick around for the Ph.D."

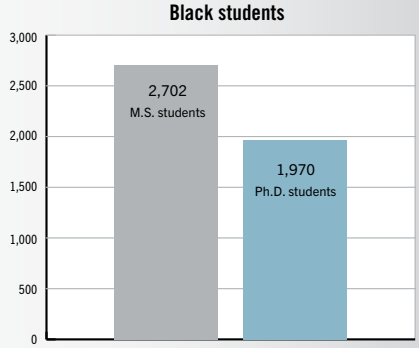
Anecdotally, both deans said that these offers are more commonly extended to students from minority-serving institutions. "It's not that they're saying, 'We don't think someone from this institution can cut it,'" McAfee said. "It's more like, 'We're concerned that we're putting ourselves at risk — and even concerned that we might be hurting the student by admitting them to a program in which, if they're not successful, they'll have fewer options when they leave than when they came in.'"

Some students seize the opportunity to attend their school of interest on any terms. Others recoil. When Zerick Dunbar was finishing his master's degree and applying for Ph.D. programs, he received one counteroffer of acceptance into a master's program instead. "I was like, 'Uh, I already have a master's?' Getting another would be a waste of my time."

While Ph.D. students outnumber master's students in the biomedical sciences overall, there are more black students pursuing master's than doctoral degrees.







Source: NSF/NCSES, Graduate Students and Postdoctorates in Science and Engineering Survey (2018)

Marenda Wilson–Pham

LaRuth McAfee

Suzanne Barbour

Recruitment and retention

The National Science Foundation's Graduate Student Survey indicates that, across the many disciplines of biology and biomedicine, about three people are pursuing doctoral degrees for every two pursuing master's degrees. This ratio is about the same for white students. But it's inverted for black students; there are three black Ph.D. students for every four black master's students. Advancing further through academic career stages, the underrepresentation of black scientists becomes more and more pronounced.

"Students are making — I think in some cases justifiable — choices to do other things," August said. "At the same time, I think we're losing an opportunity to diversify faculty, because of the culture we have in the academy."

Suzanne Barbour is the dean of the graduate school at the University of North Carolina at Chapel Hill and a longtime member of the American Society for Biochemistry and Molecular Biology's Minority Affairs Committee. She put the master's-before-Ph.D. phenomenon in the wider context of academia's inhospitability to underrepresented scientists.

"Any time there's a stopping point in the pipeline, there's a potential that you get lost," she said. "Students may get the master's and be satisfied with it. Or, due to the things that happened to them during the master's, (they may) say, 'The last thing in the world I want to do is go for a Ph.D.! I haven't been treated well in academia.'

"A lot of things have been done in the last two generations. There are all kinds of pipeline-building programs, (but) everything tends to focus on recruitment, recruitment, recruitment."

In Barbour's opinion, it is time for the focus to shift to retention of underrepresented students and to increasing diversity and inclusion in more senior roles.

Historically black colleges and universities

Briana Whitehead

The college experience can govern a student's interest in, and preparedness for, further education. A disproportionate number of black Ph.D. students attended a historically black college or university as undergraduates.

"Those are institutions that have really mastered what it means to have cultures of inclusion and to provide support structures that ensure students come out armed to succeed in whatever they do," Keivan Stassun, a physics professor at Vanderbilt University, said about HBCUs. "Many of our R1 institutions who have been working harder to increase the diversity of their student bodies still have a lot to learn from minority-serving institutions."

For Briana Whitehead, a first-year biophysics Ph.D. student at Johns Hopkins who earned a master's through a bridge program at Fisk University in Tennessee, the difference between her undergrad and her master's program was stark. When she was an undergraduate, she said, "it wasn't a community that I felt could foster my growth in being a scientist and continuing to be myself. When I went to Fisk, I was at an HBCU and I was able to be in a community where it was OK to be a black young woman in STEM."

The time she spent in the program boosted her confidence in her ability as a scientist and also her ability to compete in the admissions process. When she chose a doctoral program, she selected universities with equally strong underrepresented communities.

Students from prominent HBCUs are courted by many graduate programs. However, some faculty at research universities lack knowledge of these institutions. When Kenneth Gibbs, a program officer at the National Institute for General Medical Sciences, was a graduate student at Stanford, he served on an admissions committee; one applicant was a senior at Morehouse College, and some faculty "hadn't heard of Morehouse and didn't know how to assess (the student's) potential contributions or his ability to excel in the program."

Gibbs said his answer was, "Well, have you heard of Martin Luther King Jr.? Because that's where he went to school."

Outlook

"People in science are still *people* in science," Gibbs said. "Even though our ideals are universal, science happens in a social environment. The biases that exist in the world shape how we do science and the experience that people from different backgrounds have in science."

Many scholars have worked for years to unravel the way that those biases directly and indirectly steer young black scientists toward extra years of schooling or away from science altogether. For some of them, such as Michelle Jones–London, chief of the workforce diversity office at NINDS, students' research experience prior to graduate school is coming into focus as a research topic of its own.

"We recognize that this needs more of a careful look," Jones–London said. "We've seen what we think could be a potential difference (between well-represented and underrepresented graduate students) … the hard part is the 'why.'"

Experts say determining and redressing the causes of underrepresentation are as much a strategic priority as an ethical imperative.

"There was a time when people thought of this as an issue of just plain diversity," Barbour said. "But now, I think we have to start thinking about it in terms of the workforce and the leadership that the country needs to continue to be the global leader in research and development in the life sciences."

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

Bridge to doctorate programs

According to Keivan Stassun, a physics professor at Vanderbilt University, "Students have been figuring out on their own that where they initially can't get access to a Ph.D. program, a master's program can be a stepping stone."

Launched in 1992, the Bridges to the Doctorate funding mechanism at the National Institutes of Health is designed to offer that stepping stone but with funding to reduce the financial burden on students. It pairs minority-serving institutions that offer a terminal master's degree with predominantly white institutions that offer doctoral programs. When a student successfully completes the master's, they receive admission to the Ph.D. program.

Stassun launched Vanderbilt's Master's to Ph.D. Bridge program in collaboration with Fisk University in Nashville in 2003. (The program is independent of the NIH program.) "Almost without exception, these are students who have applied to doctoral programs and been denied admission to every one of them," he said. The program "provides a way for these students to demonstrate on site what their capabilities are."

Avery August, who ran a Bridges to the Doctorate program as a professor at Penn State in partnership with Alcorn State in Mississippi, saw some applications from undergraduates who were already well prepared to enter a Ph.D. program. He said, "We specifically counseled those students to apply directly to Ph.D. programs."

Sometimes, he added, those students were disappointed not to be accepted into the supportive community of the bridges program, so the program staff took steps to expand the extra mentoring and other activities to underrepresented students who didn't need the transitional master's step.

When a panel met to review the NIH funding mechanism in 2018, they concluded that it was unevenly successful: Some universities' programs were very effective, while others had limited success in funneling underrepresented students into Ph.D.s and later faculty positions. The committee added that a lack of longitudinal data on student outcomes made it difficult to assess accurately.

THE MEYERHOFF SCHOLARS PROGRAM

A model for increasing diversity in STEM

By Nathalie Gerassimov

In the late 1980s, Robert Meyerhoff, an MIT-trained engineer turned Baltimore businessman and philanthropist, turned his attention to changing negative narratives about black men and increasing their participation in the science, technology, engineering and mathematics fields.

Meyerhoff joined forces with a black university administrator, Freeman A. Hrabowski III, who would go on to become the president of the University of Maryland at Baltimore County. Together, they initiated a bold one-year experiment: to reproduce the supportive environment Hrabowski had experienced at Hampton Institute, now Hampton University, a private historically black university, at the predominantly white UMBC.

Some three decades later, the resulting Meyerhoff Scholars Program, or MSP, is a national model for how to increase diversity in science.

The MSP has tracked outcomes for its more than 1,200 graduates since 1993. A student who accepts an invitation to join the program is five times more likely to attend or graduate from a STEM Ph.D. or M.D.–Ph.D. program than a student who is invited to join the MSP but chooses another undergraduate program. As of 2019, the program's alumni had earned 319 Ph.D.s, including 59 M.D.–Ph.D.s and 147 M.D. or D.O. degrees, as well as 280 master's degrees, primarily in STEM fields. Most of these degrees are from prestigious institutions such as Harvard, Stanford and Yale.

