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ASBMB TODAY

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

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Looking back and ahead

Invited speakers

Scientific symposia

American Society for Biochemistry and Molecular Biology

Discover BMB | 2023

SEATTLE | MARCH 25-28

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American Society for Biochemistry and Molecular Biology

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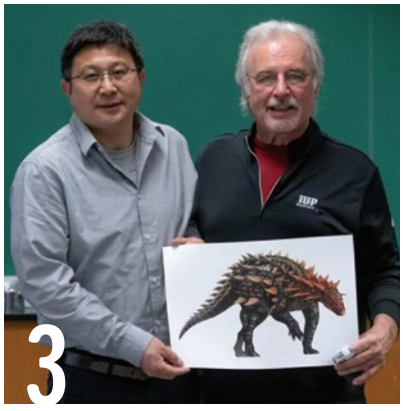

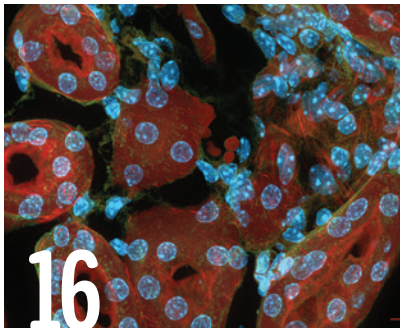

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ASBMBTODAY
THE MEMBER MAGAZINE OF THE AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

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Something for everyone at Discover BMB

By Ann Stock

When I was a junior faculty member, I hesitated to bring students to scientific conferences until they were well along in their research and had a mostly complete story to present. An experience with a grad student in my lab made me rethink this policy.

Presenting a poster sparked this trainee to feel like he owned his research. This student, who previously had sought to be led through every experiment, returned from the meeting brimming with ideas for his next experiments and suggestions for collaborations he had discussed with visitors to his poster. I learned that presenting research at a scientific conference can transform a student.

Now it's time for us to look ahead to the 2023 ASBMB annual meeting, Discover BMB, to be held in Seattle March 25–28. The deadline for abstract submissions and travel award applications is Nov. 30 — just two months away.

For some meeting and society history, see Vahe Bandarian's article on page 31 of this issue. #DiscoverBMB will be the society's first independent annual meeting in recent years. It is an important opportunity for students and postdocs who were unable to attend in-person scientific conferences during the first two years of the pandemic. If the vibrancy and energy of grad students I witnessed at two recent university-sponsored symposia are an indication, trainees are eager to present their research and gain feedback on their projects.

Check our meeting website, discoverbmb.asbmb.org, for abstract submission instructions and information about travel awards for first authors presenting research. The 2023 Program Planning Committee and the Meetings Committee will review abstracts with authors anonymized to minimize the potential for bias. They will schedule poster sessions and select abstracts for talks in 53 spotlight sessions. Abstracts will be published in a supplement to the Journal of Biological Chemistry. Don't forget to join the society or renew your membership to secure the reduced rate for abstract submission.

We'll emphasize opportunities for networking at #DiscoverBMB. The exhibit hall will be configured as a central hub for interactions, with continuous events, including:

- Opening welcome reception.
- Intermingled scientific posters and exhibit booths.
- Dedicated time for scientific poster sessions (with refreshments).
- Meet the Experts sessions with several of the day's speakers.
- Career-development and mentoring events.
- Job postings, with opportunities for candidate interviews.
- Meetup areas for scientists with similar interests.

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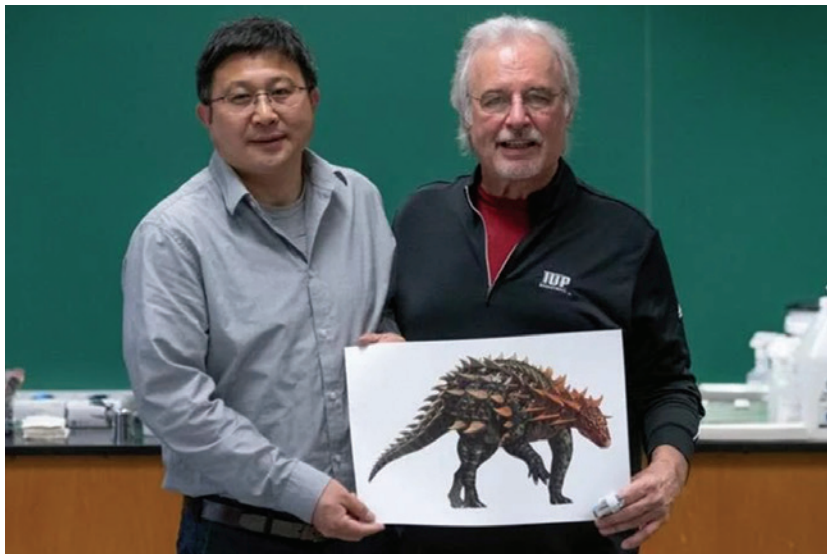
Dinosaur named for Kopchick



COURTESY OF INDIANA UNIVERSITY OF PENNSYLVANIA

Shundong Bi and John Kopchick hold a picture of the new species of dinosaur, Yuxisaurus kopchicki.

John Kopchick, a molecular biologist at Ohio University, didn't become a philanthropist in order to get a dinosaur named after himself. In fact, when he learned it was happening, he told the colleague who gave him the news, "Get out of here."

After Indiana University of Pennsylvania and Yunnan University professor Shundong Bi, a paleontologist who focuses on the early evolution of mammals, discovered a new species of armored dinosaur, he dubbed it Yuxisaurus kopchicki. Bi was motivated by a $23 million donation Kopchick made to IUP in 2018 to support construction of a new math and science center and student research.

Bi also is known for discovering the first fossil of a dinosaur brooding a nest of fossilized eggs, a find he and colleagues reported in 2019.

The honor is "one of the most remarkable and certainly unusual recognitions I've ever received," Kopchick told the Indiana Gazette, the IUP newspaper. "I am very proud and humbled to have a dinosaur with my name … wow!"

Kopchick earned his bachelor's and master's degrees from IUP and made his millions in biotechnology. After earning a Ph.D. in virology from the University of Texas Graduate School of Biomedical Sciences in Houston, he spent several years in industrial research at the Roche Institute of Molecular Biology and the Merck Institute of Therapeutic Research. He studied growth hormone and continued that line of research when he accepted an endowed professorship and became a principal investigator in the Ohio University Edison Biotechnology Institute, focusing his studies on growth, diabetes and obesity. Eventually, his lab identified a growth hormone receptor antagonist that was used to develop the drug Somavert, which is used worldwide to treat patients with acromegaly, an endocrine disorder caused by excess growth hormone secretion.

In the Indiana Gazette interview, Bi and Kopchick expressed great mutual respect and interest in working together on Jurassic growth hormones.

CONTINUED FROM PAGE 2

- Exhibitor panel discussions on industry careers.
- Games, raffles, prizes and other fun activities.
- Community outreach day for K–12 students and teachers.

The exhibit hall will be configured to maximize opportunities for interactions with exhibitors. Aside from the always-popular snacks and swag at the booths, exhibitors give researchers the latest information about new products and instruments, emerging technologies, and educational tools. And with so many early-career researchers able to meet face-to-face with representatives from the companies most relevant to BMB research, the exhibit hall provides a rich networking environment for prospective employees and employers.

Researchers — it's time to submit abstracts. Exhibitors — it's time to reserve booths. Everyone — mark your calendars. We hope you plan to come to Seattle and #DiscoverBMB in spring 2023!

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

Named chair for Schiffer at UMass

Celia A. Schiffer, a professor and chair of the biochemistry and molecular biotechnology department and director of the Institute for Drug Resistance at the University of Massachusetts Chan Medical Center, has been appointed the Arthur and Helen Koskinas professor of biochemistry and molecular biotechnology.

SCHIFFER

Schiffer's research focuses on the molecular bases of resistance, studying how mutations in drug target enzymes allow them to continue to bind their endogenous substrates but avoid binding inhibitors. This perspective on enzyme–ligand binding and defining what she calls the "substrate envelope" allows her lab and others to design robust antivirals that are less apt to be susceptible to resistance. She received the William C. Rose Award from the ASBMB in 2020 and is a fellow of the American Academy of Microbiology.

This endowed chair is one of two named for the late attorney Arthur Koskinas, who was a board member at the University of Massachusetts Memorial Foundation before his death in 2003, and his widow Helen Koskinas, who also has served as a University of Massachusetts Memorial Foundation board member in addition to extensive charitable work.

Gentry to chair UF BMB department

Matthew Gentry, until lately a professor of molecular and cellular biochemistry at the University of Kentucky College of Medicine, has been appointed chair of the biochemistry and molecular biology department at the University of Florida College of Medicine.

Gentry studies glycogen metabolism and how it goes awry in cancer and neurodegenerative disorders. Much of his early work focused on Lafora disease, a rare genetic disorder that causes progressive epilepsy beginning in adolescence. Lafora disease begins with the accumulation of insoluble polysaccharides in neurons and astrocytes. In collaboration with multiple groups and companies, Gentry's laboratory has developed several potential therapeutic approaches for Lafora disease. He has worked with patients and their families to organize scientific meetings sponsored by a patient advocacy group called Chelsea's Hope.

GENTRY

Gentry earned his Ph.D. at Syracuse University and was a postdoc at the University of California, San Diego, with Jack Dixon before joining the University of Kentucky faculty. He is a member of the American Society for Biochemistry and Molecular Biology Council, former chair of the ASBMB's Public Affairs Advisory Committee, and a member of the Journal of Biological Chemistry editorial board.

Greer joins V Foundation

Susanna Greer, until recently a senior scientific director at the American Cancer Society, has assumed a new position as the chief scientific officer at the V Foundation for Cancer Research, a North Carolina–based nonprofit. She is working with the foundation's scientific advisory committee to set funding priorities.

GREER

Greer earned her Ph.D. in microbiology and immunology at the University of Alabama at Birmingham and was a postdoc at the University of North Carolina at Chapel Hill. She spent just over 10 years as a professor studying cancer epigenetics at Georgia State University, earning tenure before she started a scientific communication consultancy and transitioned into the nonprofit world.

Greer serves on the Council and the Finance Committee of the American Society for Biochemistry and Molecular Biology and was named an ASBMB fellow earlier this year. She also has served on several National Cancer Institute committees and was previously chair of the ASBMB committee on outreach and science communication.

Rossjohn named Royal Society fellow

Jamie Rossjohn, a professor of biochemistry and molecular biology at the Biomedicine Discovery Institute, Monash University, Australia, is one of 60 scientists from around the world who recently were elected fellows and foreign members of the Royal Society.

Rossjohn, a 2022 fellow, studies immunity, disease and the vertebrate host response. His lab has used structural biology to understand how T cell receptors recognize peptides, lipids and metabolites. They have found structural mechanisms of major histocompatibility complex polymorphism that affect viral immunity, drug and food hypersensitivities, and

T cell–mediated autoimmunity. Rossjohn has pioneered molecular understanding of how T cells bind lipid-based antigens presented by the CD1 family and has provided a structural basis for how vitamin B metabolites can be presented and recognized by the immune system, revealing a new class of antigen.

Rossjohn has held research fellowships with the Australian Research Council and National Health and Medical Research Council. He is a fellow of the Australian Academy of Science,

ROSSJOHN

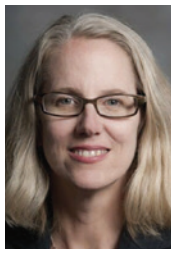
the academies of medical sciences in the U.K. and Australia, and the Learned Society of Wales.

The Royal Society, founded in the 1660s, is the oldest continually existing scientific academy in the world, and the work of its fellows and foreign members spans many disciplines.

Gillaspy appointed dean at UW

The University of Wisconsin–Madison has named Virginia Tech biochemistry professor **Glenda Gillaspy** the next dean of the UW College of Agricultural and Life Sciences.

Gillaspy earned an undergraduate degree from Auburn University and her Ph.D. in biochemistry from Case Western Reserve University and then was a National Science Foundation postdoctoral fellow at the University of California, Berkeley. She became a professor of biochemistry in the College of Agriculture and Life Sciences at Virginia Tech in 1998. After she was appointed head of the biochemistry department in 2015, the number of graduate students doubled, and she developed a mentoring program to attract and retain new faculty.



GILLASPY

In Gillaspy's lab, her research program focuses on the molecular pathways plants use to respond to the environment, an area important for developing strategies to increase crop yield and mitigate phosphates in the environment. One area of interest is a collaborative project on inositol pyrophosphate signaling molecules, which play a critical role in phosphate sensing. Her lab's outreach programs have included a plant stress exercise for local fourth graders and an authentic inquiry project with thousands of ninth-grade students at James Madison High School.

Gillaspy is excited to join the UW community, she said in an article in the UW News, noting that the College of Agricultural and Life Sciences has a unique history and composition of departments and programs. "These qualities position the college to take a preeminent role in solving complex problems facing our society with respect to food, health and sustainability," she said, "and to provide critical educational programs and experiential learning for our students."

Decker joins Valneva science board

Thomas Decker, a member of the editorial boards of the Journal of Biological Chemistry and Molecular and Cellular Biology, has been appointed to the scientific advisory board of Valneva SE, a maker of specialty vaccines, the company announced recently.

Decker is a professor of immunobiology at the Max Perutz Labs of the University of Vienna. He earned his Ph.D. at the Albert Ludwig University in 1986 and conducted postdoctoral research at the Fraunhofer Institute of Toxicology and Rockefeller University. After short stints on the faculties at the Fraunhofer Institute and the Karolinska Institute, he took a position in 1993 at the University of Vienna, where he served as chair of the microbiology and genetics department from 2001 to 2009 and became a full professor in 2002.

Decker, an immunologist, studies signaling by a group of cytokines called interferons, which activate the innate immune system's JAK/STAT signaling pathway to alter gene expression. For three decades, his lab has investigated the wiring of the JAK/STAT signaling pathway and other interferon responsive signal transduction cascades, immune cells' transcriptional and chromatin responses to those signals, and how intracellular bacteria co-opt host signaling pathways.

DECKER

In addition to JBC and MCB, Decker has served on the editorial boards of the Journal of Clinical Investigation and the Journal of Immunology and as editor for Medical Microbiology and Immunology. He has been president of the European Society for Macrophage and Dendritic Cell Research since 2018.

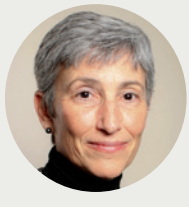
Valneva is a multinational company focused on developing vaccines for infectious diseases with significant unmet medical needs, including Lyme disease, COVID-19 and chikungunya.

AAAS inducts new members

The American Academy of Arts and Sciences has announced its 2022 inductees. The organization, founded in 1780, honors members who work in science, education, the arts and global affairs. Its members also meet to tackle problems such as accelerating climate action, improving the relationship between science and the public, and strengthening international research partnerships. Three of this year's inductees are members of the American Society for Biochemistry and Molecular Biology: Mariano Garcia–Blanco, Rachel Klevit and Aviv Regev.

Mariano Garcia–Blanco is a professor and distinguished chair in biochemistry and molecular biology at the University of Texas Medical Branch at Galveston and an adjunct professor at the Duke–National University of Singapore Medical School. His lab is known for its research on RNA-binding proteins in infection and immunity. They have identified numerous RNA-binding proteins that affect the replication of flaviviruses such as dengue, yellow fever and Zika. They also have studied the role of RNA helicase DDX39B in alternative splicing of the interleukin-7 receptor, which affects some autoimmune disorders such as multiple sclerosis.

Garcia–Blanco earned his M.D. and Ph.D. at Yale University and was a postdoctoral researcher at the Massachusetts Institute of Technology. He has founded five companies and is a member of the Association of American Physicians and a fellow of the American Association for the Advancement of Science and the American Academy of Microbiology.



Rachel Klevit is a professor of biochemistry, with secondary appointments in pharmacology and chemistry, at the University of Washington. Her lab uses structural biology techniques including nuclear magnetic resonance and hydrogen–deuterium exchange mass spectrometry to characterize proteins involved in ubiquitylation and protein chaperone activity. They are interested in the E3 ligase domain of the protein BRCA1, mutations in which can predispose carriers to breast cancer, and the protein BARD1, which functions in tandem with BRCA1. They also study small heat shock proteins, with particular interest in disordered or "fuzzy" binding.

Klevit earned her D.Phil. on a Rhodes scholarship at Oxford University and was a postdoc at Duke University. Among her awards are the ASBMB's Fritz Lippmann Award and the Protein Society's Dorothy Crowfoot Hodgkin Award; last year, she was elected to the National Academy of Sciences.

Aviv Regev is an executive vice president and head of Genentech Research and Early Development. Regev, a computational biologist, is known for her contributions to single-cell genomics. Her lab leads several major systems biology projects and has developed new experimental and computational methods for massively parallel RNA sequencing to understand cellular regulatory networks. She co-leads the Human Cell Atlas initiative with Sarah Teichmann.

Regev earned her Ph.D. at Tel Aviv University and was an independent Bauer fellow at Harvard University. Before transitioning to Genentech, she was a Howard Hughes Medical Institute investigator, a professor of biology at the Massachusetts Institute of Technology, and a core member of the Broad Institute of MIT and Harvard. Among her many honors are the ASBMB's Earl and Thressa Stadtman award, the Federation of American Societies for Experimental Biology Excellence in Science Award, and membership in both the National Academy of Sciences and the National Academy of Medicine.