The first MSP class, referred to as M1, was 19 black men from Maryland. Meyerhoff financed their tuition, fees, room and board, and books. He also took a great interest in them, their college experience, and their backgrounds and personal circumstances. That first year convinced him to continue his support of the program. Black women were admitted into the MSP starting with M2.

In the late 1990s, following the Supreme Court's decision to uphold a federal appeals court ruling that struck down a scholarship program limited to high-achieving black students, the MSP was opened to people of all races and backgrounds who are interested in increasing diversity in science.

Keith Harmon, director of the program since 2012, explains why MPS embraced this change. "If we want to change the narrative and landscape — we need everyone at the table to understand the issues and do part of the work," he said.

The MSP experience begins, before a student starts their first year, with the six-week residential Summer Bridge program. Members of the new class live together in one building and take two credited classes: a math course and Race, Science and Society, a course designed and taught since 2013 by psychology professor Shawn Bediako to examine critically how these three constructs inform and influence one another.

"All students — regardless of their background — live in a social context that basically tells them the same thing about power, who has power and who should have power," Bediako said. "They process these messages differently, however. Some students have internalized these messages and are motivated by a desire to prove themselves and their worth. Some students have externalized these messages and are motivated by a desire to change the system so that it is more equitable.

"My goal for this class is to give students the vocabulary to speak about systems of inequity and reflect on how those systems show up in society — particularly through the process and practice of science."

As part of the Summer Bridge program, Harmon said, students also attend seminars and talks designed to prepare them for the academic rigor and collaborative learning at UMBC by introducing them to best practices for undergraduate success, including learning styles, time management and networking.

"We help the students and the parents understand the sacrifices and the dedication it takes to be successful in STEM," Harmon said. "We set high standards for them, but we will not expect any less than we resource them for."

Mitsue Wiggs, the MSP assistant director and Summer Bridge coordinator, emphasizes that, in addition to academic excellence and undergraduate research, community service and civic engagement are core values of the program. As part of a for-credit class called the First Year Experience, incoming students engage in a semester-long service-learning project with one of more than 100 non-

Program founder Robert E. Meyerhoff and Freeman A. Hrabowski III, president of the University of Maryland at Baltimore County, sit center stage surrounded by program graduates and staff at the 30th anniversary celebration of the Meyerhoff Scholars Program.

profit organizations in the Baltimore area.

"It has been really successful for us to have them engaged early in their process and to really start to understand the responsibility and the benefits of serving their community," Wiggs said.

Nicole Attram, an MSP first-year student majoring in mechanical engineering, volunteered with a program called Reading Partners. She tutored elementary students who were behind grade level in reading to help improve their skills. "I chose this volunteer site because I had a difficult time learning to read when I was younger," she said, "and I thought it was only right for me to help someone as I was helped."

The institutional commitment of senior administration and UMBC faculty is the secret sauce to MSP success, Harmon said. "We would not have the success we've had, had it not been for the commitment of our faculty, especially the STEM faculty who take students into their labs and train them and teach them to think critically and deeply about the challenging problems within STEM."

Darin Gilchrist, a senior majoring in biochemistry and molecular biology, recalls that prior to becoming part of the MSP, he was interested in science but really didn't know what research was. "I don't know if I would have done undergraduate research without MSP," he said. Once at UMBC, he followed the MSP's recommendation and did undergraduate research for three years with Howard Hughes Medical Institute investigator Michael Summers and this past summer at Dana–Farber Cancer Institute at Harvard Medical School. Gilchrist is now applying to M.D.–Ph.D. programs and has interview offers from New York University, Columbia University, the University of Maryland and the University of Texas Southwestern Medical Center.

"MSP community is like a family, which I really enjoyed," Gilchrist said. "I thrived with the support from the staff and the other MSP students and alumni who helped me through my struggles, helped plan my next steps and shared my good news with me. I have no doubt that I am more successful today because of MSP."

Nathalie Gerassimov (nathalie.gerassimov@gmail.com) is a postdoctoral researcher at the Carnegie Institution of Washington department of embryology.

INCLUSIVE EXCELLENCE

A goal of lasting change

By Courtney Chandler

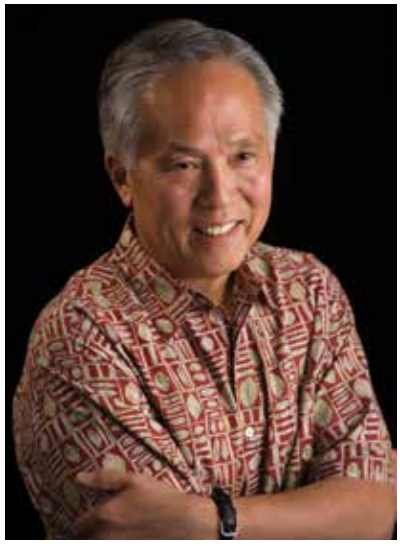
The scientific community now recognizes that diversity is important, yet historical exclusion of certain groups from the sciences hinders inclusivity and growth. This limits the range of perspectives within the community, which then loses this benefit of diversity.

Funding agencies have developed programs to increase diversity in science. But David Asai, senior director of science education for the Howard Hughes Medical Institute, thinks more needs to be done.

"These efforts have had a positive effect," Asai said, "but our overall progress has been appallingly inadequate."

This is partially due to a long-standing focus on students without a corresponding focus on the learning environment in which the students find themselves, Asai said. Many programs provide tutoring, mentoring and research experiences for specific groups of students without altering the academic structures in their schools or universities.

"While these 'fix the student' interventions might help the students who participate, they generally do not result in lasting change," Asai said. "When the grant ends, the activities end, and the system goes back to



PAUL FETTERS

David Asai

where it was before."

To overcome these limitations, the HHMI conceived a new approach to increase diversity in the sciences: the Inclusive Excellence initiative. Launched in 2015, this initiative provides grants to colleges and universities that are working to achieve significant and sustained increases in their inclusivity of all students.

Each participating school is asked to think about the populations of students that may be excluded at their institution. These may include students from racial and ethnic groups historically excluded from science, students transferring from community colleges and those who are the first generation in their families to attend college. Instead of a student-centric approach, the Inclusive Excellence initiative is focused on the institution itself.

"This approach emphasizes the building of significant and lasting changes in the institution's capacity for inclusion," Asai said.

Colleges and universities can apply to be a part of the initiative, and Asai said interest is high. In 2017, the 24 schools in the first cohort were awarded $1 million each in grant funding over five years to support institutional-level changes that create an inclusive culture for all students.

The schools work in collaboration with HHMI and the Association of American Colleges and Universities to enact these changes. The second round of awards went to 33 schools in 2018, and the application process is under way for the next round, called IE3.

Specific programs and implementation plans vary among institutions based on their needs and goals, and a single school may have multiple initiatives. For example, several schools, including the University of Wisconsin–Madison, Framingham State and the University of Utah, are working with nearby community colleges to align their curricula and advising so that students transferring into four-year universities can be successful in science, technology, engineering and

DRIVING CHANGE

The Howard Hughes Medical Institute launched a new initiative, Driving Change, in 2019 to promote a comprehensive approach to diversity and inclusion at research universities.

Each Driving Change university is expected to achieve three objectives:

1. Learn about the Meyerhoff Scholars Program at the University of Maryland, Baltimore County, and design their own student-centered program that will honor the underlying values of and achieve the outcomes of the Meyerhoff Program.
2. Design, implement and assess programs aimed at creating a significantly more inclusive learning environment for all students, especially with an eye toward closing the disparity gaps between students from excluded and nonexcluded groups.
3. Become an active participant in a learning community comprising other Driving Change universities in which the schools will share their ideas, efforts and outcomes.

Each school applying for a Driving Change grant will conduct a self-study to identify how it can create a more inclusive STEM learning environment. Letters of intent for the first round of grants are due Feb. 7.

mathematics studies.

Kenyon College and others connect inclusive behaviors in the ways faculty do their jobs, such as the way they teach and advise, to faculty rewards systems, including tenure, to provide incentives for conscious inclusive efforts. Still other schools are revising their introductory science curriculums to include course-based research experiences for beginning science students, as is the case at Towson University and Norfolk State. Inclusive Excellence allows schools to be creative and individualized with their approaches as long as they are striving for increased inclusivity and lasting change.