Michael Gottlieb

Michael Gottlieb, a global health researcher and a member of the American Society for Biochemistry and Molecular Biology since 1989, died April 27, 2021, the ASBMB learned recently. He was 76 and had cancer.

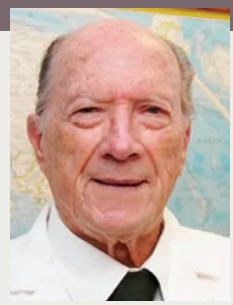
Born Oct. 18, 1944, Gottlieb earned his Ph.D. in biology from the City University of New York. He conducted postdoctoral research in the bacterial physiology unit of the Harvard Medical School and in the Laboratory of Parasitic Diseases at the National Institute of Allergy and Infectious Diseases. In 1978, he joined the faculty of the Johns Hopkins University School of Hygiene and Public Health, where his research focused on the biochemistry and cell biology of pathogenic trypanosomatid protozoa, which cause African sleeping sickness and other plant and animal diseases.

In 1991, Gottlieb returned to the NIAID as program officer in the Parasitology and International Programs Branch of the Division of Microbiology and Infectious Diseases. A decade later, he was named chief of the branch. He managed NIAID grants on parasite biology, coordinated the institute's network of international centers for tropical disease research and represented the institute in its support of the Multilateral Initiative on Malaria. He initiated the NIAID pathogen genomics research program and helped create an environment and translational research program that accelerated development of molecular diagnostics and therapeutic interventions for parasitic diseases.

Gottlieb retired from the NIAID in 2004 and joined the Foundation for the National Institutes of Health as associate director for science. As a founding member of the Grand Challenges in Global Health team at the FNIH, he worked with the Bill & Melinda Gates Foundation, Wellcome and the Canadian Institutes of Health, overseeing projects on drug discovery, genomics and discovery of new insecticides and repellents. He was principal investigator of the multinational Malnutrition and Enteric Disease Study, which focused on child health and development. He retired from the FNIH in 2018 and moved to Manhattan to focus his time on family and community activities.

In addition to the ASBMB, Gottlieb was a longtime member of the American Society of Tropical Medicine and Hygiene and an ASTMH councilor from 1996 to 2000.

Raul Ondarza–Vidaurreta



Raul Ondarza–Vidaurreta, the first biochemistry instructor on the medical faculty at the Universidad Nacional Autónoma de México and a member of the American Society for Biochemistry and Molecular Biology since 1974, died Feb. 7. He was 93.

Born Oct. 29, 1928, in Tampico, Tamaulipas, Mexico, Ondarza–Vidaurreta earned his doctorate at the UNAM and completed postdoctoral fellowships at the University of Glasgow and New York University. In 1958, he joined the UNAM faculty, and he was appointed chair of molecular biology in 1963. He founded and taught an optional class in epigenetics.

Ondarza–Vidaurreta also served as a medical sciences researcher at Mexico's Instituto Nacional de Salud Publica, where he focused on drug targets for infectious diseases and human parasites, including cancer cells infected with the Papilloma virus. At various times, he was a professor at the Scripps Institution of Oceanography, a visiting researcher in the chemistry department at the University of California, San Diego, and a fellow of the John Simon Guggenheim Memorial Foundation.

He was an adviser to and general coordinator of science committees of Mexico's Consejo Nacional de Ciencia y Tecnología from 1971 to 1982, during which time he worked to create five new research centers dedicated to ecology, biomedical research, biotechnology, chemistry, and marine biology and oceanography. He was general director of an ecological research center from 1983 to 1989 and director of the INSP's infectious diseases research center from 1990 to 1993.

Ondarza–Vidaurreta wrote more than 15 books, including biology texts, and numerous chapters and articles. Among his many honors, he received the Academia Nacional de Medicina de México's Carnot Award and an honorary doctorate from the University of Paris XIII. In addition to the ASBMB, he was a member of the National Academy of Medicine of Mexico, the Biochemical Society of Great Britain, the Mexican National Legion of Honor and the International Society for the Study of the Origin of Life. He was a founder of the Mexican Academy of Sciences and the Mexican Association of Human Genetics.

Ludwig Brand

Ludwig "Lenny" Brand, a longtime professor of biology at the Johns Hopkins University Krieger School and a member of the American Society for Biochemistry and Molecular Biology for more than 50 years, died Jan. 5, two days after his 90th birthday.

Born Jan. 3, 1932, in Vienna, Austria, Brand moved to the United States early in his life and graduated from high school in Boston. He earned a bachelor's degree in chemistry from Harvard College in 1955 followed by a Ph.D. in chemistry from Indiana University five years later. After a short stint as a research associate at the Weizmann Institute of Science in Israel, he joined the faculty at Johns Hopkins, where he developed a reputation for his enthusiastic teaching and generous personality. He remained at Hopkins until his retirement in 2012.

Brand was interested in dynamic structures of cellular components including proteins, membranes and nucleic acids. His lab used fluorescence spectroscopy and specifically single photocounting methods to study protein fluctuations on the pico- to nanosecond time scale, providing a more accurate portrayal of these molecular machines. He was one of the pioneers in the time-resolved emission spectra technique, which he employed to study GB1, a plant protein found outside the cellular membrane.

Brand was a beloved mentor and supervisor. "He cared deeply about people who worked with him, encouraged us to do what was most interesting, and never micromanaged our work," said Dmitri Toptygin, an associate research scientist, in a Hopkins obituary.

In addition to the ASBMB, Brand was a member of the American Chemical Society and a fellow of the Biophysical Society, which honored him with the Jablonski Award in 1998 and the Gregorio Weber Award in 2015. He served for five years as the executive editor of the journal Analytic Biochemistry and on the editorial boards of several other journals.

Outside of academics, Brand enjoyed listening to bluegrass music and playing the banjo, according to a family obituary. He is survived by his wife, Sheila S. Gallay.

— Anna Hu

Mark Kester

By Thomas P. Loughran & Myles C. Cabot

Mark Kester, a cancer researcher and biochemist who was well known in the lipid and sphingolipid fields, died July 20. He was 67.

Born in the Bronx, New York, on Feb. 19, 1955, Kester earned his Ph.D. in 1982 in cell biology at the State University of New York at Buffalo, previously having earned undergraduate degrees in biology and economics at the State University of New York at Stony Brook. He completed his postdoctoral work at the University of Texas Health Science Center at San Antonio and the University of Illinois Chicago.

Kester was a professor in the University of Virginia pharmacology department with secondary appointments in biomedical engineering and ophthalmology. Prior to his tenure at UVA, he was at Pennsylvania State University for more than 18 years as a professor of pharmacology at the Penn State Hershey College of Medicine and the inaugural director of the Penn State Center for NanoMedicine and Materials. Before working at Penn State, he was an assistant and later associate professor in the nephrology department at Case Western University.

Kester's earlier work focused on deciphering the role of diglycerides and ceramides in regulation of protein kinase C. Subsequently, he introduced the novel ceramide nanoliposome, jump-starting the concept of a ceramide as a drug delivery system for bioactive agents. He did exemplary work in determining the biochemical and biophysical mechanisms underlying the selective efficacy of ceramides in cancer models. His ceramide-based nanoliposomes reached clinical trials for safety in both solid tumors and acute myeloid leukemia.

Kester was an expert in the field of nanotechnologies for targeted drug delivery. At UVA, he was director of the Institute for Nanoscale and Quantum Scientific and Technological Advanced Research, which provides a collaborative platform for nanoscale research. With collaborators, he designed and engineered calcium phosphosilicate nanoparticles — noncationic, nontoxic particles that encapsulate fluoroprobes with enhanced quantum efficiencies for use in enhanced imaging and therapeutics.

Kester played a key role in helping the UVA Cancer Center achieve a comprehensive designation, both in fostering cross-campus research and in translating his work into the clinic. He was a co-principal investigator on

a P01 grant focused on targeting sphingolipid metabolism in AML.

Kester's record of research accomplishments in the field of cancer and sphingolipid-based nanotherapeutics included more than 200 peer-reviewed publications; he was first or senior author on a third of them. He co-authored "Integrated Pharmacology," recognized as a "highly commended textbook" by the British Medical Society, and he was a sought-after speaker. His research was funded by the National Cancer Institute, the National Science Foundation and the Jefferson Trust, among others. In 2018, he served as chair of the 15th Gordon Research Conference on Glycolipid and Sphingolipid Biology, held in Galveston, Texas.

In addition to his scholarly activities, Kester educated scores of undergraduate and graduate students in the classroom and as a mentor. Above all, he was an extraordinary human being, kind and passionate about all he did. He was bigger than life, motivational and a manager par excellence. He listened fervently and openly to all discussion. During free time at conferences, he always headed for the tennis court, and he had a keen sense for locating the finest cuisine even in the far reaches of the globe.

To continue Kester's scientific legacy, the family suggests gifts in his honor be made to the Kester Research Fund at the University of Virginia. Checks can be mailed to UVA, P.O. Box 37963, Boone, Iowa 50037, indicating 22264 on the memo line, or be made online at giving.uvahealth.com.

Myles C. Cabot (cabotm@ecu.edu) is a professor of biochemistry at the Brody School of Medicine at East Carolina University.

Thomas P. Loughran Jr. (TL7CS@hscmail.mcc.virginia.edu) is the director of the University of Virginia Cancer Center and a professor of medicine at the University of Virginia School of Medicine.

Conference inspires a shift in career goals

By Nicole Lynn

An undergraduate's first scientific conference is always exciting, but for Anna Crysler, Experimental Biology 2021 was especially significant. Crysler, now a recent graduate of Albion College in Michigan, was one of 12 students to win the American Society for Biochemistry and Molecular Biology's Undergraduate Research Award for proposed research that was an extension of a presentation she gave during the Antibacterial Targets and Drug Discovery poster session at EB 2021.

Crysler joined Craig Streu's lab during her sophomore year at Albion. At the time, she was considering medical school, and she saw the Streu lab as a great opportunity for personal growth and hands-on science.

"Albion College is undergraduate only," she said. "It's a great opportunity to do research because we aren't working under a graduate student, we are working directly under our PI, and the work we do is ours," Crysler said.

Crysler was introduced to the world of biochemistry through her membership in the Biochemistry Club, which also happens to be the ASBMB Student Chapter at Albion.

"I was quickly surrounded by other students who loved learning more about their field outside of class," she said. "We also volunteered at science fairs and performed demonstrations for young kids, which was inspiring to be a part of and watch kids' faces light up with excitement over chemistry and biology."

COURTESY OF ANNA CRYSLER

Anna Crysler's first national science conference was Experimental Biology 2021, an all-virtual event.

Crysler's presentation for EB 2021 focused on her work with nanobodies, which are single-domain antibodies, and how she used directed evolution in yeast to develop novel nanobodies that can be used as antibiotics and diagnostic agents. This research could help combat the ongoing problem of antibiotic resistance. The future of Crysler's project involves optimizing her design strategy and finding ways to develop an efficient workflow to produce this type of biologics.

Due to the ongoing pandemic, Crysler's first national conference was held virtually, and many of the presentations were recorded, creating a layer of complexity for many presenters.

"With it being virtual, and having to record the voiceover, I recorded myself probably 20 times before I was satisfied," she said. "I wanted it to be perfect."

With her undergraduate exposure to hands-on research and scientific presentations, Crysler's interest swayed from medical school to graduate school. The process of performing and presenting her research at the conference showed her "all of the science that is out there," she said. "It was inspiring and definitely contributed to my decision to go to grad school."

To gain experience in the biotech industry, Crysler has taken a predoctoral position with Adimab, a New Hampshire company that focuses on antibody discovery and production.

And what advice would she give undergraduates pursuing science?

"Balance is important. Weeding out every so often the things that no longer brought me enjoyment or fulfillment was important for me," she said. "Following opportunities that pique your interest makes it easier to engage in them."

Nicole Lynn (nalynn@ucla.edu) is a Ph.D. candidate at UCLA and a volunteer writer for ASBMB Today.

Leaning in to the scientific community

By Leia Dwyer

Kelly Ward has understood the value of community in the pursuit of science since she was a child. She grew up in Reading, Massachusetts, home to a school system she praises for having great opportunities for young students to be involved in science, technology, engineering and mathematics pursuits.

Ward joined Science Olympiad, a nationwide team-based science competition, in middle school, kept up her involvement all through high school and even went to the national competition.

"I really liked participating in the competitions, and you can see that today — given that I went into biochemistry," she said. "I love the process of asking a question, designing the experiment, and seeing if you've answered the question. I find it really rewarding."

Ward went on to choose Northeastern University for her undergraduate degree because it has a strong biochemistry program, research opportunities and a co-op program.

An American Society for Biochemistry and Molecular Biology Student Chapter member since the fall of her first year, Ward said she knew she wanted to be involved with the chapter as soon as she saw its thriving booth at the Northeastern student activities fair. "Everyone seemed really nice, welcoming, and passionate about their research areas," she said.

After her first year as a member, she became the chapter's secretary; she was the president last year and is serving as president again this year.

Embedded in the rich biotechnology ecosystem of Boston, Ward and her chapter have a lot of opportunities for external engagement. Under her leadership and in collaboration with the biochemistry program director, Kirsten Fertuck, the chapter hosts frequent panels with local professionals, focused on career progression and life as an industry scientist.

"We've had speakers from a variety of biotech companies in and around Boston," Ward said. "It's been incredibly beneficial to hear about their experiences and gather great advice."

Her chapter also hosts panels with Northeastern faculty about undergraduate research and graduate school. Northeastern's co-op program, where students work full time for six months instead of attending classes, ties nicely into the atmosphere of being embedded in the local scientific community and experiential learning.

Ward thinks it's important to keep the social elements of science and community engagement alive too. Her chapter hosts games nights and offers volunteer opportunities. The members partner with other Northeastern clubs as well as clubs at other Boston area colleges to grow their community and network. Her chapter has hosted Active Site, a regional conference for undergraduates sponsored by the ASBMB.

Now a senior with a biochemistry major and a data science minor, Ward wants to go on to graduate school to continue her scientific studies. She's open to a variety of programs including biochemistry or immunology but ultimately would like to continue to work in oncology.

COURTESY OF KELLY WARD

Kelly Ward is a senior at Northeastern University.

"I have been fascinated by the variety of approaches to cancer treatment that I've seen during my co-ops and on campus research," she said, "and I'd love to continue to work in this complex field."

Whatever her ultimate career goal, Ward knows she'd like a position where she can mentor younger scientists. Mentoring, she said, has been an important part of her own journey.

Leia Dwyer (leia.dwyer@gmail.com) is a Boston-area biotech and pharmaceutical industry professional.

Start or renew an ASBMB Student Chapter

The ASBMB Student Chapters program is a national network of more than 100 chapters representing more than 2,000 undergraduate students and faculty members dedicated to the advancement of research, education and science outreach.

Renew your chapter by Nov. 15.

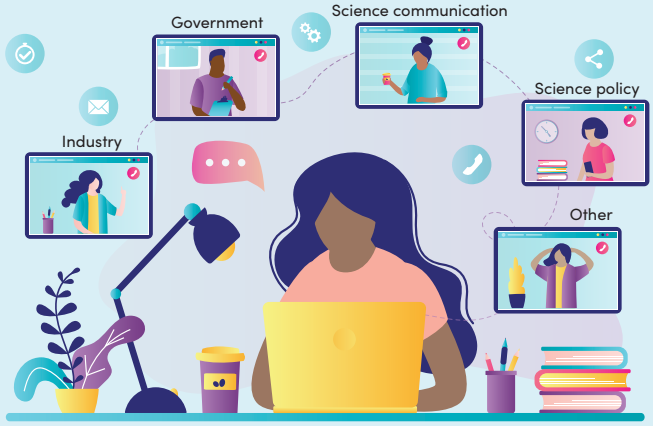
Learn more at: asbmb.org/education/student-chapters

The ASBMB Virtual Career Expo: Anything but academia

November 2 | 11 a.m.–5 p.m. Eastern

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

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



Prion origins offer disease key

By Aswathy N. Rai

Chronic wasting disease, or CWD, is a contagious, fatal prion disorder that affects cervid species such as deer, elk, caribou, reindeer and moose of all ages, captive and wild.

The Centers for Disease Control and Prevention reports that CWD is prominent in the continental U.S., Canada, Norway, Finland, Sweden and South Korea. Increased prevalence and spread of CWD endangers cervid populations in these regions. No vaccine or treatment exists.

Like any prion disease, CWD is characterized by the misfolding of a normal protease-sensitive host protein, or PrPC, to a protease-resistant isoform, or PrPSc. The misfolded pathogenic PrPSc has distinct biochemical profiles that correlate with specific disease characteristics. CWD spreads when PrPSc is shed into the environment through urine, feces, bodily fluids or carcasses or by direct animal-to-animal contact.

Mark Zabel leads a team at Colorado State University that studies prion diseases.

"Chronic wasting disease can have serious consequences," he said. "In Colorado and Wyoming, where the disease was first discovered, prevalence rates in specific herds are estimated to be between 30% and 50%. This rate in population decline can lead to local extinction of cervid species."

Although CWD is a neurodegenerative disease, in cervids, PrPSc proteins are primarily of lymphogenic origin. Once PrPSc enters the body via oral or intranasal ingestion, it is replicated in the retropharyngeal lymph nodes, or LN. The PrPSc accumulates in the obex, a region in the medulla of the central nervous system, or CNS, resulting in wasting and spongiform encephalopathy.

Typical of prion diseases, CWD is neurological, and the CNS has the highest prion concentration, so research has focused on brain-derived prions. However, the infectious prions shed in CWD primarily originate in the lymphoreticular system.

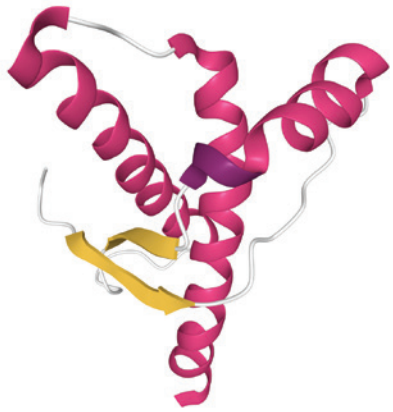
In a recent article in the **Journal of Biological Chemistry**, Zabel's team reports differences in the biochemical profiles of prion strains of lymphogenic and neurogenic origins in free-ranging white-tailed deer.

Zabel and his team report that paired obex and LN-derived prions from the same animal showed no significant differences in conformational stability, nor was interanimal variation within the same tissue substantial.

Glycoform ratio analysis showed differences in glycosylation patterns in prions derived from the obex and LN in the same animal. To the team's surprise, LN-derived glycosylation patterns showed only marginal differences among animals, but brain-derived prions showed significant differences.

Using an ELISA-based structural profiling assay, the authors also saw greater conformational diversity in LN-derived prions than brain-derived prions.

"Prions that exist in infected animals are typically not a singular species but a sort of quasi-species or a cloud of different subspecies," Zabel said. "We would argue that predominant species are selected inside the animal from a large pool of diverse prions."



Prions are misfolded proteins that can transmit their shape onto normal variants. They characterize several fatal and transmissible neurodegenerative diseases in humans and many other animals.

Based on their observations, the authors propose that predominant isoforms of neurogenic PrPSc are selected by the brain from a larger pool of LN-derived PrPSc. The neurogenic prion strains selected can vary considerably from animal to animal.

Extraneural prion strains shed into the environment may have a lower species barrier than neurogenic prions. The ability to transmit infectious prions between species increases the zoonotic potential, or the ability to infect humans, of CWD. The study underscores the importance of including strain properties alongside prion positivity as a criterion for diagnostic tests used by wildlife management agencies.

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Maternal diet's effects on liver disease in offspring

By Isabel Casas

More than half of people who become pregnant are overweight or obese at the time of conception, and obesity during pregnancy is associated with progeny who develop metabolic syndrome later in life.

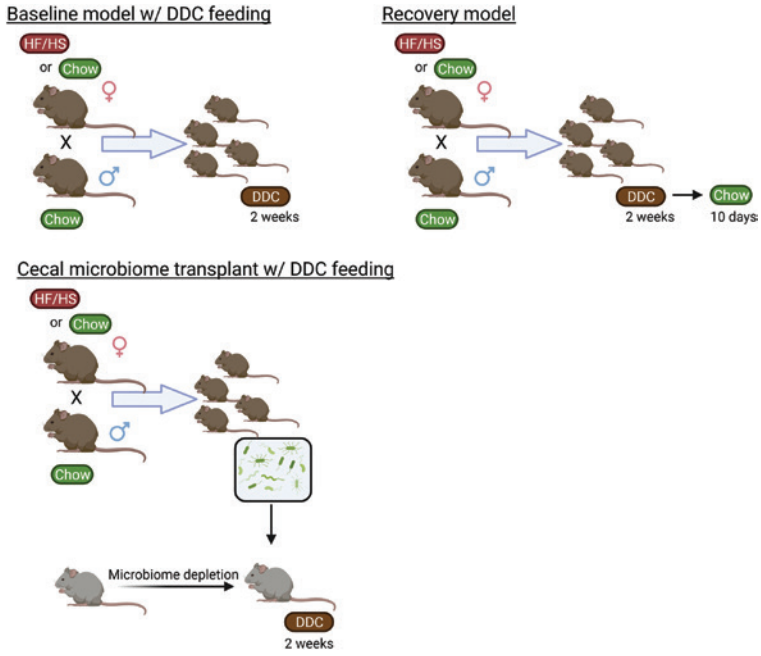
For those reasons and others, a lot of research has been done and continues to this day on the effects of maternal diet on offspring.

Studies of humans and mammalian animal models have shown, for example, that high-fat diets during pregnancy and while nursing result in offspring more likely to develop nonalcoholic fatty liver disease and to have altered bile acid homeostasis.

Scientists at the Washington University School of Medicine in St. Louis recently undertook a study to learn more about how maternal obesity might influence the development of cholestasis, a liver disease for which therapies are limited.

In cholestasis, bile cannot reach the duodenum, the first portion of the small intestine, where it is supposed to facilitate food digestion. The disease can be brought on by several factors, including duct obstructions or narrowing, toxic compounds, infection and inflammation, disturbance of intestinal microbiota, and genetic abnormalities.

In their study, published in the **Journal of Lipid Research**, Michael D. Thompson and collaborators at Washington University fed female mice conventional chow or a high-fat, high-sucrose diet and bred them with lean males.



DAVIDSON ET AL./JLR

The term "cholestasis" is derived from the Greek phrase meaning "bile halting." The graphic above shows how the researchers bred, fed and completed cecal microbiome transplantation. HF/HS is short for high-fat, high-sucrose, and DDC is short for 3,5-diethoxycarbonyl-1,4-dihydrocollidine.

They fed the offspring DDC, which is short for 3,5-diethoxycarbonyl-1,4-dihydrocollidine, for two weeks to induce cholestasis. After this feeding period, the offspring ate conventional chow for 10 more days. They found that offspring from females on the high-fat, high-sucrose diet had increased fine branching of the bile duct and enhanced fibrotic response to DDC treatment and delayed recovery times from it.

Earlier this year, the team reported changes to offspring microbiome after maternal consumption of high-fat, high-sucrose chow, so they decided to feed antibiotic-treated mice cecal contents from the offspring that had been fed conventional chow or high-fat, high-sucrose, followed by DDC for two weeks. They found that cholestatic liver injury is transmissible in these mice models, further supporting the role of the microbiome in this disease.

DOI:10.1016/j.jlr.2022.100205

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MicroID2: Streamlined for better biotinylation

By Inayah Entzminger

Protein interactions are a big field. Proteins network for both intercellular and extracellular signaling pathways, many of which require the relevant proteins to be close together.

Researchers often use proximity-dependent biotinylation to characterize these interactions. In this process, an enzyme that labels proteins with biotin is attached to a protein of interest using CRISPR-based or plasmid-based expression strategies. When biotin is added to the experimental system, any protein in close proximity to the protein of interest is tagged and researchers then can purify and identify it.

Proximity-dependent biotinylation recently was used to discover sites where mitochondria contact the endoplasmic reticulum. The outer mitochondrial membrane is difficult to map by purification; the process quickly destroys the membrane, and membrane enrichment techniques are not perfect. By using biotinylation, researchers in the Ting lab at Stanford University accurately captured and identified proteins on the outer mitochondrial and endoplasmic reticulum membranes of living human cells.

James Londino's lab at the Ohio State University Wexner Medical Center in Columbus, Ohio, has modified the structure of a state-of-the-art proximity-dependent biotinylation protein, BioID2,that is derived from Aquifex aeolicus bacteria. Benjamin Johnson, a graduate student and first author of a recent paper in the journal **Molecular & Cellular Proteomics**, explained that by removing the C-terminus of BioID2, the Londino lab created MicroID2, a smaller biotin ligase with fewer nonspecific labeling events than its predecessors.

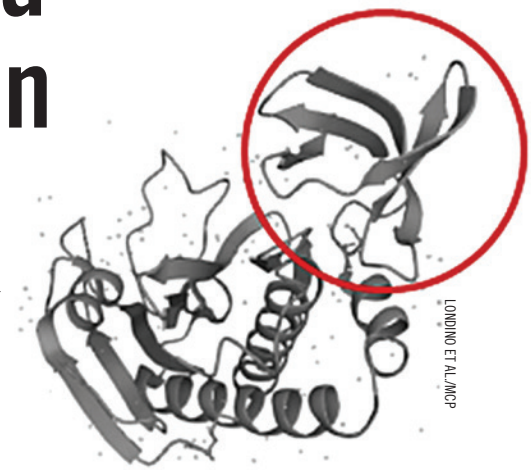
"We asked, 'Do we need this entire construct in order to facilitate labeling?'" Londino said.

The size of the ligase matters because larger constructs can cause mislocalization of the protein and disruption of endogenous signaling. This means the host cell will not perform its signaling pathways and other reactions as it would without the insertion of this new protein, skewing the validity of any results. A too-large construct may appear to associate with proteins in artificial ways.

The biotin ligase has a minimum size limit, however. Truncation of the BioID2 C-terminus beyond 63 amino acids completely inactivated the biotinylation activity. Deletion of 10 amino acids from the N-terminus also inactivated the enzyme.

The researchers performed other mutations to develop MicroID2, including substitutions at the active site, that increased the labeling efficiency. Additional mutations reduced nonspecific labeling, allowing more accurate analysis of protein–protein interactions.

"When we're overexpressing these constructs, they're going to be continuously labeling," Londino said. "Even when we completely deplete biotin from the media, there's still going to be a certain amount of biotin labeling that occurs. By reducing the ability of these constructs to scavenge biotin … we were able to reduce the overall amount of background labeling."



LONDINO ET AL./MCP

After the removal of the C terminus (circled in red), the enzymatically relevant sections of the BioID2 bacteria Aquifex aeolicus BirA remain intact in MicroID2.

Johnson described MicroID2 as the smallest biotin ligase yet developed that maintains a high level of activity, but the lab is not done optimizing the construct. Next steps include further exploration of stable integration of the ligase and optimization of its stability.

The Londino lab plans to use these constructs to examine how ubiquitin ligases target specific proteins for degradation. As a lab studying ubiquitin biology, "we are pretty well positioned" to use this tool to examine protein stability, Johnson said.

DOI:10.1016/j.mcpro.2022.100256

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From the journals

By Isabel Casas & Nivedita Uday Hegdekar

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

An oncoprotein's role in kinase pathway activation

The Kaposi's sarcoma–associated herpes virus is the main etiological agent of Kaposi's sarcoma, which manifests as patchy cancerous tumors on the skin and mucus membranes. It most often affects people with immune deficiencies, such as those with HIV/AIDS.

The virus — known as KSHV and human herpesvirus 8 — belongs to the same family as Epstein–Barr virus, which is responsible for causing infectious mononucleosis and several cancer types and recently has been implicated in the development of multiple sclerosis.

The virally coded oncoprotein vFLIP is known to upregulate the inhibitor of kappa B kinase, or IKK, complex, activating the canonical nuclear factor κB signaling pathway, a major factor in KSHV pathogenesis.

The physical interaction of vFLIP and the IKK kinase regulatory component, IKK gamma, is essential for persistent activation and has been studied widely; however, scientists have not yet determined how the kinase subunits are active mechanistically.

In a recent **Journal of Biological Chemistry** article, Claire Bagnéris, Swathi L. Senthil Kumar and collaborators at the Institute of Structural Molecular Biology in London report that vFLIP alone is sufficient to activate the IKK kinase complex. The researchers used a combination of cell-based assays and biophysical and structural biology techniques.

The authors also found weakly stabilized, high-molecular-weight vFLIP-IKKγ assemblies relevant to the activation process.

In the end, this novel study determined that vFLIP-induced NF-κB activation relies upon structurally specific vFLIP–IKKγ multimers that are essential to activate kinase subunits by autophosphorylation.
DOI: 10.1016/j.jbc.2022.102012

Assessing vitamin D status in critical care

Vitamin D helps regulate calcium and phosphorus levels, plays a role in maintaining proper bone structure and regulates immune function. Vitamin D deficiency results in bone diseases, such as rickets, as well as cancer and cardiovascular and diseases, and is associated with increased risk for respiratory infections, including COVID-19.

When absorbed by the body, vitamin D is metabolized to 25-hydroxyvitamin D, or 25OH-D, which often is used as a biomarker to measure vitamin D levels in the body. Liquid chromatography–tandem mass spectrometry, or LC-MS/MS, is the gold standard for quantitative 25OH-D determination, and this technique has several advantages over previously used immunoassays, including greater selectivity, lower detection limits and improved precision.

Researchers at McMaster University and the Children's Hospital of Eastern Ontario Research Institute have developed a high-throughput method for assessing vitamin D status from blood specimens based on direct infusion–MS/MS, or DI-MS/MS, following click derivatization using 2-nitrosopyridine, which is optimized for quicker analysis than LC-MS/MS and greater accuracy than a commercial immunoassay.

In a comparative test study, Erick Helmeczi and a team found that 25OH-D concentrations from reference blood samples measured by DI-MS/MS were less biased than the commercial immunoassay when compared to LC-MS/MS. They found that, compared to DI-MS/MS, the commercial immunoassay, often used for screening in clinical trials, underestimates the prevalence of vitamin D deficiency in critically ill children who might benefit from high-dose vitamin D supplements.

These findings, published in a paper in the **Journal of Lipid Research**, show that DI-MS/MS can be used to assess vitamin D status rapidly and reliably in clinical trials and large-scale studies. The researchers will focus future efforts on adapting this method for the purpose of reporting clinical values.
DOI: 10.1016/j.jlr.2022.100204

Secretomics shed light on cells' immune response

Hepatocytes — cells in the liver that play essential roles in metabolism and detoxification —have important secretory and immunological functions. Inflammatory

processes produce signals (such as cytokines interleukin-1 and -6) that induce the acute-phase response, which in turn provokes secretion of proteins with immunomodulatory functions to restore homeostasis.

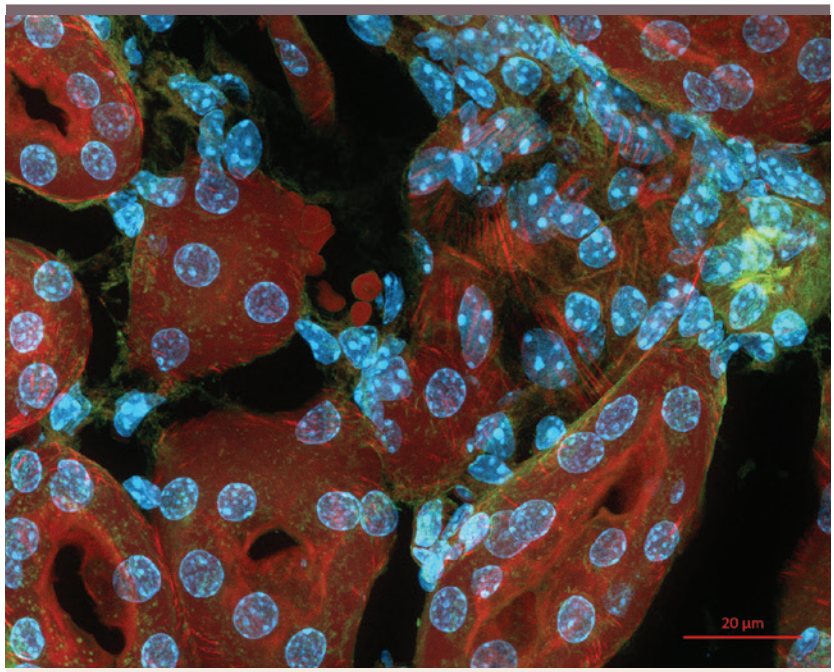
The secretome of a cell or an organism consists of proteins secreted by the endoplasmic reticulum–Golgi secretory pathway and other direct or vesicle-based mechanisms. The systematic investigation of secreted proteins by mass spectrometry–based proteomics, however, has faced several challenges, as most approaches use serum-free culture conditions to avoid serum-induced interferences, thus negatively affecting the observable time window, cellular functions and viability.

In a recent article in **Molecular & Cellular Proteomics**, Sascha Knetch and colleagues at GlaxoSmithKline in Germany developed an interval-based secretomics workflow that determines protein-secretion rates in short serum-free time windows. The authors also implemented a labeling strategy in which they were able to pull up to 11 protein samples into a single mass spectrometry run. This approach allowed for the first comprehensive analysis of time-dependent secretion of liver cell models in response to these pro-inflammatory cytokines.
DOI: 10.1016/j.mcpro.2022.100241

The proof is in the linker

Iron acts as an electron carrier and a co-factor in many proteins; this makes it an essential nutrient for living organisms, including pathogenic bacteria such as Staphylococcus aureus, which is responsible for deadly nosocomial infections.

The iron-regulated surface determinant system is a family



CARL ZEISS MICROSCOPY

Microscopy image of a mouse kidney section.

Novel player involved in kidney injury response

Fibrosis involves the excessive accumulation of extracellular matrix, or ECM, which may result in loss of function when normal tissue is replaced by scar tissue, such as after injury. In the case of kidney disease in particular, fibrosis is the final step in chronic disease characterized by the accumulation of interstitial fibroblasts and myofibroblasts in addition to ECM accumulation.

Follistatin-like 1 is a secreted protein. While the role FSTL1 plays in heart and lung injury and development of fibrosis have been studied widely, researchers have not determined the role this protein plays in kidney injury and progression to chronic disease.

In a recent article in the **Journal of Biological Chemistry**, Yu Zhang and colleagues from the School of Biomedical Sciences at the Chinese University of Hong Kong and the Center of Nephrology and Urology at Sun Yat-sen University in China report that FSTL1 plays a profibrotic role in the kidney.