Institutions submit proposals that are reviewed by HHMI staff as well as scientists and educators who provide advice to the HHMI review panel during the application process. Preproposals for the IE3 cycle were due Jan. 14, and more than 400 schools indicated that they intended to apply; up to 30 will be awarded grants.

"Working toward inclusive excellence is a never-ending process, and the process is dynamic," Asai said.

The Inclusive Excellence initiative is relatively new, but Asai said HHMI staff members already have gained insight about what it takes to create meaningful culture change in an institution.

"Working toward inclusive excellence is a never-ending process, and the process is dynamic," Asai said. "The institutional context changes all the time, often unexpectedly, and the work toward inclusive excellence must navigate these changes."

The lessons of the first two rounds will help the HHMI improve the program and other inclusivity efforts including their recently announced Driving Change program.

For the learning community to improve as a whole, Asai said, its members need to reflect on and share their experiences. For example, each grantee institution is part of a small peer implementation cluster, typically composed of four schools, that meets regularly. During these sessions, groups of faculty and staff from each Inclusive Excellence school share with one another what they are learning and how they can improve further. As an increasing number of schools become involved in the Inclusive Excellence learning community, this mutual support will help promote lasting and meaningful change.

Courtney Chandler is a postdoctoral researcher at Johns Hopkins University and columnist for the ASBMB Careers Column focusing on industry. Follow her on twitter @CourtneyEChan.

PROGRAM AT NORTHEASTERN AIMS TO FIX THE INSTITUTION

By Leia Dwyer

In the higher education-dense Boston region, Northeastern University always has stood out for its rich tradition of experiential learning. So it comes as no surprise that Mary Jo Ondrechen has employed this concept in launching the Inclusive Excellence program at Northeastern, with a focus on flipped classrooms and encouraging faculty to share with each other best practices for diversity and inclusion.

Though she speaks in an unassuming way about her initiatives at Northeastern, Ondrechen herself navigated higher education at a time when few resources supported diversity and inclusion, so she has a deep personal connection to these efforts. As both a woman studying physical chemistry with very few female faculty mentors and a member of the Mohawk Nation, she says she felt invisible but always did her best to push ahead despite challenges.

Ondrechen and Wendy Smith, professors of chemistry and biology, respectively, heard the call for preproposals for the first round of the Inclusive Excellence competition back in 2015. After their full proposal was selected by the Howard Hughes Medical Institute for funding, the project launched at Northeastern during the 2017 fall semester and has continued for two years.

The goal of Inclusive Excellence is to make the science majors more welcoming to diverse students, Ondrechen said, including first-generation college students.

"We don't need to fix the students," Ondrechen said. "We need to fix the institution."

A professional evaluator measures the Northeastern program's success with both students and faculty and is just starting to acquire early data. Students and faculty associated with the program take before-and-after surveys, and the change in number of students graduating with science, technology, engineering and math degrees will be a key metric of success.

Ondrechen doesn't mince words about traditional academia. Research shows that lecturing is "just about the worst way to teach," she said. However, most faculty learned by this method, so they employ it in their classrooms today. She aims to educate her colleagues on the benefits of interactive classrooms where students drive their own, often collaborative, learning — classrooms where they feel more engaged and, as a result, more included.

COURTESY OF MARY JO ONDRECHEN

As a woman studying physical chemistry with few female mentors and a member of the Mohawk Nation, Mary Jo Ondrechen says she felt invisible when she was a student but always did her best to push ahead.

Ondrechen employs the flipped classroom approach in her own teaching, reversing the traditional split of homework versus lecture and putting more emphasis on active, team-based problem solving in the classroom as opposed to instructor lectures. Research shows that while this flipped approach is good for all students, it offers the greatest benefits to women and minorities, she said. She was happy to eliminate individual quizzes in her quantum chemistry and spectroscopy class in favor of team-based quizzes, she said; students can solve harder problems together through discussion and collaboration than they would be able to tackle individually.

As part of Northeastern's Inclusive Excellence program, workshops educate faculty on basic principles of diversity and inclusion in the classroom. Ondrechen said attendance at some of these workshops has exceeded her expectations. The workshops are followed by teaching circles where about a dozen faculty members gather to discuss their practices and open tough conversations about bias and inclusion that faculty then carry with them back to their own classrooms.

Ondrechen emphasizes the advantages of these peer-to-peer discussions and notes that the small, easily implemented changes often have the greatest impact. One of her favorite examples is eliminating implicit bias in calling on students in the classroom by using a stack of index cards with students' names and drawing at random.

And the best measure of success in an interactive classroom? "The noise level."

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For vulnerable populations, the thorny ethics of genetic data collection

By Adrian Pecotic

To be equitable, genetics research needs more diverse samples. But collecting that data could present ethical issues.

In 2009, researchers collected DNA from four elderly men in Namibia, each from one of the many San indigenous communities scattered across southern Africa. A year later, analyses of the men's DNA were published in the journal Nature — alongside that of South African human rights activist Desmond Tutu. The intention, in part, was to increase the visibility of southern, indigenous Africans in genetic-based medical research. Soon after, a nongovernmental organization representing indigenous minorities in Southern Africa took issue with the consent procedures used to gather the data and wrote to Nature's editors accusing the paper's authors of "absolute arrogance, ignorance, and cultural myopia."

The San case highlights the thorny ethics of collecting genetic data. Yet today, to make medicine more equitable, scientists see the importance of sampling DNA from more diverse populations. Most genetic research uses DNA from descendants of Europeans, which means the related medical applications — such as genetic tests to see the likelihood of developing a certain disease, called polygenic risk assessments — can only benefit those populations. In 2018 in the United States, for example, the National Institutes of Health launched All of Us, a research program that aims to collect DNA, electronic health records, and other data, from about one million Americans with emphasis on including many different groups of people.

"When we do genetic studies, trying to understand the genetic basis of common and complex diseases, we're getting a biased snapshot," said Alicia Martin, a geneticist at the Massachusetts General Hospital and the Broad Institute, a biomedical and genomics research center affiliated with Harvard and the Massachusetts Institute of Technology.

Research to capture these snapshots, called genome-wide association studies, can only draw conclusions about the data that's been collected. Without studies that look at each underrepresented population, genetic tests and therapies can't be tailored to everyone. Still, projects intended as correctives, like All of Us and the International HapMap Project, face an ethical conundrum: Collecting that data could exploit the very people the programs intend to help.

Researchers with All of Us have collected data from about 1,600 Native Americans, some of whom live in cities outside of sovereign lands, where tribal approval is not necessary for genetic research, according to Krystal Tsosie, a geneticist at Vanderbilt University who is co-leading a study in collaboration with a tribal community in North Dakota.

"Obviously there's an interest in monetizing biomarkers collected from diverse populations and underrepresented populations," Tsoise said, so without adequate protections, "the concern becomes about exploitation."

Shifting gears

Medical genetic research generally works like this: Geneticists use powerful computers to compare the genomes of people affected by a particular disease to healthy controls.

Researchers mark genetic patterns that are common in people with, say, diabetes, but not the controls, as "associated" with the disease. The more samples geneticists feed to the algorithms, the more likely that the findings reflect reality.

But studies restricted to descendants of Europeans will only find associations between diseases and "variants that are common in European ancestry populations," said Martin — if those variants are common enough to be found.

Scientists use the results to develop polygenic risk scores, which count the risky variants on someone's genome to estimate their susceptibility to a disease. But if studies don't use the genomes of non-white populations, the tests won't pick up on the problematic variants in different groups of people. One 2019 Nature Genetics study, on which Martin was an author, determined that these blind spots reduce the accuracy of polygenic tests by approximately two and five times in South or East Asian, and black populations, respectively.

In many cases, the groups whose DNA is missing have worse health care outcomes than their white counterparts; genetic medicine could worsen these disparities. "I think there's a huge responsibility," said Martin. "If we look at the history of the field, over the past decade we've gone from participants in genetic studies being 96 percent European ancestry to about 80 percent. We've shifted gears a little bit, but not nearly enough to be able to serve minority populations."