The team used several molecular biology and imaging techniques — including single-cell RNA-Seq analysis and immunofluorescence — to show that Fstl1 was enriched in stromal cells in obstructed mouse kidneys and that FSTL1 expression was induced in fibroblasts during kidney fibrogenesis in mice and in human patients.

In addition, the authors showed FSTL1 overexpression increased renal fibrosis and activated the Wnt/beta-catenin signaling pathway, whereas inhibition of FSTL1 lowered Wnt/β-catenin signaling.
DOI: 10.1016/j.jbc.2022.102010

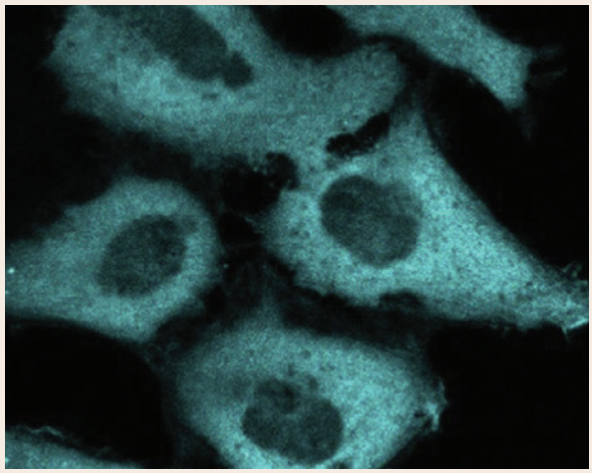
— Isabel Casas

A new site-specific cholesterol control option

Cholesterol is an essential component of mammalian cell membranes. Its unesterified, or free, form, localized within plasma, controls mechanical properties of the lipid bilayer such as rigidity and permeability. Cholesterol also directly interacts with a wide variety of cellular proteins at the plasma membrane, thus regulating cell signaling.

Researchers manipulate cellular cholesterol levels either through chemical extraction and enrichment of cholesterol by methyl-beta-cyclodextrin, or MβCD, and MβCD-cholesterol adducts, respectively; or by inhibition of new cellular cholesterol biosynthesis by statins. These methods are convenient but lack site-specific control of cholesterol levels within cells. Moreover, they can cause nonspecific cholesterol depletion that exerts harmful effects on cells including cell death and nonspecific alteration of cell physiology.

Ha Pham and a team of researchers from the University of Illinois Chicago and the University of Western Australia, Perth, have developed a new system that allows inducible, site-specific cholesterol depletion. They created a genetically encoded bacterial cholesterol oxidase whose membrane binding activity is altered in a way that allows spatiotemporally specific control of its membrane targeting by chemically induced dimerization with a partner protein located in a specific membrane site. The team documented the system and their findings in a recent research paper published in the **Journal of Lipid Research**.



WONHWA CHO ET AL./JLR

This image shows the distribution of fluorescently labelled Streptomyces sp. bacterial cholesterol oxidase in HeLa cells.

In combination with quantitative imaging of cholesterol and signaling activity assays, this novel system will allow for unambiguous determination of site-specific functions of cholesterol in diverse cell membranes, including the plasma membrane and the lysosomal membrane.

DOI: 10.1016/j.jlr.2022.100178

— Nivedita Uday Hegdekar

of proteins that sequesters iron from the host to support bacterial growth and is therefore a potential therapeutic target. The surface protein IsdH consists of three near-iron transporter, or NEAT, domains connected by linkers, and it is responsible for capturing hemoglobin.

In a recent **Journal of Biological Chemistry** article, Sandra Valenciano–Bellido and colleagues at the University of Tokyo characterized the linker region between the NEAT2 and NEAT3 domains using multiple biophysical techniques to understand better the role it plays in heme extraction.

The researchers showed that the linker region contributes to the stability of the bound protein and this, in turn, influences the flexibility and orientation of the NEAT3 domain in its interaction with hemoglobin.

The authors suggest this model explains how the linker region facilitates NEAT3 positioning to sequester heme, and they argue that the study adds to researchers' understanding of the mechanism of heme extraction of human hemoglobin by IsdH.

DOI: 10.1016/j.jbc.2022.101995

Targeting signaling pathway convergence

PI3K–mTOR and MEK/MAPK signaling pathways are essential for the regulation of cell survival and other cellular functions. In addition, they are the most frequently dysregulated pathways in cancer.

Some cancer therapies based on kinase inhibitors are effective in tumors that are addicted to prosurvival signals and target individual members within these pathways. This leads to drug resistance and transient responses. To overcome this limitation, researchers are now investigating cotreatments

with PI3K/AKT and MEK/MAPK inhibitors; however, the mechanisms leading to sensitivity remain unclear.

In a recent **Molecular & Cellular Proteomics** article, Maruan Hijazi and collaborators at the Centre for Genomics and Computational Biology at Queen Mary University of London report developing a phosphoproteomics approach based on liquid chromatography– tandem mass spectrometry to study the effects of co-treatment on the kinase eEF2K, a convergence point for both pathways.

The authors found that inhibition of eEF2K by siRNA or with a small-molecule inhibitor reversed the anti-proliferative effects of the cotreatment with PI3K plus MEK inhibitors in a cell model–specific manner. The authors conclude that eEF2K is a key mediator of these pathways and a target for synergistic cotreatment in cancer cells.
DOI: 10.1016/j.mcpro.2022.100240

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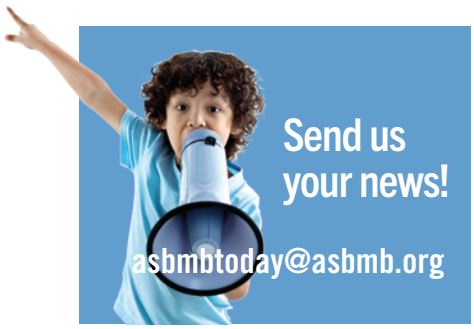
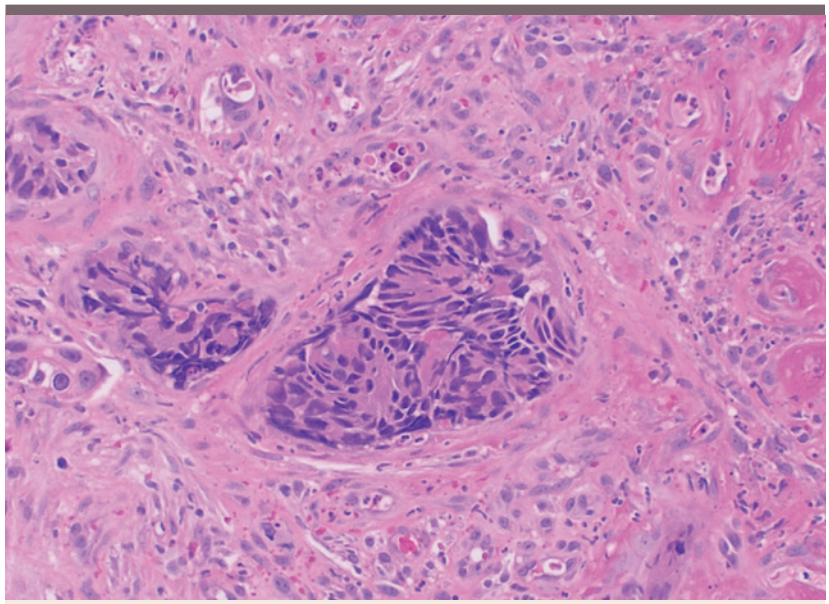




MIKAEL HÄGGSTRÖM /WIKIMEDIA COMMONS

Histopathology of colorectal adenocarcinoma with lymphatic invasion.

A new way to view colorectal cancer cell differentiation

Colorectal cancer is among the most common cancers. Its risk factors include genetics, aging and lifestyle choices, such as smoking. Treatment has proved difficult, as this type of cancer is heterogenous and often has an asymptomatic clinical course, resulting in late diagnosis. Identifying reliable biomarkers for diagnosis and disease progression is essential.

Research groups previously have determined that altered glycosylation states, in glycosphingolipids particularly, can be associated with malignant transformation in colon cancer. While protein glycosylation in this cancer is studied widely, researchers have not yet explored glycosphingolipid expression of patterns and their contributions to colorectal cancer.

In a recent study published in **Molecular & Cellular Proteomics**, Di Wang and collaborators at the Center for Proteomics and Metabolomics at Leiden University Medical Center in the Netherlands performed an in-depth analysis of glycosphingolipid glycans of 22 colorectal cancer cell lines using porous graphitized carbon nano–liquid chromatography coupled with electrospray ionization–mass spectrometry. The authors found that glycosphingolipid expression varies among different cell lines.

They also found that glycosphingolipid expression correlates with relevant glycosyltransferases involved in their biosynthesis as well as with transcription factors implicated in colon differentiation. The authors conclude that this glycomic study provides novel insights into glycosphingolipid glycan regulation for future functional studies in colorectal cancer research.
DOI: 10.1016/j.mcpro.2022.100239

— **Isabel Casas**

Is chronochemotherapy coming?

The debate over timing cancer medicines

By Laurel Oldach

Between a congressional effort to end daylight savings time, a New York Times feature on timed drug delivery, and reviews of circadian biology in several major journals, circadian medicine has had a buzzy year. The excitement is particularly high among oncology researchers.

At various intervals since the 1970s, long before the molecular gears of the circadian clock were understood, timed delivery of cancer medication has seemed to be just over the horizon. In 1979, when a group of oncologists published the paper "On methods for testing and achieving cancer chronotherapy," cancer was the second most common cause of death in America, following heart disease. In 2020, the same was true — but cancer was catching up. In the intervening 40 years, scientists have learned a huge amount about how cancer works and how to treat it. Some cancers that once would have been a death sentence are now curable. Others have remained intractable despite decades of study and billions of dollars of research investment.

Now, with a better understanding of the molecular underpinnings of humans' circadian clocks and more sophisticated measurements of physiological phenomena, researchers are taking a fresh run at the idea of circadian cancer therapy.

"There is an immense excitement (in the field)," said Francis Lévi, a French oncologist who has worked for decades on basic mechanisms and clinical studies of chronochemotherapy. He and his colleagues say they have begun to observe that drugs can be more effective, or cause fewer side effects, if delivered at certain times of day.

But others point to the long and disappointing history of circadian medicine as a reason to be cautious about the hype. The clock, said biochemist Aziz Sancar, "interfaces with everything. It's logical to think that it should have an effect … but you have to demonstrate it experimentally."

If treating cancer better were as simple as using the same drug at a different time of day, Sancar argues, wouldn't we know that by now?

Daily rhythms of disease

Anyone who has awoken at 4 a.m. after a long-distance trip knows that the circadian cycle is a powerful regulator of human behavior. Its rhythms also can regulate disease. People with rheumatoid arthritis feel the most pain in the morning, while gout and asthma attacks are more than twice as likely at night. People with Alzheimer's disease tend to become upset and uneasy around sundown.

Responses to external stimuli change by time of day too. In a famous experiment from the 1960s, mice injected at noon with lipopolysaccharide, a bacterial toxin mimicking sepsis, died 80% of the time; those injected at midnight died just 20% of the time. Conversely, some cholesterol drugs are best taken at night, when cholesterol synthesis is highest.

Disruption of circadian rhythms has been linked to diseases, especially cancer. In epidemiological studies of shift workers, disruption to clock functions has been linked sometimes, but not always, with higher cancer rates (see "Clock disruption and carcinogenesis" on page 29). Meanwhile, studies on a variety of cancer biopsies indicate that some retain a daily cycle in clock proteins and proliferate in daily waves, but their timing relative to the rest of the body can vary.

In a recent study of breast cancer metastasis in the journal Nature, researchers at several hospitals in Switzerland reported that blood samples taken at 4 a.m., when patients usually would be asleep, contained many more circulating tumor cells than samples taken at 10 a.m. Cells from each time point also showed different growth profiles. When grafted into mice, the nighttime cells grew much more aggressively, suggesting that, independent of number, they might be better able to seed metastases.

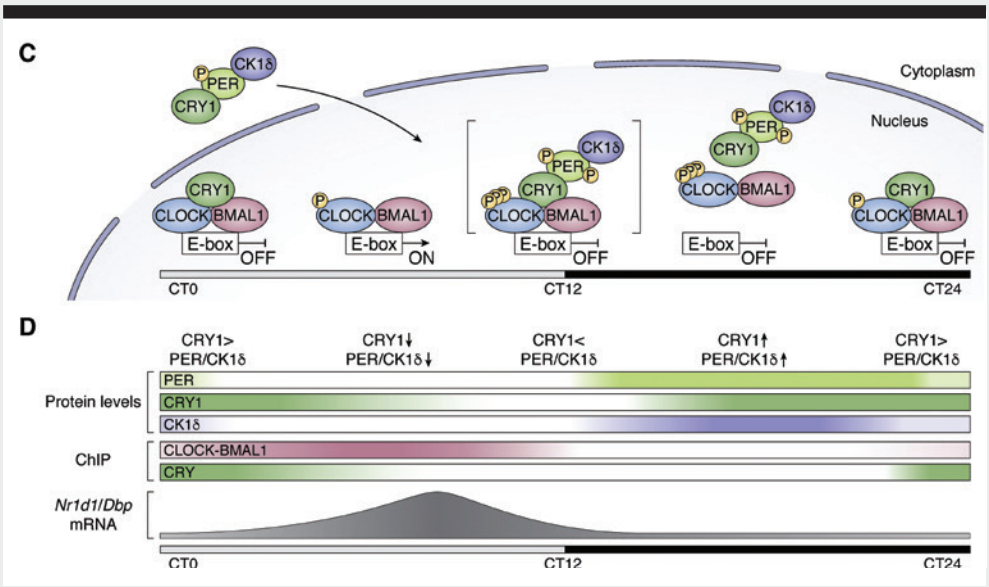
Using transcriptomics, the researchers showed that circulating tumor cells captured at night expressed many genes related to mitosis, while those collected by day devoted more energy to translation and ribosome biogenesis. Oddly, however, the tumor cells also seemed to have no cellular time keeper; they had lost oscillation of their clock proteins.

How the cellular clock runs

The molecules that run the human circadian clock are expressed in almost every cell. The first described was a protein called CLOCK, short for "circadian locomotor output cycles kaput." CLOCK works with binding partner BMAL1 as a transcription factor. When the two bind unfettered to DNA, they drive transcription of numerous genes. But that free access is possible for only part of the day. Most of the time, BMAL and CLOCK have additional binding partners that disrupt their ability to

COURTESY OF IRINA BEZSONOVA

An illustration by biophysicist Irina Bezsonova shows a portion of the CLOCK protein's 3-dimensional structure.



YANG ET AL., J BIOL CHEM 2021

A figure from a recent review in the Journal of Biological Chemistry shows how complexes form and separate, regulating DNA expression to generate circadian rhythms.

bind to DNA.

Their window of opportunity peaks a little after midday. As evening nears, their transcriptional activity produces a group of inhibitor proteins called cryptochromes, or CRYs, and period proteins, or PERs. When a cryptochrome binds the CLOCK–BMAL dimer, it recruits a pile-on of other proteins that becomes a powerful repressive complex.

One kinase in the complex gradually phosphorylates CLOCK. Carrie Partch, a structural biologist at the University of California, Santa Cruz, who works on the assembly and diversity of circadian protein complexes, said that the enzyme's inefficiency is a feature, not a bug. "We think that clocks rely on poor enzymes to help add the delay that leads to a 24-hour (cycle)."

By nightfall, CLOCK and BMAL are incapacitated. They relax their hold on the DNA. This turns off the faucet of CRY and PER protein production. As the night wears on, degradation reduces levels of CRYs and PERs, while phosphatases reverse CLOCK phosphorylation. As that happens, CLOCK and BMAL regain their ability to bind to DNA. One CRY, with especially high binding affinity, sticks around until dawn — at which point, it too begins to be degraded, eventually freeing CLOCK–BMAL to transcribe again.

Boiled down to its barest essentials, the cycle is simple. Night: off. Day: on. Repeat at roughly 24-hour intervals in almost every cell in the body. The central clock in the brain corrects any slippage.

The central clock

That central clock is composed of a cluster of neurons near the optic nerve, called the suprachiasmatic nucleus, or SCN, which receives light information directly from the retina, independent of the visual system.

Erik Herzog, a professor at Washington University in St. Louis, studies SCN function and communication. "In the same way we think about the atomic clock in Boulder, Colorado, sending out a pulse every morning at 3 a.m. … the SCN sends out daily signals to get everybody on local time," Herzog said.

If a smartwatch were cut off from the atomic clock, it would continue to run but might drift out of accuracy. The same is true for cells: Each can oscillate on its own, but signals from the SCN keep them synchronized. Other parts of the brain turn pulses from the SCN into fluctuations in body temperature and circulating hormones melatonin and cortisol, each of which peaks at a signature time of day.

The SCN is a powerful pacesetter, but its control, researchers recently have learned, is not absolute. A short list of tissues, particularly in the skin and cornea, respond directly to light, even if the SCN has been rigged to run on a different schedule than

an animal's external environment. Also, in the course of human aging, central and peripheral clocks lose synchronicity.

Still, the SCN has an important coordinating role. For example, it is key to determining a person's chronotype, or daily behavior pattern. Not every individual responds to light cues the same way; polymorphisms in clock genes, including the CRY and PER genes that mediate the CLOCK–BMAL pile-on, can determine how long an individual's clock takes to complete a cycle — probably because they change the kinetics of protein complex formation, Partch said. Manipulating those genes in only the SCN can be enough to change an animal's chronotype and turn a morning mouse to an evening mouse.

Whatever its inherent speed, as the cycle repeats itself in cells, it produces an ambient rhythm in gene expression. Nearly half of coding genes, and many noncoding RNAs, show circadian patterns in at least one tissue. Those transcripts affect the proteome, metabolome and cellular behaviors such as the cell cycle, DNA damage responses and apoptosis. Physiological functions such as sleep, body temperature, immune activity and feeding vary by time of day. Small wonder that researchers are asking whether medical interventions might also answer to the clock.

In discussions of drugs and the circadian rhythm, two types of interventions come up. A physician or a patient might try to adjust the clock through light therapy, timing cues such as exercise, or small molecules that interfere with the circadian oscillatory system. Or they might try to time medicines to reach their highest efficacy by working with biochemical and behavioral patterns that oscillate daily.

Drugging the clock

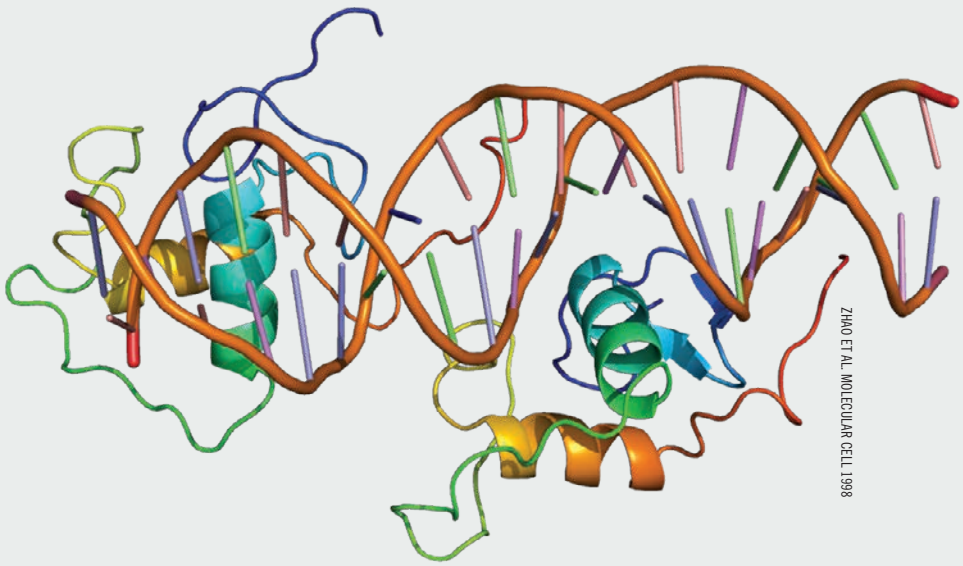
Scientists have found some evidence that bringing patients' circadian rhythms into alignment using light and other cues can be beneficial. Timing food intake and exercise may help with Type 2 diabetes, and some (but not all) studies have concluded that cycling light conditions in a neonatal intensive care unit speeds development. But small molecules that alter the function of individual clock proteins have, so far, had little effect.

The clock is hard to drug, according to pharmacologist Tom Burris of the University of Florida, whose lab developed agonists for the clock protein called REV-ERB, a nuclear receptor that regulates BMAL1 expression. The drugs' effects on mice are subtle; to see them, his lab had to dose the animals after they had been in the dark for several days. He thinks that's because clock proteins are highly redundant, making the circadian cycle robust.

"I don't think we can reset the entire rhythm, but we can modulate pieces of it," Burris said. Because various clock proteins link to assorted other cell systems, he added, tweaking some of them might be useful, even

Physiological functions such as sleep, body temperature, immune activity and feeding vary by time of day. Small wonder that researchers are asking whether medical interventions might also answer to the clock.

REV-ERB is a transcription factor, shown here binding to DNA.



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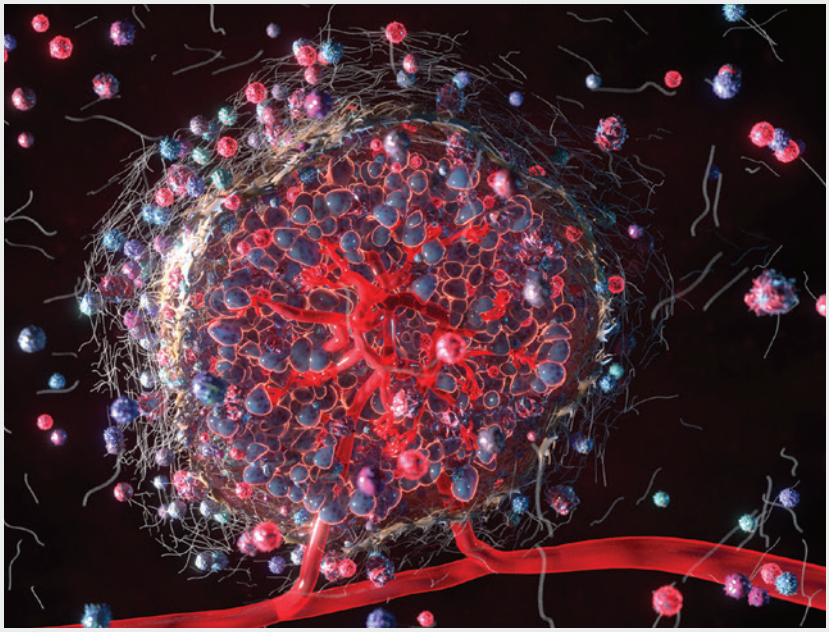


The number and metastatic potential of circulating cancer cells can change by time of day. Researchers hope to find the optimal time to use drugs that target proliferation.

if REV-ERB activation does not reset the sleep–wake cycle altogether.

Several groups have studied the effects of the REV-ERB agonists on tumor cells. Sometimes, their effects look promising. A lab at the Salk institute observed that they seemed to reduce autophagy and cause programmed cell death selectively in cancer cells. However, critics point out that the drugs also have effects in mice that lack the REV-ERB gene, suggesting that they may act through other targets.

Burris expects that, over time, "we're going to understand more about how the oncogenic pathways are coupled to the circadian rhythm and be able to hijack some of the targets that are shared."

Still, because of this complexity, more physicians have focused on timing a drug for greatest efficacy. Jeffrey Field, a pharmacologist at the University of Pennsylvania, put it this way: "The evidence for drugging the clock is probably weaker than clocking the drugs."

Clocking the drugs

An influential review article published in the journal Science in 2019 found that 75% of 106 trials testing the same drug at two times of day showed differences in either toxicity or efficacy. Roughly 20 of those trials tested cancer drugs. Drugs with a shorter half-life were more likely to show a time-of-day effect.

In a study that cited that work, researchers in the labs of Jeffrey Field and Penn colleague Amita Sehgal tested 126 drugs at six-hour intervals, comparing their effects on osteosarcoma cells that had a functioning circadian clock and others that did not. They found that the timekeeping cells were more sensitive to about half of the drugs at some times of day than at others. Focusing on a group of drugs that target the chaperone protein HSP90, which they previously had shown connects the clock with the cell cycle, they found that they were most effective if given just after the chaperone hit its lowest daily expression level.

"Proliferation was affected because a specific part of the cell cycle was regulated by the clock, and that part of the cell cycle is also targeted by many chemotherapeutics," Sehgal, a circadian biologist, said.

In this case, timing the drug to match the circadian clock meant also timing it to match the cell cycle, which the clock can influence. Sehgal and Field proposed that links between the cell cycle and circadian rhythm may be among the most important reasons that some drugs show circadian effects. But other pathways also fluctuate with time of day: Researchers have suggested exploiting rhythms in DNA repair or inflammation, both of which interact with the clock, to get the

most out of extant drugs. Unraveling causality in these complex interactions can be a challenge.

"Often I get the question, 'Is the efficacy that you're getting because you're regulating the circadian system or some other piece?'" Burris said. "I've often said, you just can't say that, because they're connected."

Besides hitting a target at the right time — which may mean that target concentration is high or low, depending on the drug — there's a second mechanism by which dosing time might give a drug an advantage: It may cause lower toxicity at certain times of day. Most legacy chemotherapy drugs kill healthy and tumor cells somewhat indiscriminately, causing harmful side effects. Whether it's killing more cancer cells or damaging other tissues less, improvement to a drug's therapeutic index — the distance between an effective dose and a dose that causes harmful side effects — could be beneficial.

Finally, a drug may be metabolized differently over time. Besides the desired target and any collateral proteins that cause off-target effects, molecules that may cycle include the liver enzymes that convert a drug to its active form, the transporters that carry it into its target cell or across the blood–brain barrier, the enzymes required for degrading or secreting it, and other players that deliver an active pharmaceutical ingredient to the tissue where it acts.

Sehgal suggested that retrospective studies of people who happen to take a drug at different times are a good way to scan for effects without getting lost in mechanistic details. "Maybe that's not the optimal time from the perspective of the daily rhythm in cortisol, but maybe it is from the point of view of when the target is up."

Confusing clinical trials

Russell Van Gelder, a physician–scientist who chairs the ophthalmology department at the University of Washington, is skeptical that dosing at a specific time of day will yield dramatic medical advances. He said, "You're taking extremely complicated physiologies that have multiple clock components running at the same time and assuming that there's some phase that's optimized and will have a very clear effect."

He cited a history of clinical failures to show conclusive circadian effects. For example, a 2006 study of timed chemotherapy for patients with metastatic colorectal cancer found that timed dosing only helped some patients. Median survival was comparable between the study's arms, but timed therapy reduced the risk of an earlier death in men by 25% and increased it by 38% in women.

No one is certain why women fared worse than men in this study. Author Francis Lévi, the oncologist in France, vehemently disputed the characterization of this study as a failure. Lévi's group subsequently has conducted many studies defining the lowest-toxicity timing for various chemotherapies and continues to observe sexual dimorphism in optimal dosage times. He said, "It's a complex issue, and this is why it has taken a long time and is not yet finished."

But when a recent news article on circadian medicine cited the study but only mentioned the improved survival among men, Aziz Sancar, a biochemist at the University of North Carolina who shared the 2015 Nobel Prize for discovery of a DNA repair enzyme that helps to set the clock, was galvanized to speak up about his doubts about the field

Many clinical trials of timed chemotherapy have varied not just the time when drug is administered, but also the infusion regimen or length or the total dosage, making their results difficult to interpret.

at large. Sancar's lab had spent time looking for evidence that an optimal time exists when DNA-damaging chemotherapeutic agents might be most effective.

Doubled survival time among men, Sancar said, simply wasn't what the 2006 study reported. "That got distorted, and all of a sudden people said chronotherapy cures cancer."

Meanwhile, Sancar remained concerned about the half of study participants who had fared worse on timed treatment. "He felt that … this enthusiasm for timed chemotherapy could actually be harming people, or subgroups of people, and not helping them," said longtime colleague Van Gelder.

In two review articles published back to back last year in the journal Science (with co-author Van Gelder) and the Journal of Biological Chemistry (with colleagues from UNC), Sancar laid out an argument that enthusiasm for chronochemotherapy exceeded the evidence that supports it.

Sancar's argument is highly detailed but returns to several themes: He says that the chronochemotherapy literature glosses over negative data, overstates positive findings in reviews and generalizes inappropriately from small studies.

For example, he pointed to a widely cited 1985 paper reporting that a group of 31 women with ovarian cancer who received adriamycin in the morning and cisplatin in the evening experienced fewer side effects than those whose treatment schedule began in the evening; that study could not be replicated, Sancar said. In a study of thousands of patients with metastatic ovarian and uterine cancers, he added, the Gynecology Oncology Research Group "concluded that chronotherapy did not help."

In an interview, Sancar also bemoaned widespread bias against publishing negative results, especially if they contradict previous findings. He said that he wants to see rigorous tests of the chronochemotherapy hypothesis considered objectively — including the disappointing studies.

Summing up their joint work, Van Gelder said, "It's not that circadian rhythms don't have anything to do with cancer. They have a great deal to do with cancer. It's very clear that tumors disrupt rhythmicity, rhythmicity governs tumors, and there are deep mechanistic relationships between clock genes and oncogenes. However, the relationships don't readily predict the appropriate timing for treatment."

Presented with these critiques, Lévi wrote, "An ophthalmologist and a biochemist can hardly understand the methodologic constraints of clinical research and how much we learn from them to advance medicine irrespective of hypothesis validation." One important finding from clinical studies, he said, has been that there is significant divergence between individual responses based on sex,

lifestyle and genotype, meaning that drug timing probably will need to be personalized to be effective.

Lévi also cited a recent systematic review of chronochemotherapy studies that appeared in The Lancet Oncology. The review considered 18 clinical trials published from 1994 to 2021; Lévi was an author of six of them. Most investigated the effects of dosage timing on infused chemotherapeutic drugs, especially combinations including cisplatin and oxaliplatin. The study found that 11 of the 18 trials reported a reduction in toxicity, or harmful side effects, and none showed any reduction in efficacy. However, the review's authors cautioned, it was impossible to isolate the effects of timing, since many of the studies also had altered the duration of infusions or the overall dosage patients received.

The case of temozolomide

"Historically, the research hasn't been done carefully," admitted Erik Herzog, the Washington University biologist. That makes it difficult for researchers to get support to test new circadian medicine hypotheses, such as the one he has been working on with WUSTL colleagues Joshua Rubin, a neuroscientist, and Jian Campian, a neurooncologist.

Herzog and Rubin teamed up to study timing in glioblastoma. They became interested in temozolomide, or TMZ, the best available treatment. The drug works by alkylating purine bases in DNA, causing double-strand breaks that halt replication. Patients take the pill daily for five days, take three weeks off to recover, and repeat indefinitely. TMZ has been a front-line treatment since 2005, but it's no panacea; a glioblastoma patient can expect to live on average 16 months after diagnosis.

Emily Slat, a student in Herzog's lab, found that cultured glioblastoma cells from both mice and humans keep a daily rhythm, and the time when they receive TMZ matters. Treating tumor cells early in the day killed many more of them. Herzog said that the timed effect seems to depend on DNA repair, not cell proliferation.

"If you give temozolomide at a time of day when the clock is revved up and driving the expression of repair enzymes, you may not have much success with the drug," Herzog said. "In fact, there are times of day when it looks like temozolomide does almost nothing."

When she saw the results, Campian was intrigued but cautious. "I didn't want to pull off a large study, put in a lot of resources, and then it doesn't work," she said.

Many treatments, she knew, have looked promising in preclinical models, only to fail in patients. Besides, trials are expensive. A principal investigator must pay institutional review board fees, compensate research assistants to screen and enroll patients and keep records in order, and devote staff time to analyzing data. Even though the drug in question already was prescribed to nearly every patient at the clinic, it was difficult to secure pharmaceutical companies' interest without patent protection. When Campian wrote grants to the National Cancer Institute and several foundations, those groups also did not bite.

Instead, the team found an experiment already underway at their clinic. Many physicians, Campian said, recommend that patients take TMZ in the evening, when the nausea and fatigue it causes may be easier to bear. Other doctors recommend that it be taken in the morning.

WUSTL had a diverse enough

> **"It's not that circadian rhythms don't have anything to do with cancer. ... It's very clear that tumors disrupt rhythmicity, rhythmicity governs tumors, and there are deep mechanistic relationships between clock genes and oncogenes."**
>
> **RUSSELL VAN GELDER**

ATIKA ATIKAWA / WIKIMEDIA COMMONS

Despite the challenges, many researchers expect chronochemotherapy to be proven effective eventually. An artistic rendering shows the CLOCK protein.

group of prescribers for a retrospective study, which was easier to arrange since it would not impact clinical decisions. Among 166 patients who had passed through the clinic and whose dosing time could be determined, the study team found no difference in survival time between groups. However, among patients with methylation of the gene for DNA repair enzyme MGMT — a biomarker that physicians already know sensitizes cells to TMZ treatment — they saw a dramatic benefit from morning dosing.

Campian and Herzog next planned a small feasibility study that the university supported. They would ask patients to take TMZ either in the morning or the evening and compare their outcomes. Contrary to received wisdom, they found that among thirty-five patients on different dosing schedules, no significant differences in adverse side effects arose. However, there was also no significant difference in survival.

"It disappointed us, for sure," Herzog said. But, he added, the study was too small to detect a positive effect reliably, especially one that might apply only to patients with methylated MGMT. In addition, the team did not control for patients' chronotypes, or for disruptions to circadian rhythm that the cancer itself can cause. Continuing the study, the team has begun to use wearable activity monitors to determine how a patient's internal clock compares to the wall clock.

To determine for sure whether there is any difference between taking TMZ in the morning and the evening, doctors would need to recruit several hundred patients, Campian said. She'd like to run such a study, because to her it seems more promising to get the greatest possible efficacy out of a drug that already has been shown to be effective and safe — safe, at least, as chemotherapeutic agents go — than to run the risks of developing a new treatment. She said that she is disappointed that funders do not seem to agree.

"It's going to be a long time before (chronochemotherapy) becomes the norm, primarily because of the expense," Herzog said. He added that studies that start by using cultured cells from patients to identify the times of greater drug efficacy for an individual may be a more cost-effective way forward.

Herzog said that most physicians and grant reviewers expect timing to have at best a mild effect on how well medicine works. He predicts that if robust evidence on one drug could be collected, it would help make the case for circadian therapies. But without much industry interest, it isn't clear how such a blockbuster finding could happen.

"Once a drug company would show something, the others will too," Lévi said. But he thinks that the industry as a whole is conservative and that no company is likely to move first on a concept that has failed in the past.