Jantina De Vries, a bioethicist at the University of Cape Town, agreed that "representation in genomics research can bring health benefits," particularly if it is paired with measures to build research capacity so that, eventually, "there are researchers at every level" within the groups themselves.

Collecting broader genetic samples poses a host of challenges. Efforts to collect and study the genomes of indigenous peoples, for example, have been controversial since the early '90s. The first such project, called the Human Genome Diversity Project, or HGDP, was meant "to explore the full range of genome diversity within the human family" by collecting DNA samples from about 500 distinct groups, with an emphasis on indigenous peoples that might soon "vanish." Indigenous-rights organizations criticized the project, taking issue with being treated as mere objects of scientific interest and potential for commercialization. All of Us, more recently, has run into similar objections from the National Congress of American Indians.

STAEHLER/WIKIMEDIA COMMONS

A San woman drills a hole in a slice of ostrich egg and adds it to a jewelry chain. After researchers published an analysis of DNA from four San men in Namibia, an organization representing indigenous minorities took issue with the consent procedures used to collect the samples.

Collective consent

The concerns are linked to the long history of exploitative encounters between researchers and vulnerable populations. The Tuskegee Study — in which the U.S. Public Health Service withheld treatment from African American men with syphilis — lasted from 1932 until 1972, ending less than 20 years before the HGDP proposal. And in 1989, researchers from Arizona State University collected DNA samples from the Havasupai Tribe and reused the data for

IAN BEATTY/WIKIMEDIA COMMONS

A San tribesman in Namibia.

research to which the participants hadn't consented: on schizophrenia, inbreeding, and migration history. Tsosie said this context has created a "climate in which we've seen tribes deciding to disengage from biomedical research completely."

All the geneticists and ethicists this author spoke with agreed that community engagement is crucial to establish trust. But they didn't agree on the degree of the engagement. Some believed that gaining the consent of communities is necessary for ethical research, while others said it was enough to have respect and open dialogue between researchers and the people they'd like to study.

But both approaches are difficult in the context of collecting and analyzing genetic data, since geneticists take DNA from individuals to make conclusions about entire populations. For instance, the San paper in Nature extrapolated findings regarding individual genomes to discuss the genomes of the broader communities. "One's genome is not their own specifically; one's genome is informed by their recent ancestry, their family structures, and their more distant ancestry," said Tsosie. Geneticists are never "talking about an individual that's siloed."

The gap between individual and collective consent is partly responsible for the continued friction between genetic science and indigenous peoples. Collective consent, said Tsosie, who is herself Navajo, is "more culturally consistent with how tribal groups govern themselves."

In 2017, Andries Steenkamp, a San leader, and Roger Chennells, a lawyer, wrote that the Nature study failed in this regard by only getting "informed consent from the indigenous individuals who participated."

Not everyone agrees that collective consent can or should be a requirement for all genetic studies. For instance, de Vries said, "it depends what sort of community we're talking about," drawing a contrast between small, rural, communities and larger populations spread across several cities or countries. "If we're talking about the entire Yoruba population, who would you even talk to?" she added. The Yoruba are an ethic group of more than 20 million individuals, most of whom live in Nigeria, with smaller populations in Benin, Togo, and across several diaspora communities. De Vries believes the onus lies on researchers to "think in terms of respecting communities," rather than in terms of collective consent.

Gaining collective consent involves logistical hurdles, especially for large-scale projects. The NIH's All of Us program, for example, wasn't able to get input from each of the 573 federally-recognized tribes. According to Tsosie, during the planning stages, "there was talk of gaining tribal input, but that plan seemed to be abandoned early on." The All of Us website does have a section on tribal engagement, but only offers "formal consultation and listening sessions" for ongoing projects, not guidance on how to approach these issues before a project starts.

Among non-indigenous policymakers and scientists, Tsosie noted, there's a "magical notion" that stakeholders from every tribe can be brought together in one room "when, in reality, that is not how we make consensus decisions for ourselves."

Respecting groups

Even more difficult than logistics may be conceptualizing the genetic studies to begin with — for example, deciding which people belong in which groups. "One of the greatest political acts, acts of power, that we perform as human beings is dividing ourselves up for the purpose of knowing and governing ourselves," said Jenny Reardon, a sociologist who specializes in genomics at the University of California, Santa Cruz.

Globally, indigenous peoples are so culturally distinct from one another that a single understanding of a community won't resonate with everyone. Finding a method for data collection "that crosses all indigenous groups is going to be really hard," said Vanessa Hayes, a geneticist at the Garvan Institute of Medical Research and the University of Sydney in Australia who conducts fieldwork in South Africa. "Because, straightaway, that's assuming all indigenous people are the same."

Without common ground, scientists must do the hard work of understanding each unique community. As Hayes put it, "every group that you work with, you have to respect that group, and take the time to understand what is important in that group."

Hayes was one of the authors of the 2010 Nature study on the San, and she was responsible for obtaining consent, gathering samples, and discussing the results with the community. While Steenkamp and Chennells suggested the researchers were hasty in their data collection and ignored governance structures, Hayes countered that, at the time of the study, she'd already been working in these communities for more than a decade and they were working directly with government agencies. She'd been in contact with the Working Group of Indigenous Minorities in Southern Africa, or WIMSA — the NGO which would eventually criticize the study — before it began. But, she said, "when I went back to the community and asked if they knew who WIMSA was, they said 'no.' I asked them if they wanted WIMSA to represent them, and they said, 'Hell no.'"

(As an organization, WIMSA is currently being restructured. The South African San Council, which now represents the San communities of South Africa, declined an interview, citing a requirement for financial compensation and a signed contract.)

Hayes followed the principles of collective consent, she said, just at a lower level than formal institutions like WIMSA or the San Council: "Their decision was made as a group. They are the group, they are the band, they are the family." She added, "No one can represent them that is not them."

The difficulties in defining a group make collective consent even more challenging.

In the clearest of circumstances, where an established organization exists, approval processes can be difficult to navigate and can take months. But within some indigenous and minority groups, issues of representation remain controversial. Often, a scientist will have to invest a lot of time interacting with potential subjects in order to judge what consent procedures are appropriate. Few scientists have the necessary time and resources.

STAEHLER/WIKIMEDIA COMMONS

A San man in Namibia adds finished giraffe bone to the arrow shaft made of hard grass.

There is no easy way to choose which organizations to deal with, especially when there are internal disagreements about representation. Or, as Reardon put it: "The folks that are trying to democratize the science are going to have the same problem as the people who were attempting to treat it as 'We're just going to go out and get these groups, and study them from a scientific perspective.'"

Although the repeated controversies surrounding research and indigenous groups may have slowed their inclusion in genetic science, the researchers this author spoke with said ensuring these concerns are heard and addressed is a vital part of the work. Indigenous groups are demanding a greater say in research that concerns them, whether under the All of Us program or conducted by individual researchers in Africa. Resolving the ethical ambiguities is no easy task, but, as Hayes asked: "Why should it be easy?"

This article was originally published on undark.org.

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JBC/Tabor award winners to speak at annual meeting

By George N. DeMartino

Winners of the 2020 Journal of Biological Chemistry/Herbert Tabor Early Career Investigator Awards will give talks on April 5 at the American Society for Biochemistry and Molecular Biology Annual Meeting in San Diego.

The awards, named for Herb Tabor, who served as JBC's editor-in-chief from 1971 to 2012, recognize early-career first authors of standout JBC papers published the previous year for their creativity and scientific excellence.

After carefully reviewing nominations from JBC readership, consulting experts in the field and evaluating the quantitative impact of the papers, a committee of JBC associate editors selected six award-winning first authors.

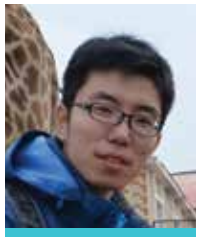
"We are very pleased to celebrate these early-career investigators who have authored top-notch papers in JBC that report exciting and significant research," said Lila Gierasch, distinguished professor at the University of Massachusetts Amherst and editor-in-chief of JBC. "These awardees are outstanding representatives of the future leaders of biological chemistry."

At the ASBMB annual meeting, five of the six award winners will give talks about their research findings, which span a diverse array of topics within biological chemistry. Read more about the five 2020 speakers in the following pages.