From chemotherapy to immunotherapy

At a recent American Society for Clinical Oncology meeting, Lévi counted five abstracts showing circadian effects of various drugs in different cancers. "I think the excitement about timing, and the magnitude of the benefit, is now an important fact," he said.

Many of those drugs were antibodies, some of which activate the immune system. In contrast with broad-spectrum DNA-disrupting agents, these are biological drugs with single specific targets and may lend themselves to cleaner mechanistic hypotheses, Van Gelder said. Although they have very long half-lives, which blunts the effects of dose timing in small molecules, some antibodies have shown significant time-of-day effects, a puzzle no one has explained yet.

Immunotherapies, which recruit quiescent immune cells, may benefit from the immune system's strong inherent circadian rhythms. Checkpoint inhibitors, antibodies that block a mechanism cancer cells use to evade immunity, are an example; one analysis suggests they may work best when more T cells can infiltrate the tumor and worst when T cell infiltration is low.

Some practical questions about implementing chronochemotherapy are closer than ever to being answered. For example, if a drug works best at certain times of day, do clinicians need to figure out whether a patient has a certain chronotype, or whether their individual tumor is cycling, before moving forward with treatment? Clinical researchers can control for patient chronotypes during trials using wearable activity monitors. To determine whether a tumor is in phase with its host, researchers may culture a tumor biopsy and add a luciferase reporter of circadian gene expression; or they may isolate circulating tumor cells and use an algorithm to evaluate the transcriptome and determine its point in the circadian cycle.

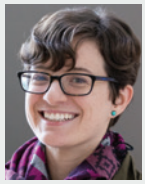
"We need to determine who are the patients with good rhythms, who are the patients with poor rhythms, and determine whether chronotherapy will be more or less effective," Lévi said. But as long as it remains difficult to finance studies of chronochemotherapy, he added, "We will not know. We will not advance."

Despite the challenges of demonstrating a conclusive effect for chronochemotherapy, many researchers expect the approach to bear fruit eventually, especially as the tools for personalized medicine improve doctors' ability to tailor treatment plans for individuals.

Still, Van Gelder said, "I think the odds that we're going to find some drug that is completely ineffective at one circadian phase and phenomenally effective at another are fairly low." After all, most drug targets that fluctuate in response to the clock change by at most a few fold. "They don't go from zero to a thousand."

Nonetheless, Sancar said, the prospect of curing cancer with circadian rhythms is an appealing one, even for him. "All scientists, all human beings want their work to be relevant."

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



CLOCK DISRUPTION AND CARCINOGENESIS

Does circadian disruption cause cancer? In humans, the answer has seemed to be yes. But preclinical models have yielded confusing results, making it hard to say why people who do shift work develop cancer at higher rates in epidemiological studies.

"It's been almost a two-decade-long conversation now," said biologist Carrie Partch at the University of California, Santa Cruz. "I don't think there's a really clear answer … in terms of 'a particular cancer has a particular type of effect on the clock,'" or a particular disruption of the clock promoting particular cancers.

In mouse models, she said, removing different clock genes from different genetic backgrounds has led to results that are difficult to compare. In cell lines, it can be tricky to choose an appropriate control for an oscillating tumor tissue.

According to Aziz Sancar at the University of North Carolina at Chapel Hill, publication bias — the tendency for positive results to get more attention than negative findings — makes it harder to evaluate the evidence. For example, he described a colleague who had difficulty publishing her observation that, contrary to a previous high-profile paper, mice lacking two Period genes do not show higher cancer rates than their unmodified relatives.

According to French oncologist Francis Lévi, there are at least eight types of cancer whose prognosis is significantly worse if circadian signaling is disrupted. But studies also have shown that cancer — and its associated stress and difficult medical treatments — can disrupt sleep, which may impair circadian rhythms. The complex causal relationships complicate not only studies of whether circadian disruption can cause cancer but also studies concerning chronochemotherapy.

A gathering for our community

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Discover BMB 2023: History reinvents itself

By Vahe Bandarian

Attending a society conference to share research results is a rite of passage and a cornerstone of the scientific process. For many of us, the American Society for Biochemistry and Molecular Biology is our go-to community, and the ASBMB conference is a yearly pilgrimage.

Discover BMB, our 2023 meeting, is the first in many years where the ASBMB will convene independently. This return to our roots is an inflection point in our history and an opportunity to innovate and reimagine.

As chair of the ASBMB Meetings Committee, my goal is to make sure everyone who attends the 2023 meeting comes away inspired to do their best work and to catalyze the lifelong personal connections that are the bedrock of science.

A personal watershed

The only national conference I attended as a graduate student was the 17th International Congress on Biochemistry and Molecular Biology held in conjunction with the 1997 ASBMB annual meeting. I remember my excitement arriving in San Francisco for the conference, the talks and the poster sessions. I remember the nervous thrill of presenting my work to luminaries in the field and receiving their comments.

ROWENA MATTHEWS

I still can feel the handset of the pay phone that I used to call my adviser, George Reed, at the University of Wisconsin–Madison to tell him about all the feedback I'd received and relay his friends' well wishes. At the conference, I met with my future postdoctoral adviser, Rowena Matthews, and we talked about potential projects.

That conference was both a personal and professional watershed for me, and I've looked back on it with utmost fondness over the past 25 years. Through my many moves and spring cleanings, I have not parted with the bag from that conference, because it evokes so many fond memories.

VAHE BANDARIAN

Vahe Bandarian saved this bag from his first ASBMB meeting in 1997.

A society gathers

The ASBMB was founded as the American Society for Biological Chemists on Dec. 26, 1906, during a meeting on the second floor of the Belmont Hotel in New York, which had opened for business earlier that year. The Belmont, by all accounts, was an amazing 1,006-room property located across the street from Grand Central Station.

Documents from the first meeting show that the society's inaugural chair was Russell H. Chittenden and that 29 members were in attendance. The ASBC was established to provide practitioners of the new field of biological chemistry with an independent forum to discuss science that was interdependent with the American Chemical and American Physiological societies — as far as we know, many of the inaugural members were also members of one or both.

In the 116 years since its founding, the society has grown from 81 members, who were nominated and voted in, to the inclusive 10,000-member strong ASBMB. The founders could not have imagined that their society would grow to one that nurtures biological chemists from around the world at every stage of their careers. Attendees at our

The American Society for Biological Chemists held its first meeting in 1906 at the Belmont Hotel.

meeting now include high school students.

The primary goal of the first annual meeting, held May 8–9, 1907, was to provide a platform for dissemination of research. Forty-three papers were presented, mostly by charter members.

Since then, the ASBMB meeting has been canceled only a handful of times, most recently in 2020 as COVID-19 surged globally. It has taken many forms, often held in conjunction with other societies like the conference I attended in 1997, but it always has been true to its origin as a forum for discussing science and for conducing the business of the society.

#DiscoverBMB

The guiding principles for programming the 2023 meeting are inclusion and community building.

Posters: Introduced to ASBMB meetings in 1975, poster sessions are being reimagined as the social and exhibition hub of the conference. Rather than holding these sessions midday, we're moving all posters to the end of the day. We will provide refreshments to help keep energy and enthusiasm levels in the stratosphere and to drive traffic to both the posters and exhibitors.

Interest groups: We will designate spaces within the exhibit hall as meetup zones for interest groups. We are imagining these as gathering places for scientific discussion and social interaction. No more trolling the hall on your phone trying to locate your collaborator — just tell them to find you in meetup zone 1, 2 or 3.

Receptions: We're planning a societywide opening reception to welcome everyone and a closing reception to bid everyone farewell. These bookending events will provide amazing opportunities for folks to discuss science and establish new friendships and collaborations.

Scheduling: We are mindful of start and stop times each day, with no formal session starting earlier than 9 a.m., so late-night scientific discussions can flow. Award lectures will be interspersed with other programming throughout the day — and as part of reimagining the conference, we are building in time for Q&A after each award talk.

Of course, we plan to continue interest groups and the spotlight sessions, which provide valuable opportunities for subdisciplines to get together and speaking slots for early and midcareer investigators. This is just an early glimpse of our plans — stay tuned for more information.

The Meetings Committee will collaborate with ASBMB staff over the coming months on many details. In fact, we already met in Philadelphia during the 2022 meeting. We all hope the move to a stand-alone conference will be a hit with our members. We're going into this with open minds and with the goal of making 2023 memorable. Whether this is your first ASBMB meeting or one of many, we want you to come away feeling invigorated as you return to the bench and anticipate 2024 with excitement.

As I tell my students, any experiment worth doing is worth repeating. Consider 2023 as an experiment, the first of many over the next few years as we work toward a stand-alone ASBMB meeting that serves and strengthens our community.

Come to Seattle for Discover BMB and celebrate the new meeting with us!

Vahe Bandarian (vahe@chem.utah.edu) is a professor of chemistry at the University of Utah and chair of the ASBMB Meetings Committee. Follow him on Twitter: @Vahooster.

ADVANCES IN ORGANISMAL AND CELLULAR METABOLISM

Different field, different problem, same solution: metabolism!

By Nika Danial & Gary Patti

Metabolism has captured the interest of researchers across many different biological disciplines. In some fields, interest in longstanding metabolic questions has been renewed. In other areas, new metabolic connections are being made for the first time. No matter the topic, however, metabolism studies evoke pathway charts and methodological approaches that may not be common knowledge in all disciplines, and this could hinder dialogue between investigators. Moreover, many of the same metabolic patterns are observed consistently in different disease settings, animal models and cell types.

The purpose of our symposium at Discover BMB, the annual meeting of the American Society for Biochemistry and Molecular Biology, which will be held in March in Seattle, is to bring together researchers from disparate areas of biology who speak the common language of metabolism. We want to facilitate interactions between investigators who may be thinking about the same metabolic themes, but who are not typically at the same meetings or conferences. The presentations will not be organized by discipline but rather by metabolism topic, with the aim of stimulating new discussions and collaborative opportunities.

Our symposium will feature research examining metabolism at multiple levels — ranging from whole body to cells and organelles. We will hear how the same metabolic programs are implicated not only in diseases such as cancer and neurodegeneration but also in fundamental biochemical processes including immune response and vision.

Keywords: Metabolism, metabolomics, lipids, physiology, interorgan communication, mitochondria, lysosomes, isotope tracing.

Who should attend: Anyone interested in metabolism at any level in any context.

Theme song: "What Makes You Beautiful" by One Direction, because metabolism lights up all of our worlds — and in honor of the infamous "What Makes Glycolysis" parody (look it up!).

This session is powered by Ox phos (platinum-level sponsor) and substrate-level phosphorylation (gold-level sponsor).

SPEAKERS

Metabolic physiology
Gary Patti (chair), Washington University in St. Louis
Deb Muoio, Duke University
Nada Kalaany, Harvard Medical School
Matt Gentry, University of Kentucky

Metabolism in health and disease
Jason Tennessen, Indiana University
Jing Fan, University of Wisconsin

Organelle metabolism
Nika Danial (chair), Harvard Medical School
Dale Abel, University of California, Los Angeles
Roberto Zoncu, University of California, Berkeley
Natalie Niemi, Washington University in St. Louis

Nika Danial (nika_danial@dfci.harvard.edu) is an associate professor of medicine at Dana–Farber Cancer Institute and Harvard Medical School and the co-director of the T32 training program in cancer chemical biology and metabolism at DFCI.

Gary Patti (gjpattij@wustl.edu) is a professor in the departments of chemistry and medicine at Washington University in St. Louis and the senior director of the Center for Metabolomics and Isotope Tracing.

ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING IN STRUCTURAL BIOLOGY, DRUG DESIGN AND SYSTEMS BIOLOGY

Computation is the new experiment

By Rommie E. Amaro & Celia A. Schiffer

After decades of playing second fiddle, computation is now taking center stage — achieving critical insights that experimentation alone cannot provide. We are witnessing a dramatic rise in artificial intelligence–based methods coupled with year-on-year improvements of physics-based approaches. We now can fold a protein accurately from sequence alone!

Game-changing methods in protein and enzyme design are hurtling toward us. Scientists now can integrate numerous experimental data sets into computational models to explore previously unseen elements at (and across) scales never before achieved. Computational simulations are rewriting textbooks — from molecules to system dynamics and function. Machine learning is transforming drug design and development.

All in all, you will not find a symposium at Discover BMB, the annual meeting of the American Society for Biochemistry and Molecular Biology, filled with more excitement and possibility than ours. Buckle up for a thrilling ride in March in Seattle!

Keywords: Artificial intelligence, structural biology, simulation, drug discovery, bioinformatics, systems biology, machine learning.

Who should attend: All who want to find out how computation is transforming biological problem-solving.

Theme song: "Respect" by Aretha Franklin, because computation deserves it.

This session is powered by a 1.2 gigawatt flux capacitor.

SPEAKERS

Structure determination

Debora Marks, Harvard Medical School
Rommie E. Amaro (chair), University of California, San Diego
Ramanathan Arvind, Argonne National Laboratory; University of Chicago
Jason Perry, Gilead Sciences Inc.

Drug design

John Chodera, Sloan Kettering Institute
David Baker, University of Washington
Steve Capuzzi, Vertex Pharmaceuticals
Celia Schiffer (chair), University of Massachusetts Chan Medical School

Bioinformatics / Systems biology

Marian Walhout, University of Massachusetts Chan Medical School
Janet George, Intel Corporation
Ivet Bahar (chair), University of Pittsburgh School of Medicine
Henry van dem Bedam, AtomWise Inc.

Rommie E. Amaro (ramaro@ucsd.edu) is a professor in the chemistry and biochemistry department at the University of California, San Diego. Follow her on Twitter: @RommieAmaro.

Celia A. Schiffer (celia.schiffer@umassmed.edu) is professor and chair of the University of Massachusetts Chan Medical School Department of Biochemistry and Molecular Biotechnology and director of the Institute for Drug Resistance.

BIAS IN, BIAS OUT IN DATA SCIENCE

Control our thoughts and better science will follow

By Allison C. Augustus–Wallace

The COVID-19 pandemic has shined a light on the disproportionate burden that certain diseases and conditions — such as diabetes, metabolic syndrome and mental health disorders — have on historically excluded, marginalized communities. It also has drawn attention to the negative impacts of implicit biases and the social construct of race.

The American Society for Biochemistry and Molecular Biology Maximizing Access Committee's symposia at Discover BMB in Seattle in March will examine the effects of implicit biases on science at the genomic level, including experimental design and data interpretations, and how they contribute to health disparities. This topic is of particular importance with the emerging use of genetics in the development of artificial intelligence mechanisms.

We must seek remedies and mitigate health disparities. This means asking tough questions, even of ourselves as scientists. We must examine how our implicit biases warp our lens as biomedical researchers. We must revisit our scientific past to understand better our present and, thus, prepare for our future.

Keywords: Genetics, race, implicit bias, data interpretation, health disparities, artificial intelligence.

Theme song: "Free your Mind" by En Vogue is a song that speaks to daily stereotypes, implicit biases and microaggressions that historically excluded, marginalized people face. If only those who make such judgments would free their minds, peace for all of us would follow.

This session is powered by our need, as scientists, to be mindful of our implicit biases — and the potential roles they play in our research questions, experimental designs and data analyses — so that we can mitigate them and thereby health disparities.

SPEAKERS

Race as a human construct: We are only human, not a race

Kayunta Johnson–Winters (chair), University of Texas at Arlington
Amanda Bryant–Friedrich, Wayne State University
Chris Gignoux, University of Colorado Anschutz Medical Campus
Daniel Dawes, Morehouse School of Medicine Satcher Health Leadership Institute
Allison C. Augustus–Wallace, Louisiana State University Health Sciences Center New Orleans

How selection bias and data interpretation contribute to disparities in health outcomes and artificial intelligence development

Sonia Flores (chair), University of Colorado Denver
Irene Dankwa–Mullan, IBM Watson Health
Lucio Miele, Louisiana State University Health Sciences Center New Orleans
Robert T. Maupin Jr., Louisiana State University Health Sciences Center New Orleans
Rosalina Bray, National Institutes of Health Office of Extramural Research

Implicit bias

Ruma Bannerjee (chair), University of Michigan
Mahzarin Banaji, Harvard University

Allison C. Augustus–Wallace (awall1@lsuhsc.edu) is an associate professor at Louisiana State University Health Science Center in New Orleans and a member of the ASBMB Maximizing Access Committee.

BIOCHEMISTRY OF ELEMENTAL CYCLING

Microbial engines of global change

By Sean J. Elliott & Jennifer Dubois

Right now, redox cycling of the elements is happening on a genuinely global scale. These cycles are driven by the intricate electron-transfer chemistry of microbial organisms. Whether engaging in the molecular construction projects of the carbon, nitrogen or sulfur cycles or simply moving electrons to make a bioenergetic living, these smallest of creatures harness metals as cofactors to cycle and recycle the environment around us continuously.

Our symposia at the American Society for Biochemistry and Molecular Biology annual meeting — now called Discover BMB — in Seattle in March will cover several topics relating to the biochemistry and microbiology of elemental cycling, where complex metalloenzymes often are used to achieve startling transformations. Recently elucidated mechanisms, insight into how metallocofactors are harnessed to power the redox reactions of life around us, and surprising insights into the connections between metals, microbes and electrons all will be discussed.

With concerns for sustainability and a new energy economy, the microscopic world of biological chemistry has much to teach us.

Keywords: Metalloenzymes, enzyme mechanisms, microbiology, biochemistry, biogeochemistry.

Who should attend: All who are fascinated by how microorganisms shape the world around us and how the environment, in turn, shapes microbial biochemistry.