Kirstine Lavrsen


Febin Varghese


Cindy Yang


Wenchao Zao


Manisha Dagar

The JBC/Tabor award winners

- **Kirstine Lavrsen**, a postdoctoral researcher with the Danish Cancer Society in Copenhagen, identified an enzyme that converts normal colon into cancerous tissue by attaching sugar to certain cellular proteins.
- **Febin Varghese** was a graduate student at Imperial College London when he discovered the molecular mechanism by which a bacterial oxidase functions via its interaction with another enzyme.
- **Yue (Cindy) Yang** was a graduate student at Weill Cornell Medical School when she discovered that dihydronicotinamide riboside is a critical regulator of the cellular concentration of NAD+.
- **Wenchao Zhao**, a graduate student at the Institute Rheinische Friedrich-Wilhelms-Universität Bonn, developed animal models to reveal how missense mutations of a protein result in pathology.
- **Manisha Dagar**, a graduate student at Amity University Haryana, India, discovered that phosphorylation of HSP90 by protein kinase A is essential for the nuclear translocation of androgen receptor.
- **Ayumi Nagashima-Kasahara** was a postdoctoral scientist at the University of Tokyo when she identified a transcriptional co-repressor that plays a key role in sensing and mediating volatile organic compound signals in plant cells. Nagashima-Kasahara is on maternity leave and will present her work at the 2021 ASBMB annual meeting in Indianapolis.

George N. DeMartino (George.DeMartino@UTSouthwestern.edu) is a professor of physiology at the University of Texas Southwestern Medical Center and a JBC associate editor.

JBC/TABOR AWARD

Lavrsen finds endless possibilities in PTMs

By Nivedita Uday Hegdekar

When she was an undergraduate at the University of Copenhagen, Kirstine Lavrsen became fascinated by the impact of posttranslational modifications, or PTMs, on cellular function. She was working with Hans Wandall's group at the university's glycomics center, researching the role of glycosylation in cancer and how cancer-associated changes in O-glycans could be used to target solid tumors. "So many protein glycosylations are modified in cancer," she said. "The research possibilities were endless."

A native of Denmark, Lavrsen earned her bachelor's and master's degrees in molecular biomedicine from the University of Copenhagen. Pursuing a Ph.D. in cellular and genetic medicine seemed like the natural and best next step, she said, and she continued her doctoral research in Wandall's laboratory.

For her Ph.D., Lavrsen researched the role of O-glycosylation in colorectal carcinogenesis. She identified an important role for a PTM enzyme, GalNAc-T6, in conversion of normal colon tissue into cancerous tissue through its ability to O-glycosylate a small subset of proteins. She then used antibodies targeting cancer-specific O-glycans to distinguish between cancerous and normal tissue and to induce cancer-specific cell death.

"Recent findings show that PTMs have been playing a bigger role in cancer development than earlier thought," Lavrsen said. She hopes that further understanding of PTMs in cancer cells will lead to improved early diagnostic tools, targeted drugs and immunotherapies.

PTMs continue to fascinate Lavrsen. She now works as a postdoctoral researcher in Marin Barisic's lab at the Danish Cancer Society, investigating the role of another PTM, detyrosination of tubulin, during cancer development.

Lavrsen appreciates the analytic and creative blend of research work. When not in the lab, she enjoys spending time with her young children.

This is an exciting time in cancer research, she said, and she is optimistic about where the research will take her.

Kirstine Lavrsen

Sugar-adding enzyme makes colonic cells cancerous

Epithelial cancers are characterized by aberrant expression of O-glycans sugar molecules in cancerous cells. Addition of these sugar molecules is mediated by a post-translational modification — O-glycosylation — through a large family of GalNAc transferases, or GalNAc-Ts.

Analyzing transcriptomic and immunohistochemistry data, Hans Wandall's research group found that GalNAc-T6 was the only GalNAc-T that was highly expressed in colon cancer and was absent from healthy colon tissue. To investigate the specific role of GalNAc-T6 in the development of colon cancer, the group used CRISPR/Cas9 to develop isogenic colon cancer cell lines with a knockout/rescue system for GALNT6. GalNAc-T6 expression was associated with a cancerlike dysplastic growth pattern, whereas GALNT6 knockout cells showed a more normal differentiation and phenotype. Mass spectroscopy identified that GalNAc-T6 targeted a subset of proteins involved in cell-cell adhesion.

This study highlights the importance of a post-translational modification in cancer development, and its publication in the Journal of Biological Chemistry earned Kirstine Lavrsen a Journal of Biological Chemistry/Herbert Tabor Early Career Investigator Award.

Nivedita Hegdekar (nivedita.hegdekar@umaryland.edu) is a graduate student at the University of Maryland working toward a Ph.D. in biochemistry and molecular biology and an M.S. in patent law. Follow her on Twitter @NiveditaHegdek1.

JBC/TABOR AWARD

Varghese roams from forests to enzymes

By Guananí Gómez–Van Cortright

When Febin Varghese is not puzzling out enzyme structures in the lab, there's a good chance he's out on the trail.

"When I was really young, I used to watch a lot of documentaries on National Geographic and Discovery Science and such," Varghese said. "We would watch as a family, and I think that's where it all started."

This early interest in the natural world sparked Varghese's lifelong study of biology both out in the forest and deep inside molecular structures. "I love being in the lab, but I try my best to take breaks," he said. "Something about being in the mountain air, up in the clouds, stepping away to clear your head, is really refreshing."

After earning a doctorate at Cambridge University, Varghese embarked on a 15-month backpacking journey throughout Southeast Asia, Australia and New Zealand.

He then returned to the world of metalloenzymes as a postdoc at the Imperial College of London, where researchers in his lab peered into the mystery of how associated proteins protect nitrogen fixation in the presence of oxygen. The project combined Varghese's interest in energy-conserving metalloenzymes with the potential for long-term environmental applications — an excellent fit. For his contribution to the study as first author on the paper published in the Journal of Biological Chemistry, Varghese won a 2020 JBC/Tabor Award.

"I was very surprised, I wasn't expecting it at all," he said of the award. "It's an honor to be recognized, but a lot of people's work went into this paper. Collaboration is everything in science."

Febin Varghese

Protecting nitrogenase

Nitrogen is abundant in the atmosphere yet scarce in the biosphere; only prokaryotes are equipped with the enzymes necessary to fix atmospheric nitrogen into bioavailable forms. To subvert this limitation and boost crop production, researchers are studying nitrogen-fixing enzymes with the goal of genetically engineering crop plants that can express nitrogenase of their own.

Iron-only nitrogenase, encoded by fewer genes than other nitrogen-fixing enzymes, is a promising candidate for this endeavor. However, it becomes inactive in the presence of oxygen; this barrier must be overcome for it to be expressed functionally in crops.

To explore how the structure of iron-only nitrogenase responds to oxygen, Varghese and colleagues at the James W. Murray lab at the department of life sciences at the Imperial College of London investigated the structure and oxygen-reducing role of Anf3, a protein associated with nitrogenase function.

By characterizing the crystal structure of Anf3 at atomic resolution, the team saw that its heme and flavin adenine dinucleotide cofactors were unexpectedly close to each other.

"The structure itself was a surprise," Varghese said. "We knew (Anf3) had a heme and an FAD cofactor, but that they were so close together and that there was a cooperative effect was unexpected."

Further experiments suggested that electron transfer between the two cofactors contributes to Anf3's ability to reduce oxygen, thus protecting iron-only nitrogenase from being inactivated. Anf3 protein is a promising candidate for enhancing functional nitrogenase in aerobic environments.

Guananí Gómez–Van Cortright (guananigvc@gmail.com) is a recent Reed College graduate, outdoor educator and science teacher.

JBC/TABOR AWARD

Yang follows the science where it takes her

By Elizabeth Stivison

Yue (Cindy) Yang grew up in a university environment in her home country of China, and from a young age she pictured herself as a professor at a university. Her father is a mechanical engineering professor and her mother is a dentist, and both helped inspire her to seek a life of science, though her inspiration is also internal.

"I've always loved science," Yang said, "especially biology."