Theme song: "Electric Boogie (The Electric Slide)" by Marcia Griffiths.

This session is powered by electrons, and so are you.

SPEAKERS

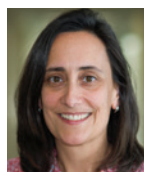
The enzymology of the carbon cycle
Jennifer Dubois (chair), Montana State University
Stephen Ragsdale, University of Michigan
Sean Elliott, Boston University
Cecilia Gomez Martinez, University of California, Berkeley
Kylie Allen, Virginia Tech

Frontiers of the nitrogen cycle
Eric Hegg (chair), Michigan State University
Yilin Hu, University of California, Irvine
Lisa Stein, University of Alberta
Akif Tezcan, University of California, San Diego

Metals, microbes and minerals
Sean Elliott (chair), Boston University
Eric Boyd, Montana State University
Jennifer Dubois, Montana State University
Jeff Gralnick, University of Minnesota
Christine Morrison, Colorado School of Mines

Sean J. Elliott (elliott@bu.edu) is a professor at Boston University. Follow him on Twitter: @prof_sje.

Jennifer Dubois (jennifer.dubois1@montana.edu) is a professor at Montana State University.



CELL SIGNALING — NEW TOOLS AND EMERGING CONCEPTS

Shining lights on the cell

By Jin Zhang & Kevin H. Gardner

The cellular machinery is a remarkable system that is able to regulate myriad life processes with exquisite specificity by responding to a variety of environmental cues. This essential regulation is achieved through a network of highly dynamic signaling molecules that are regulated both spatially and temporally.

Inspired by nature's fluorescent proteins and photosensors, biochemists have made tremendous advances toward developing new classes of genetically encoded protein tools to detect and control signaling activities with high spatiotemporal precision. With these new tools, new kinds of biochemistry, molecular biology and cell biology are being discovered on a regular basis.

For the American Society for Biochemistry and Molecular Biology annual meeting, Discover BMB, in Seattle in March, we have assembled symposia featuring some of the top experts in these diverse fields who will discuss new tools for manipulating and visualizing the activity of enzymes and other classes of protein activity in living cells across a range of settings. As an example of the impact of these tools, we will highlight the emerging field of liquid–liquid phase separation as an organizing principle of cell signaling uniquely identified by advances in our ability to probe and control biomolecules in vitro and in cells.

Keywords: Optogenetics, fluorescent biosensors, protein engineering, phase separation.

Who should attend: Biochemists, cell biologists and protein engineers interested in novel protein-based tools to observe and control cellular behavior as well as new concepts in cellular organization that have emerged from use of these reagents.

Theme song: "Blinding Lights" by The Weeknd.

This session is powered by high-quality photons — from the UV to the infrared.

SPEAKERS

Toolkit for native biochemistry: Sensors, actuators and computational tools
Kevin H. Gardner (chair), City University of New York Advanced Science Research Center
Klaus Hahn, University of North Carolina at Chapel Hill
Sabrina Spencer, University of Colorado Boulder
David van Valen, California Institute of Technology

Spatiotemporal control of cellular signaling
Jin Zhang (chair), University of California, San Diego
Mark von Zastrow, University of California, San Francisco
Lukasz Bugaj, University of Pennsylvania
Anton Bennett, Yale University

Liquid–liquid phase separation as a signaling paradigm
Christine Mayr (chair), Memorial Sloan Kettering Cancer Center
Zhijian "James" Chen, University of Texas Southwestern Medical Center
Sarah Veatch, University of Michigan
Shana Elbaum-Garfinkle, City University of New York Advanced Science Research Center

Jin Zhang (jzhang32@ucsd.edu) is a professor at the University of California, San Diego, and co-director of the Cell Signaling Center at UCSD. Follow her on Twitter: @jinzhanglab.

Kevin H. Gardner (kgardner@gc.cuny.edu) is a professor at the City College of New York and director of the CUNY Advanced Science Research Center's Structural Biology Initiative. Follow him on Twitter: @nmrkaygee.

FRONTIERS IN CARBOHYDRATE SYNTHESIS AND RECOGNITION

Carbohydrates for life, health and diseases

By Catherine L. Grimes and Xi Chen

What molecules determine human ABO blood groups? What do influenza viruses grab when they infect a human? What define the serotypes of bacterial species? What are the most diverse protein post-translational modifications? The answer to all of these questions is "carbohydrates."

Indeed, carbohydrates are indispensable biomolecules and components that are essential for life. They are key recognition components of many biological and pathological events. Synthesizing glycans and understanding the roles of carbohydrates used to be daunting tasks but, thanks to recent progress, have become easier.

The exciting talks in our symposium at Discover BMB, the annual meeting of the American Society for Biochemistry and Molecular Biology, which will be held in March in Seattle, will highlight recent advances made on several fronts: glycan synthesis, tools developed, chemical biology, and the roles and the applications of carbohydrates in health and diseases.

The topics include human and bacterial glycans, biocatalysis, chemoenzymatic synthesis, glycomics, glycoproteomics, anti-glycan antibodies and the roles and applications of carbohydrates in learning, memory and treatment of adult diseases.

We aim to engage aficionados as well as those interested in learning more about how to implement these approaches in their own research.

Keywords: Biocatalysis, carbohydrates, glycans, glycoscience, synthesis, recognition.

Who should attend: Anyone interested in the recent advances in the synthesis, roles and applications of glycans and glycoconjugates.

Theme song: "Watermelon Sugar" by Harry Styles.

This session is powered by a sugar rush.

SPEAKERS

Synthesis of glycans for exploring their roles in health and diseases
Xi Chen (chair), University of California, Davis
Catherine L. Grimes, University of Delaware
Rita Gerardy–Schahn, Hannover Medical School
Steven D. Townsend, Vanderbilt University
Jerry Troutman, University of North Carolina at Charlotte

Chemical glycobiology and tools for glycoscience
Catherine Grimes (chair), University of Delaware
Mireille Kamariza, Harvard University
Jeff Gildersleeve, National Cancer Institute
Lingjun Li, University of Wisconsin
Tania Lupoli, New York University

Carbohydrate biocatalysts and glycan-binding probes/materials
Catherine Grimes (chair), University of Delaware
Xi Chen, University of California, Davis
Barbara Imperiali, Massachuetts Institute of Technology
Kelley Moremen, University of Georgia
Vered Padler–Karavani, Tel Aviv University

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Xi Chen (xiichen@ucdavis.edu) is a professor at the University of California, Davis. Follow her on Twitter (@ChenGlycoGroup).

LIPID DYNAMICS AND SIGNALS IN MEMBRANE AND PROTEIN STRUCTURE

Lipids, lipids everywhere!

By Mike Airola and Robert V. Stahelin

Lipids not only taste delicious (at least in our opinion) but are the major components of biological membranes and play essential roles in most aspects of human biology. In fact, if we look closely at the lipids and membranes of eukaryotes and prokaryotes, we see they contribute to fundamental roles in compartmentalizing cells, stress responses, metabolism, gene regulation, inflammation, and activating both cell protective and cell destructive mechanisms.

As such, the study of lipids and membranes remains a critical and emerging area for cutting-edge research — one that has great potential to impact human health and the understanding and treatment of diseases.

Our symposia at Discover BMB, the annual meeting of the American Society for Biochemistry and Molecular Biology, in Seattle in March will bring together leading investigators in lipid metabolism and membrane function in replication of microorganisms and viruses, communicate novel protein structural information in lipid metabolism and transport, and promote the understanding of membrane structure and biophysics in cell physiology.

Keywords: Enzyme regulation, lipid droplets, lipid domains, membrane structure and tension, sphingolipids, infectious disease.

Who should attend: Lipid and membrane enthusiasts and anyone interested in learning more about lipid metabolism, lipid–protein interactions or membrane structure.

Theme song: "Insane in the Membrane" by Cypress Hill.

This session is powered by Hass avocados, rich in healthy fats.

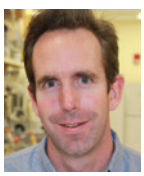
SPEAKERS

New roles for lipids in microorganisms and viruses
Michael Airola (chair), Stony Brook University
Robert V. Stahelin, Purdue University
Elizabeth Johnson, Cornell University
Eric A. Klein, Rutgers University–Camden
Nihal Altan–Bonnett, National Institutes of Health

Molecular insight into lipid metabolism and transport
Abdou Rachid Thiam (chair), Centre national de la recherche scientifique, Ecole Normale Supérieure de Paris
Michael Airola, Stony Brook University
Angeline Lyon, Purdue University
Eric Ortlund, Emory University School of Medicine
Saskia Neher, University of North Carolina at Chapel Hill

Membrane structure and dynamics
Robert Stahelin (chair), Purdue University
Abdou Rachid Thiam, Centre national de la recherche scientifique, Ecole Normale Supérieure de Paris
Sarah Keller, University of Washington
Suzanne Scarlata, Worcester Polytechnic Institute
Ilya Leventhal, University of Virginia

Mike Airola (michael.airola@stonybrook.edu) is an assistant professor at Stony Brook University. Follow him on Twitter: @Airola_lab.



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ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING IN STRUCTURAL BIOLOGY, DRUG DESIGN AND SYSTEMS BIOLOGY

The era of 'smart' organelles

By W. Mike Henne & Cheryl A. Kerfeld

Organelles are the fundamental units of cellular organization, and our understanding of their roles in cell physiology has evolved dramatically since they first were described in the early 20th century. Though organelles originally were thought of as simple compartments for biochemical reactions and confined to eukaryotes, new studies have revealed "smart" roles for them in fine-tuning metabolism as well as serving as platforms coordinating signaling and quality-control pathways in both bacteria and eukaryotes.

Recent work illuminates the organizational principles governing how organelles cleverly coordinate cell quality control. These reveal how organelles create microenvironments for metabolic pathways, how they facilitate interorganelle communication to sense and respond to specific cues, and how the phase properties of lipids and proteins equip organelles to protect cells from stress and maintain organismal homeostasis.

Our symposia at the American Society for Biochemistry and Molecular Biology's annual meeting, Discover BMB, in Seattle in March illustrate these themes and feature work in an array of fields, including prokaryotic and eukaryotic cell biology, cancer biology, and phase separation biophysics.

Just like in the song "Whatever It Takes" by Imagine Dragons, organelles are equipped to do whatever is necessary for cells to adapt and survive the ever-present challenges of life.

Keywords: Bacterial microcompartments, interorganelle communication, protein and lipid phase separation, mitochondrial metabolism.

Who should attend: Anyone interested in learning how organelles are constructed, organized and responsive to signals. Also people interested in the phase properties of proteins and lipids in organelle biology.

Theme song: "Whatever It Takes" by Imagine Dragons.

The session is powered by lipids, proteins and cellular stress.

SPEAKERS

Bacterial organelles
Luning Lu, University of Liverpool
Cheryl Kerfeld (chair), Michigan State University
Arash Komelli, University of California, Berkeley

Phase separation in organelle structure and function
David Savage, University of California, Berkeley/ Howard Hughes Medical Institute
Martin Jonikas, Princeton University
Mike Henne (chair), University of Texas Southwestern Medical Center
Alex Merz, University of Washington School of Medicine
Anthony Vechiarelli, University of Michigan

Inter-organelle communication
Karin Reinisch, Yale University
Laura Lackner, Northwestern University
Sarah Cohen, University of North Carolina at Chapel Hill
Rushika Perera (chair), University of California, San Francisco

Cheryl A. Kerfeld (kerfeldc@msu.edu) is a distinguished professor at Michigan State University.

W. Mike Henne (mike.henne@utsouthwestern.edu) is an associate professor at the University of Texas Southwestern Medical Center at Dallas. Follow his lab on Twitter: @HenneLab.

PROTEIN MACHINES AND DISORDER

Living in a bubble

By Y. Jessie Zhang & Ivaylo Ivanov

In our cells, proteins assemble into dynamic macromolecular machines whose function and regulation underlie life's essential processes. One example is gene expression, in which cells depend on biomolecular machines to harness the information in DNA.

Understanding the inner workings of these intricate assemblies is among the great challenges in the biomedical sciences. Knowledge was, until recently, severely limited by their sizes and complexity.

Therefore, our field has been greatly excited by the incredible advances in cryo-electron microscopy and its "resolution revolution," which we will feature in our symposia at the American Society for Biochemistry and Molecular Biology annual meeting, Discover BMB, in Seattle in March.

A contrast to the highly structured protein complexes lies in the often underappreciated structurally disordered protein regions, which also will be in the limelight during our symposia. Recent studies have shown that, far from being useless, these disordered regions can cause liquid–liquid phase separation — an omnipresent phenomenon in eukaryotic cells underpinning the formation of membraneless organelles.

Localization of protein machines within membraneless organelles allows them to work more efficiently or achieve necessary regulatory interactions. Conversely, condensate disruption compromises the function of the protein machines within, leading to human diseases.

Keywords: Protein complexes, gene expression, genome maintenance, intrinsically disordered regions, lipid–lipid phase separation, computational biology, cancer, neurodegeneration.

Who should attend: Anyone who works with proteins with ordered or disordered regions. (Well, isn't that everybody?)

Theme song: "With a Little Help from My Friends" by the Beatles. (The protein machines work so efficiently with the help of the condensates formed by disordered regions of the proteins.)

This session is powered by structured proteins (yang) and droplets (yin).

SPEAKERS

Protein machines at the intersection of genome maintenance and gene regulation
Ivaylo Ivanov, Georgia State University
Huilin Li, Van Andel Institute
Tanya Paull, University of Texas at Austin
Yuan He, Northwestern University

Methodology investigating disordered proteins and condensates
Jeetain Mittal, Texas A&M University
Jessie Zhang, University of Texas at Austin
Xavier Darzacq, University of California, Berkeley
Simon Alberti, Technische Universität Dresden

Disordered protein in diseases
James Shorter, University of Pennsylvania
Hao Jiang, University of Virginia
Pinglong Xu, Zhejiang University
Rebecca Page, University of Connecticut

Y. Jessie Zhang (jzhang@cm.utexas.edu) is a professor at the University of Texas at Austin.

Ivaylo Ivanov (iivanov@gsu.edu) is a professor at Georgia State University.

REGULATION OF RNA

Keep your friends close and your RNAs closer

By Stacy Horner & Daniel Dominguez

The importance of understanding RNA biology never has been more apparent. Not only did an RNA virus cause a global pandemic, COVID-19, but an RNA-based vaccine has the power to end it. RNA biology is complex and fascinating, and alterations to its function often lead to disease.

How much do you really know about RNA? How is RNA regulated? What does RNA do in the cell? What happens when RNA regulation goes wrong? What are the latest approaches to studying RNA function?

Our symposia at Discover BMB, the annual meeting of the American Society for Biochemistry and Molecular Biology, in Seattle in March is organized around these important questions and will feature a diverse set of experts on these topics.

Keywords: RNA modifications, epitranscriptome, RNA localization, splicing, viral RNA, RNA binding proteins, RNA structure.

Who should attend: Everyone who is curious about the diverse biology regulated by RNA, how RNA works and the latest methods to study its function.

Theme song: "Message in a Bottle" by The Police.

This session is powered by ribonucleic acid, its modifications and the interacting proteins.

SPEAKERS

RNA binding proteins and disease
Daniel Dominguez (chair), University of North Carolina at Chapel Hill
Brenda L. Bass, University of Utah
Alfredo Castello, Medical Research Council–University of Glasgow Centre for Virus Research
Kristen Lynch, University of Pennsylvania School of Medicine

RNA modifications: discovery and function
Stacy Horner (chair), Duke University School of Medicine
Lydia M. Contreras, University of Texas at Austin
Kate Meyer, Duke University School of Medicine
Jordan Meier, National Cancer Institute

Novel RNAs: localization, form, function
Silvi Rouskin, Harvard Medical School
Eliezer Calo, Massachusetts Institute of Technology
Grace Chen, Yale University
Matthew Taliaferro (chair), University of Colorado Anschutz Medical Campus

Stacy Horner (stacy.horner@duke.edu) is an associate professor at Duke University. Follow her on Twitter: @TheHornerLab.

Daniel Dominguez (didoming@email.unc.edu) is an assistant professor at the University of North Carolina School of Medicine.

EDUCATIONAL PROFESSIONAL DEVELOPMENT

Learn, reflect and lead

By Margaret I. Kanipes

The American Society for Biochemistry and Molecular Biology Education and Professional Development Committee will present three symposia on distinct but essential matters in BMB education at Discover BMB, the society's annual meeting, in Seattle in March.

One symposium will be about artificial intelligence. A lot of people think of AI as in the future, but in fact it is already here. It is changing the way biomedical research is conducted. How do we introduce students to BMB while intertwining AI and machine learning so that they will learn to think like biochemists and data scientists? The goal of this session will be to see how others have brought AI tools into the classroom to make this material accessible to all students.

Another will be about intentional leadership development. How do we help people learn and grow to work toward a common goal? This session will focus on navigating the tough parts of leadership. We'll cover leading in fast-changing environments, working with difficult people and sustaining effective leadership.

The third will be about cultural humility — the dynamic, lifelong process of self-reflection and self-evaluation yielding insights about our identities and biases. This process affects how we show up in our classrooms to provide an inclusive environment where we can create future STEM leaders.

Keywords: Artificial intelligence, cultural humility, professional development, big data, machine learning, biases, leadership, education, inclusive excellence.

Who should attend: Faculty, educators, graduate students, postdocs and administrators.