After earning a bachelor's degree from the Chinese University in Hong Kong, Yang wasted no time in continuing her education and moved to the U.S. to get her master's. She chose the University of Nebraska so she could study with Ji-Young Lee in the nutritional sciences department. Yang was drawn to the lab's astaxanthin work, and she enjoyed Lee's mentorship so much that when Lee moved to the University of Connecticut, Yang followed, joining the Ph.D. program there and continuing her work in the lab.

During her Ph.D., Yang studied the health effects of astaxanthin, an antioxidant carotenoid compound found in algae. She thrived in the lab, loving the freedom to follow the science.

"Sometimes you go into a lab and everything is established, and you just follow and do what everyone has been doing," she said. "But when I was in Dr. Lee's lab, we'd have to find what the next step is and decide for ourselves what to do. It was a great experience."

She took these skills into her postdoctoral fellowship at Weill Cornell Medicine, where she studies NAD+ metabolism in Anthony Sauve's lab and recently was promoted to instructor. That young girl who always saw herself as a professor seems to be well on her way, following where the science takes her.

Cindy Yang

A new pathway to increase cellular NAD+

Cindy Yang finds the work in Anthony Sauve's lab incredibly exciting. The innovative and collaborative environment in the lab allows her to dive deep into the NAD+ field with all its nuance and potential to improve human health.

The job of NAD+ is to transfer a hydrogen from one molecule to another. This central activity means that NAD+ is a cofactor for over 500 enzymatic reactions in the cell and is essential to life. Researchers now see that modulating cellular NAD+ levels can have wide-ranging effects in the cell and in the whole body, such as preventing metabolic syndrome and neurodegeneration; it may even slow aging in general. This has inspired many clinical trials and patents, but with typical compounds that increase NAD+ in the cell, the dosage required to see any effect is extremely high.

Yang and her colleagues discovered that a new compound, dihydronicotinamide riboside, or NRH, increases NAD+ levels in cultured cells to an unprecedented level with a lower dose and in as little as an hour. NRH also appears to act as a precursor to NAD+ through a novel pathway. While a novel pathway means a lot of work must be done to find out what exactly is happening in the cells, this new work is opening the door to increasing our understanding of NAD+ metabolism and its effects on human health and may lead to efficient modulation of NAD+ in the clinic.

Elizabeth Stivison (elizabeth.stivison@gmail.com) is a postdoc at Columbia University studying mechanisms of DNA repair and a careers columnist for the ASBMB.

JBC/TABOR AWARD

Selenium led Zhao from icy hometown to German hospitality

By Nathalie Gerassimov

Wenchao Zhao is fascinated by selenium or, more accurately, what happens when it is lacking.

A trace element in soil, selenium is an essential nutrient for many species, including humans. Its deficiency is associated with Keshan disease, a cardiomyopathy first identified in the Keshan county of Heilongjiang province in northeastern China, bordering Russia. Zhao's hometown is Harbin, the capital of that province, a city of more than five million people known for cold weather and the world's biggest ice festival.

Keshan disease used to be widespread in China, especially in Heilongjiang province, before the government started a selenium supplementation program in the 1970s. Research into the mechanism of selenium action in physiology remains important, not least because a form of thyroid disease is caused by mutations in the selenium pathway.

Zhao decided to study the effect of selenium deficiency using chickens when he was doing master's degree research in his hometown. This descriptive research prompted him to seek laboratories studying the molecular mechanism of selenium action. Ulrich Schweizer's lab at the University of Bonn's Institute of Biology and Molecular Biology was a perfect fit, although Zhao spoke no German.

Zhao describes himself as "super lucky" to have Schweizer as his mentor. In addition to tutoring him in the lab, Schweizer helps him adapt to his unfamiliar German life. When Zhao couldn't find an apartment right away, he lived at Schweizer's house for his first month in Bonn.

Zhao is now writing his Ph.D. dissertation and hopes to finish his degree this spring. He doesn't have firm post-graduation plans; learning to manipulate sequencing data from his research is a short-term goal.

When not working in the lab or playing basketball or soccer with his friends, Zhao is learning German. His favorite and most-used phrase is "Alles gut" — all is well.

Wenchao Zhao

Tissue-specific stability of key regulator of selenoprotein synthesis

Selenoproteins, characterized by the presence of selenocysteine, the 21st amino acid containing selenium in its sidechain, are essential to human health. Their main roles are in the antioxidative response and thyroid function. Not surprisingly, selenoprotein deficiency is associated with cancers, heart disease and neurodegeneration.

The biosynthesis of selenoproteins relies on selenocysteine insertion sequence-binding protein 2, or SECISBP2. Human mutations in SECISBP2 associate with clinical phenotypes of variable severity. Wenchao Zhao's research, published in the Journal of Biological Chemistry and selected for the JBC/Herbert Tabor Early Career Investigator Award, investigated the effect of two human mutations using mice.

Zhao and his colleagues found that while one mutation behaves like a null allele, the other shows a different phenotype in the liver and the brain. Specifically, the R543Q mutant of the SECISBP2 protein is unstable and undetectable in liver but retains residual function in brain.

Zhao's research contributes to our understanding of why so many diseases of ubiquitous proteins affect specific organs, he said. "A mutation may not be equally detrimental in every cellular context, since cellular context can affect the stability of that protein."

Nathalie Gerassimov (nathalie.gerassimov@gmail.com) is a postdoctoral researcher at the Carnegie Institution of Washington Department of Embryology.

JBC/TABOR AWARD

Dagar dissects a prostate cancer driver

By Alyson Smith

Many cancer treatments block hormones that drive tumor cell division and metastasis. These therapies only shrink tumors temporarily, however, as cancer cells can use alternative signaling pathways to reduce their hormone dependence. Drugs that target these pathways may halt tumor growth and extend patient survival.

Manisha Dagar has uncovered the details of a signaling pathway that drives advanced prostate cancer.

Dagar has always been interested in science, especially biology. Her mother encouraged her to pursue higher education and a research career. She earned an undergraduate degree in biotechnology, and a summer internship at the National Centre for Disease Control in New Delhi gave her the lab experience she needed to pursue a Ph.D. at Amity Institute of Biotechnology, Amity University in Haryana, India.

At Amity University, Dagar decided to study the molecular biology of cancer. She joined Gargi Bagchi's lab where she studies androgens, the male sex hormones, in prostate cancer. Previous research revealed that protein kinase A, which phosphorylates proteins to change their functions, can activate androgen signaling in the absence of hormones. Dagar and colleagues in the lab discovered how this aberrant activity contributes to prostate cancer progression.

Dagar studied protein kinase A function in a cell line derived from a prostate cancer patient. After optimizing protocols to measure protein levels in these cells, Dagar could track how blocking protein kinase A phosphorylation activity changed androgen signaling. Her work has revealed new drug targets that could treat advanced prostate cancer.

Dagar successfully defended her Ph.D. thesis in January. She hopes to pursue postdoctoral research studying cell signaling. Outside the lab, she enjoys reading and traveling.

Manisha Dagar

Targeting molecular chaperones to stop prostate cancer

Testosterone and related androgen hormones act through the androgen receptor, which is stabilized in the cytoplasm by the molecular chaperone HSP90. When the receptor binds an androgen, it releases HSP90 and enters the nucleus to regulate gene expression. Androgens thus direct the development and maintenance of the prostate gland but also drive prostate cancer.

Manisha Dagar and her colleagues knocked down protein kinase A to learn how this enzyme affects androgen receptor nuclear entry. They discovered that protein kinase A phosphorylates HSP90, causing it to release the androgen receptor. The receptor then binds HSP27, a different molecular chaperone, which helps it enter the nucleus. Once in the nucleus, the receptor can bind certain DNA regions to turn on genes.

Blocking protein kinase A activity blocked testosterone-induced HSP90 phosphorylation, androgen receptor-HSP90 dissociation, androgen receptor-HSP27 binding, androgen receptor nuclear entry, changes in gene expression and increase in proliferation of prostate cancer cells.

"By targeting HSP90 phosphorylation by protein kinase A, androgen signaling in prostate cancer cells can be blocked," Dagar said. "This can be used as a therapeutic target for treatment of prostate cancer."

As first author on the paper reporting this research, Dagar received a 2020 Journal of Biological Chemistry/Herbert Tabor Early Career Investigator Award.

Alyson Smith (alysonscsmith@gmail.com) is a recent Ph.D. graduate from Scripps Research in La Jolla, California. Follow her on Twitter @cellbionerd.

Attending a conference when you don't have the budget

By Bonnie L. Hall, Rebecca Roberts, Julia Koeppe & Paul A. Craig

Attending the American Society for Biochemistry and Molecular Biology Annual Meeting or any professional conference can be rewarding but expensive. Here are a few ideas to manage costs, to help those professional development dollars go as far as possible. It might be too late to take some of these steps for the ASBMB meeting in San Diego this April, but keep them in mind for other meetings and for ASBMB 2021 in Indianapolis.

Registration and other meeting costs:

Register by the early-bird deadline. If you're not a member of the host society, consider joining; the reduction in registration costs is often more than the cost of membership.

Volunteer. If you help to put on the conference, you might get a partial or full waiver of your conference fee and maybe some free meals.

Apply for travel awards from the host society. These often have early deadlines, so pay attention.

If you're traveling with infants or children, ask about free childcare on site (slots are often first-come first-served, so plan ahead).

Lodging:

Pick a hotel a mile from the conference center that includes breakfast. The nightly rate will be less because of the distance, and you won't have to pay for one meal each day.

Consider finding lodgings on Airbnb, VRBO or HomeAway. You might find a room or an apartment closer to the conference center than the conference hotel at the same price as a hotel a mile away. If you're traveling with a group from your campus or company, several of you could share the space.

Have a roommate (or if you rent a house, multiple roommates) at the conference. Some conferences provide roommate matching services if you are attending alone.

Consider staying with a friend or relative who lives in the city.

Connect with people from other labs or institutions; attendees from multiple groups can stay together to reduce costs.

Meals:

Attend the opening ceremony. Often, it includes a buffet of some sort. It's not gourmet food, but it's not bad. Sometimes, there's even free beer and wine.

Look for free food breaks. At many conferences, finger foods or snacks are served in the midmorning or midafternoon.

Stay somewhere with a refrigerator and microwave; stock up at a local grocery store, then carry your lunch. You can have fresh fruits, beverages and sandwiches for less than half of what you would pay at a restaurant. Remember to bring reusable utensils and a plate or bowl to make this option less frustrating.

Grocery stores often have hot buffets where you can get an inexpensive dinner plus a few meals to reheat in your room later if you have a microwave.

Pay attention to the vendors. Sometimes they host workshops that include meals.

Pay attention to workshops that are part of the meeting. If they start at noon, trays of sandwiches or fruit might be included.

Get out of the conference center for breakfast and/or lunch. Picking up coffee or a sandwich on your way to or from the meeting is often substantially less expensive than on-site food options. Walk a couple of blocks away to find cheaper restaurants with shorter wait times (lots of conference attendees will go to the place across the street).

If you stay at a hotel, ask about a concierge level for your stay. This might cost a bit more, but it often includes breakfast, snacks, beverages and evening hors d'oeuvres. So meal costs are almost zero.

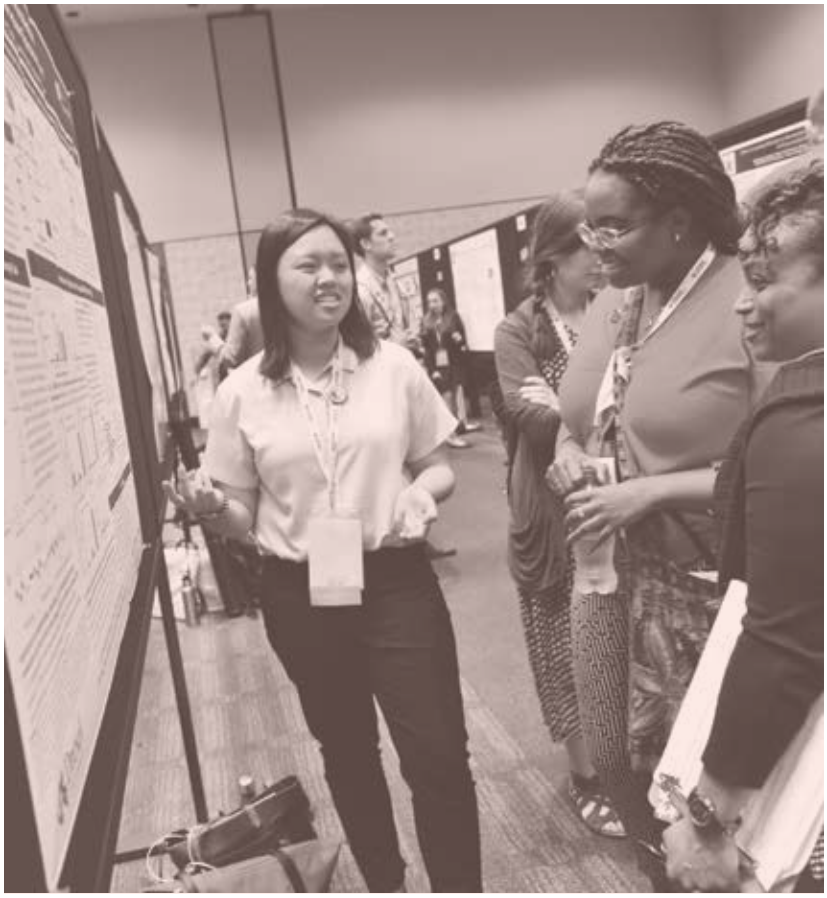
Bring a refillable water bottle and hit the water fountain (both in the airport and at the convention center). Fill your own reusable coffee mug at the meeting coffee/tea breaks.

If you have dinner out with colleagues, don't be shy about asking for a take-home bag for leftovers and avoiding pricey drinks. Politely ask for a separate check (use the excuse of institutional reimbursement rules) to avoid the dreaded "let's split the bill."

If you've brought children with you, look for restaurants with kids-eat-free options.

Airfare and transportation:

Purchase your plane ticket well in advance. This is especially advisable if



ASBMB

you're flying on Southwest Airlines. You also can use Google Flights to track ticket prices.

Bring good walking shoes and enjoy the chance to move while walking to the conference site.

Look for a hotel on a bus or trolley line or one with a free shuttle.

If you've been invited to speak at a nearby university, try to schedule the visit around the conference time to combine travel costs.

Research how to get from your home to the airport: catch a ride, use public transportation or find less expensive off-site airport parking.

Find out how to get from the airport to the hotel; public transportation or a hotel shuttle service will be the least expensive. Coordinate sharing taxi rides with others to reduce costs. Introduce yourself to people with poster tubes at the luggage carousel — they often are going to the same conference and can share ride costs.

If your funding is limited, these ideas should help make attending a conference more accessible. We hope this means we'll meet you at a conference social or in the airport luggage claim area.

Note: The authors are all members of the BASIL Consortium (https://basilbiochem.github.io/basil/) at various points in our careers as educators and researchers. We are located on small and large campuses, public and private institutions, primarily undergraduate institutions as well as those with M.S. and Ph.D. programs.

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A beginner's guide to minority professor hires

By Michael D. L. Johnson

What makes a good principal investigator? What makes a great one? Often, there is a certain mold that hiring committees look for in applicants. By and large, the first two cutoffs are funding and great papers. However, most of us in the professoriate do more than acquire grants and submit papers. We advise students, sit on committees and teach — all things that are essential to being a successful professor because they show that you can juggle more than just science.

Many underrepresented minorities, or URMs, take on a lot of those intangible items, not only because people ask us to serve in a multitude of areas for the sake of having representation, but because we also want to be that representation. As a postdoctoral fellow looking to be hired as an assistant professor, I performed service, mentoring, teaching and more. Doing some of these intangible activities can make it hard to measure current and future success as a principal investigator, and thus, may be a major problem facing URMs looking to join a research-intensive professoriate.

We advise students, sit on committees and teach — all things that are essential to being a successful professor because they show that you can juggle more than just science.

How are these intangible activities scored during a faculty application review? When in the process are they scored? Are they scored?

The argument against looking deeper into the pool of applicants is that it takes time, money and lots of effort. Hundreds of applications have to be distilled down to five or so people to interview in person. Practicality has to be valued, especially given the juggling act of being a professor with so many things to do. How does an institution that wants to add more URM faculty do so?