Theme song: "Golden" by Jill Scott or "Man in the Mirror" by Michael Jackson.

This session is powered by what it takes to build STEM leaders for the future.

Margaret I. Kanipes (mikanipe@ncat.edu) is a professor at North Carolina Agricultural and Technical State University and director of the honors program. Follow her on Twitter: @KanipesMargaret.

Apply now for a travel award

The following awards are available to help ASBMB members submitting abstracts as first authors to present their work at #DiscoverBMB in March in Seattle:

- Dependent-Care Grant
- Early-Career Faculty Award
- Graduate Student Diversity, Equity and Inclusion Award
- Graduate Student or Postdoctoral Researcher Award
- Student Chapters Award
- Undergraduate Faculty Award

American Society for Biochemistry and Molecular Biology
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Deadline for applications: 5 p.m. Eastern on Nov. 30

Award winners will be notified in mid-January.

ASBMB
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ASBMB FELLOWS

Nominate the next ASBMB fellows

Selection as a fellow of the American Society for Biochemistry and Molecular Biology is an honor bestowed upon our most distinguished members.

The program encourages nominations that reflect the breadth and diversity of the society's membership. Nominees must be regular, industry, emeritus or affiliate members of the ASBMB.

Submit a nomination by Nov. 14.

asbmb.org/fellows

Mentoring wins over training in diversifying science

And it's more important for broadening participation

By Shantá D. Hinton

On April 14, I was reminded of the powerful relationships that mentoring cultivates and how it impacts lives.

On that day, I attended the homegoing for Joshua Emmanuel Owusu–Koramoah, a 2020 College of William and Mary graduate, a chemistry major and a linebacker on the football team, who had been found murdered the week before.

The circumstances of Joshua's death were terrible and tragic, but being at that service reminded me that great or even good mentorship integrates our lives — resulting in the pinnacle goal of belonging. Instructors often consider "their" student one who completed a course with them, was their academic advisee, or worked in their research lab. Joshua was not a student in my course, nor was I his advisor, nor was he in my research program, but he was my student because we were both William and Mary. Therefore, I did not hesitate to mentor him. In fact, it is an honor that I'm glad I accepted.

I am guilty of using the words "training" and "mentoring" interchangeably, but there is a distinct difference between the two. I credit my family and my mentors for helping me develop my mentoring style. I learned from peers, students and colleagues and through observing that programs that are limited to training provide students with fewer advantages than programs with a good mentoring component. Mentoring helps students to develop coping mechanisms to handle stress, uncertainty and unknowns that are an integral part of a scientific career. I have become an advocate for understanding the difference between training and mentoring — and will continue to work at using the two terms correctly.

Mentorship is a selfless act; it focuses on serving the best interests of the protégé. Training is oriented toward conveying competence in techniques to lead to a completed product. Yes, mentorship also encompasses this, but it transcends to more and is much more rewarding.

Mentoring provides a continuous foundation, while training is a finite duty. From my perspective, training is comparable to an assembly line: Individuals are required to do a defined task to complete their job. For example, some labs assign students to complete the PCR portion of a project. Students are provided with the samples and reagents and taught the protocol to complete the project successfully. This is training; it only requires the use of the student's hand. Mentorship involves the student as a whole person.

Thus, how can we expect training programs alone to increase a sustainable pipeline of diversity in science, technology, education and mathematics? Belonging remains the elusive goal that will increase diversity in any discipline and, quite frankly, any positive relationship.

My Ph.D. advisor, William R. Eckberg at Howard University, and Winston A. Anderson, who received the Presidential Award for Excellence

in Science, Mathematics and Engineering Mentoring, mentored me as a grad student and still do. Coming from a predominantly white university (University of North Carolina at Chapel Hill) to Howard provided me with a comfortable place to develop and grow as a scientist. There was no doubt that I belonged.

The most pivotal moment for me to excel beyond my own expectations was my postdoctoral experience under Nicholas K. Tonks at Cold Spring Harbor Laboratory. When he stated the minimal journal publishing he expected from all of us, I belonged. His expectations for me were the same as for anyone else; we might reach the goal differently, but we all were expected to achieve it, no matter our sex, gender identity or race. It is noteworthy that he paid attention to all of our different scientific and cultural backgrounds, and that helped the science to excel.

Tatiana Prioleau, a biology major and 2021 William and Mary graduate, was my undergraduate researcher and is now a protégé. She stated it best: "Anyone can train you but not everyone can be a good mentor."

Notice the adjective is "good" and not "great." We seek to be great mentors; however, becoming a good mentor will accomplish our goal of providing an environment of diversity and inclusion, which should catapult our proteges to belonging.

Good science mentors allow their proteges to grow and develop into independent thinkers under their supervision. They allow their proteges to make mistakes while teaching them that troubleshooting is a major part of learning, not belittling them, and encouraging them to press forward. These mentors are committed to the success of the individual student while understanding that this fruitful relationship also will enhance their own research programs.

When students are encouraged to think independently, they develop ownership of their projects. This ownership benefits any research program; it cultivates a work ethic, innovation, creativity and sustained motivation. When students know that they are listened to and heard, they begin to feel a sense of belonging. They know that they belong when their mentor's (or principal investigator's) actions coincide with important mentor–student conversations they have had.

Mentor and protégé do not, will not and should not always agree. However, they must have a mutual understanding that both have the same goal, which is success for each other.

A good research mentoring program consists of:

1. Providing an inclusive atmosphere that allows protégés to become successful from failures, not demeaned for them.

2. Meeting each protégé where they are in their research career, understanding that people have been exposed (or not) to research at different levels.

3. Challenging them by setting high standards, which the mentor will help them to reach.

4. Providing structure for the protege to balance their personal and professional life.

5. Providing a welcoming environment where proteges will want to belong and where they will be motivated to meet the research program goals.

A great mentor elevates the relationship by removing any doubt that the mentor believes in the success of the protege. This connection allows a student to become confident and comfortable asking questions without worrying what the mentor thinks of them. And it allows both to be vulnerable, which in turn allows both to grow and develop; the mentor grows through accepting different perspectives expressed by their students.

Both mentoring and training programs require patience and understanding. However, I hope I've made the differences between the two clear. Training and mentoring should not be mistaken for each other.

A training program, once completed, will enhance a resume or CV. Once the training is concluded, the relationship may end — and so may the trainee's enthusiasm for science. The structure of a training program often doesn't create an environment where trainees will feel they belong and will fall in love with the inquiry of science. Sure, training checks off a box, but checking off a box doesn't make a student want to solve the mystery or puzzle. It also doesn't help diversify science.

Mentoring programs build mutual respect, connections and, possibly, lasting friendships between the mentor and protege. These help facilitate an identity that includes belonging. Belonging is critical to diversifying STEM — and the minimum of good mentorship is that an individual is comfortable and accepted as a vital member of the community.

Shantá D. Hinton (sdhinton@wm.edu) is a professor and associate chair in the biology department at the College of William and Mary in Williamsburg, Virginia.

Upcoming ASBMB events and deadlines

OCTOBER

National Dental Hygiene Month

1 Student Chapter Outreach Grant fall deadline

10 *World Mental Health Day*

15 *National Latinx AIDS Awareness Day*

NOVEMBER

Native American Heritage Month

Diabetic Eye Disease Month

Pancreatic Cancer Awareness Month

2 ASBMB Virtual Career Expo

14 ASBMB fellows nomination deadline

15 Student Chapter renewal deadline

18 *LGBTQ+ in STEM Day*

30 Discover BMB on-time abstract and travel award application submission deadline

DECEMBER

3 *International Day of Persons with Disabilities*

6 Deuel Conference on Lipids early registration deadline

'Our technology allows you to name the nameless'

By Martina G. Efeyini

Swathi A. Kumar is senior director of marketing at Verogen, a company that produces next-generation sequencing solutions for forensic investigations. Before joining Verogen in 2019, she worked for seven years at Illumina. She talked to ASBMB Today about her training and work experience.

1 What did you do at Illumina?

Illumina was clearly the disrupter in the sequencing space and emerging as early winner of competitive next-generation sequencing technologies. I was an early adopter of its applications and tools and could see the impact that digitizing DNA would have on so many fields. The applications were enormous. I joined their bioinformatics team. I got to do research and development and eventually sales and marketing.

2 Tell me about Verogen.

Verogen is a venture capital–backed DNA biometrics–based human identification company.

Crime labs, globally, still use 30-year-old technology. It is inefficient, restrictive and not sensitive enough to support the multitude of applications the forensic community needs. Our goal is to empower them with newer technology that is cheaper, more efficient and more accurate. That's really important if you want to provide an answer to those who've been victims of crime, or if you want to exonerate the innocent who were put in a prison based on inefficient technologies, or even if you want to identify victims of genocide, mass disasters or the thousands of John and Jane Does. Our technology allows you to name the nameless.

Swathi A. Kumar

CURRENT POSITION
Senior director of product and marketing at Verogen

CAREER PATH
Ph.D. in genetics and statistics, The Pennsylvania State University

FIRST JOB OUTSIDE OF ACADEMIA
Bioinformatics scientist at Illumina

FAVORITE MOLECULE OR PROTEIN
"It's a toss-up between GATA-1, a master regulator in blood cell formation, and two of its friends, EKLF and TAL 1. They participate in a tightly orchestrated dance aided by multiple epigenetic markers that determine the development of the right blood cells at the right time. I like those three proteins."

3 What does a day in your work life look like?

It's important to be close to our customers in crime labs — lab directors and technicians — to understand challenges they are facing. It could also mean engaging with law enforcement to understand limitations of current approaches or folks working on forensic standards and policy. Another equally important portion is ensuring that input is available to the smart people building all of these tools. It is also key for me to understand how we might commercialize a product, evaluate partnerships and competition, and determine how to build our brand and demand.

4 Who uses these products?

Justice systems. Public and private crime labs. Groups that have an interest in putting a name to unidentified remains. We spend a fair bit of time educating groups that have an interest in ensuring that governments are investing in better technologies in service of victims of crime.

5 What skills helped you prepare for your career?

Curiosity and resourcefulness. Taking a systems view to any problem set. Finally, developing a customer-oriented mindset is critical, because not all good ideas are successful in the market.

(This interview has been condensed and edited. To read a longer version, go to asbmb.org/asbmbtoday.)

Martina G. Efeyini (mefeyini@gmail.com) is a science communicator and STEM education advocate, and a careers columnist for ASBMB Today. Follow her on Twitter: @mefeyini.

CLASSIFIEDS

Staff Fellow — (Interdisciplinary Chemist) — Orthopedic Devices
U.S. Food and Drug Administration

The Division of Health Technology 6C is recruiting Staff Fellows (Interdisciplinary Chemists) to serve as orthopedic medical device reviewers. You will have the opportunity to apply your scientific knowledge and experience to conduct comprehensive qualitative and quantitative evaluations of scientific and technical data associated with orthopedic devices regulated by the Center. You will collect and synthesize data from multiple sources to offer recommendations and guidance to improve the safety, quality, reliability, and performance of orthopedic medical devices. Further, you will exercise sound technical judgement and utilize science and regulatory policy knowledge in your decision-making when responding to inquiries from industry, patient and healthcare professional advocacy groups, other government entities, and stakeholders, both internal and external.

https://careers.asbmb.org/job/staff-fellow-interdisciplinary-chemist-orthopedic-devices/64792161/

Destination Biochemistry Postdoctoral Scholars
Vanderbilt University

This year, two early-stage scholars may be appointed as the Destination Biochemistry Cohen Postdoctoral Scholar or Destination Biochemistry Danzo Postdoctoral Scholar. Applicants for the early-stage scholar awards should have outstanding records of accomplishment in their graduate studies and have received their Ph.D. degree no more than 6 months in advance of their application. These scholars will receive a competitive stipend with benefits plus a supplement of $10,000 for two years and a signing bonus of $5,000. Scholars will be nominated for positions on institutional training grants and external fellowships; will have a mentoring committee of at least three faculty members; and will benefit from many career development activities and other resources of the Office of Biomedical Research Education and Training. Highly productive scholars will be considered for appointment as Destination Biochemistry Advanced Postdoctoral Scholars.

https://careers.asbmb.org/job/destination-biochemistry-postdoctoral-scholars/64654122/

Biology Faculty Open Rank
Nova Southeastern University

The Department of Biological Sciences at Nova Southeastern University invites talented educator/investigators to join our emerging program building on strengths in Genomics and Evolutionary Biology. Successful candidates will join a growing team in a vibrant and collaborative environment. We are located in a beautiful setting just a few short miles from the ocean in sunny south Florida. In addition to teaching undergraduate and graduate courses in their area of expertise, faculty also have wide latitude in the development of their research program and the mentorship of undergraduate and graduate students. Applicants with research experience in genomics and bioinformatics are particularly encouraged to apply.

https://careers.asbmb.org/job/biology-faculty-open-rank/64371444/

Research Scientist/Engineer
U.S. Food and Drug Administration

The Center for Devices and Radiological Health (CDRH) is seeking a senior level scientific and regulatory expert to serve as a technical expert and advisor to the Division Director for the Sterility and Infection Regulatory Science Program. This Program is a high priority and visible program in the Office of Science and Engineering Laboratories (OSEL) and addresses key focus areas on advancing regulatory science in novel sterilization modalities, reprocessing of reusable medical devices and anti-microbial device technologies to reduce health care associated infections. The program delivers regulatory science tools facilitating device innovation and creating consistency in device testing methods where existing standards and guidance do not exist. In this position, reporting directly to the Division of Biology, Chemistry, and Materials Science (DBCMS) Director, you will advance the mission of OSEL and directly impact the health outcomes and the quality of life of the American people. You will be responsible for providing strategic, technical and program leadership, and exercising sound scientific and evidenced-based technical judgment in all areas of sterility and infection control.

https://careers.asbmb.org/job/research-scientistengineer/64493289/

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

ASBMB
American Society for Biochemistry and Molecular Biology

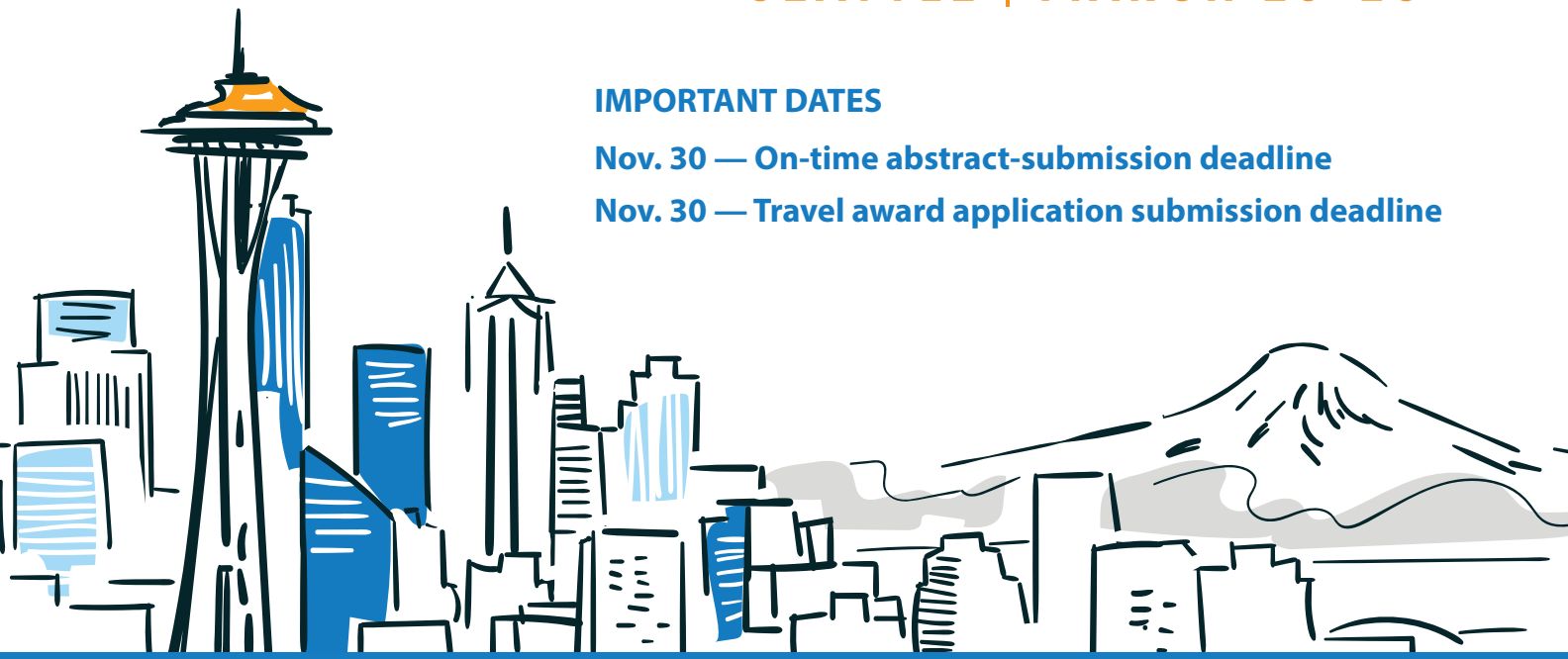
Have you marked your calendar?

ASBMB has a new annual meeting.

American Society for Biochemistry and Molecular Biology

Discover BMB | 2023

SEATTLE | MARCH 25-28



IMPORTANT DATES

Nov. 30 — On-time abstract-submission deadline

Nov. 30 — Travel award application submission deadline

Visit discoverbmb.asbmb.org