The increasing number of URM doctorates hasn't been reflected in URM faculty hires. Despite a 930% increase in URM Ph.D.s since 1985, there has been no significant change in the percentage of URM biomedical professors at research-intensive universities. The best solution is to hire more URMs, but no unilateral solutions to do so exist or they would have been implemented already. Given this information, here are some things I propose that might help faculty searches increase their URM faculty candidates:

- Recognize and evaluate the intangibles of prospective professors.
  - Talk with and seek advice from minority professors at your institution and ask them what their background was, how they got recruited and what made them feel more welcome at one place over another. Let this be the start of the conversation, not the end.
- Identify URM individuals and encourage them to apply for open positions at your university. A selection of databases to look through includes:
  - Awardees of the Hannah Gray Award from the Howard Hughes Medical Institute
  - Awardees of the National Institutes of Health Blueprint Diversity Specialized Predoctoral to Postdoctoral Advancement
  - Awardees of the Ford Postdoctoral Fellowship
  - Awardees of the Burroughs Wellcome Fund Postdoctoral Enrichment Program
  - MinorityPostdoc.org
  - Diversify Microbiology
  - Diversify EEB (Ecologist and Evolutionary Biologists)
  - Diversify Immunology
  - Diversify Chemistry
- Share job openings within groups and communities that commonly self-identify on social media, such as #BLACKandSTEM, LatinxandSTEM and #diversityinSTEM.
- Create university initiatives to encourage or facilitate minority hires, such as having a designated slot to hire a URM faculty. Add to the prestige by naming it after a donor.
- Align your department/institution as a place that values diversity by making public statements on your

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webpage about diversity.

- Require new hires to submit a diversity statement with their application and make it a part of the decision-making process. It helps to surround yourself with people who value diversity.
- Re-evaluate what kind of candidate you are looking for and see if it excluded the people you talked to in the first bullet point.
- Provide URMs with a platform to present their research by inviting them to a research seminar.

Overall, as an institution, you must be willing to spend money and time for these efforts because, after all, commitment without currency is counterfeit.

This article first appeared on the American Society for Microbiology's website, asm.org

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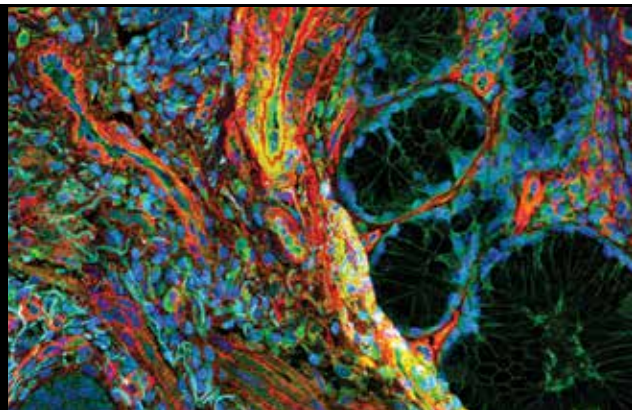


Upcoming ASBMB events and deadlines

FEBRUARY

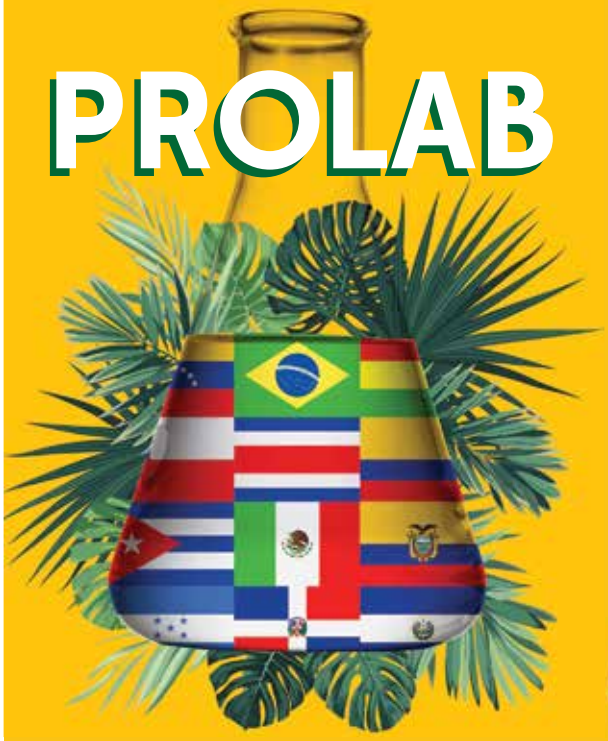
14 Deadline for ASBMB Outstanding Chapter Award applications
19 Deadline for ASBMB–Deuel Conference on Lipids registration
29 **Rare Disease Day**

MARCH

National Colorectal Cancer Awareness Month
1 Deadline for Student Chapters Outreach Grant
3–6 ASBMB–Deuel Conference on Lipids meeting

APRIL

World Parkinson's Awareness Month
4–7 2020 ASBMB Annual Meeting held in conjunction with Experimental Biology
25 **World Malaria Day**



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CLASSIFIEDS

Tenure Track Faculty Positions
Vanderbilt University,
Tennessee, United States

The Department of Molecular Physiology & Biophysics (MPB) at Vanderbilt University invites applications for a tenure-track faculty appointment. MPB has a long and distinguished scientific history and currently has 23 primary faculty members with active research programs studying biophysics, gene regulation, genetics, membrane transport, metabolic/endocrine disorders, neuroscience, signal transduction, single-cell biology, and structural biology. Applicants must have a Ph.D. and/or M.D. degree and an outstanding record of scholarly achievement that demonstrates the potential to establish a highly productive and innovative research program. A generous start-up package will be provided to facilitate cutting-edge investigations into fundamentally significant biomedical research questions.

https://careers.asbmb.org/jobs/view/tenure-track-faculty-positions/52487077/

Postdoctoral Fellow
Yale, New Haven,
Connecticut, United States

Postdoctoral positions are available in the Ben Mamoun Laboratory at Yale to study the agents of human malaria and babesiosis and their interactions with their mammalian hosts and arthropod vectors. Ph.D., M.D./Ph.D. and MD candidates with strong experience in the fields of cellular, molecular biology, genetics and biochemistry are encouraged to apply. Yale University offers a competitive postdoctoral salary, a comprehensive benefits package, and an excellent work environment.

https://careers.asbmb.org/jobs/view/postdoctoral-fellow/52892325/

Biology Tenure Track Faculty
IUPUI, Department of Biology,
Indiana, United States

The Department of Biology at Indiana University–Purdue University Indianapolis (IUPUI) invites applications for a tenure-track faculty position at the assistant professor level, but appointment at a more senior level is possible for applicants with suitable experience to begin August 1, 2020. Competitive salary and start-up funds are available. A Ph.D. and postdoctoral experience are required. Applicants must demonstrate the ability to initiate and sustain an externally funded program of research, dedication to effective student mentoring and the ability to teach courses at the graduate and undergraduate levels. Applicants at a senior level must have an established record of research excellence and external funding, and a demonstrated commitment to mentoring students. Candidates able to contribute to teaching in microbiology and biochemistry are particularly welcome. Research strengths in the department span a range of topics in cellular, molecular, developmental and neuro- biology.

https://careers.asbmb.org/jobs/view/biology-tenure-track-faculty/52487080/

Postdoctoral Research Fellow
University of Connecticut,
Farmington, Connecticut, United States

An NIH funded postdoctoral research position is available immediately in the Weller lab in the Department of Molecular Biology and Biophysics at the University of Connecticut School of Medicine in Farmington CT. The Weller lab uses biochemical, biophysical and molecular genetic approaches to study the mechanisms and enzymology of DNA replication in Herpes Simplex Virus. HSV infects almost 70% of the world's population, and we have discovered that this important viral pathogen has evolved an unusual replication strategy that uses recombination-dependent replication to produce progeny genomes. Our newly funded R01 focuses on a virally-encoded ssDNA binding protein that plays many roles during viral DNA replication, participating protein-protein interactions necessary for the initiation of DNA synthesis, the cooperative binding to ssDNA, filament formation and the annealing of complementary ssDNA.

https://careers.asbmb.org/job/postdoctoral-research-fellow/52783956/

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

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