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ASBMBTODAY

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

"The magic isn't the squid... The magic is the protein."

NEWS

FEATURES

PERSPECTIVES

ASBMB'20 **ANNUAL MEETING**

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

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EDITOR'S NOTE

Caution: Tchotchkes at work

By Comfort Dorn

tchotchke *(noun)* \'chäch-kə , -kē; 'tsäts-kə\: knickknack, trinket
Origin: Yiddish *tshatshke* trinket, from obsolete Polish *czaczko*
First Known Use: 1971 —*Merriam Webster Unabridged*

On my office windowsill I have a plastic margarita glass full of paper umbrellas, a small pot of succulents, a pottery jar wearing a scarf and hat, a plastic butterfly ring, a fidget spinner and a sign that reads "Crazy cat lady."

These are my office tchotchkes. They're usually more spread out, but I wanted to pose them:

We all have these things, right? The random objects that accumulate in our workspaces and make them our own. Look around your desk/office/lab. What do you see? You can probably tell a story about where each of these non–work-related things came from — and that's what I want you to do.

Regular readers might recall that we devote our August issue to the topic of careers. We invite you to submit essays and articles related to your career path, sharing what you've learned. We want to know what works (and what doesn't) as ASBMB members seek and find the jobs that fit.

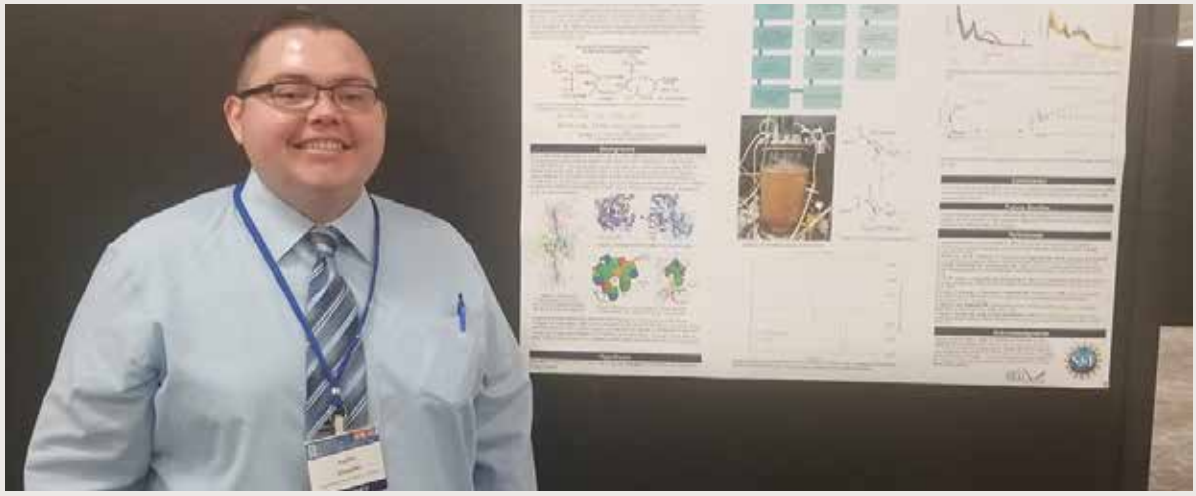
We still want those serious, useful articles and essays (deadline: June 15), but we also want your tchotchkes.

Take a picture of the knickknacks in your workspace (bonus points if you're in the photo too) and tell us their story: Where did you get them—and when? What do you think about/feel when you look at them?

You don't need to write a lot. Keep it under 100 words. Then send your picture (as a jpg file) and words to asbmbtoday@asbmb.org by June 15. We'll share them in our August 2020 issue.

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

Correction
The data sources for infographics in the story "A Matter of Degree" in the February issue were incorrect. Please refer to the web version of the story at asbmb.org/asbmbtoday for correct data citations. In the same article, Zerick Dunbar's school was misidentified; he attends Meharry Medical College in Nashville. Also, Taylor Carmon's compensation from Alabama A&M University was misstated; he is paid a stipend.



Young researchers present science

The Emerging Researchers National Conference in STEM, hosted by the American Association for the Advancement of Science and the National Science Foundation, is an opportunity for underrepresented undergraduate and graduate students to present their research to peers and professors.

Among this year's presenters were nine student members of the American Society for Biochemistry and Molecular Biology, along with three faculty members. (See the full list of presenters at our website.)

Stephen Gonzalez, a student at California State University, Fullerton, pictured above, said, "One of the conversations that really stuck with me was with one of my poster judges … We got into a great talk about my research. I cherished his time there, since he really made me grow more scientifically and as a presenter."

Doudna, Charpentier share Wolf prize in medicine

The 2020 Wolf Prize in medicine will be awarded jointly to **Jennifer Doudna** and **Emmanuelle Charpentier**, whose work led to the discovery of the gene-editing tool clustered regularly interspaced short palindromic repeats–CRISPR-associated protein 9, or CRISPR–Cas9.

Doudna is the Li Ka Shing chancellor's chair in biomedical and health sciences and a professor of molecular and cell biology and professor of chemistry at the University of California, Berkeley, and a Howard Hughes Medical Institute investigator. She studies how RNA molecules control the expression of genetic information. In 2013, Doudna won the American Society for Biochemistry and Molecular Biology's inaugural Mildred Cohn Award in Biological Chemistry.

Charpentier is a biochemist, microbiologist and geneticist recognized as an expert in regulatory mechanisms underlying processes of infection and immunity in bacterial pathogens. She is scientific and managing director of the Max Planck Unit for the Science of Pathogens in Berlin, an institute that she founded with the Max Planck Society.

Doudna and Charpentier determined the mechanism of RNA-guided bacterial adaptive immunity by the CRISPR-Cas9 system, enabling them to harness the system for efficient genome engineering in animals and plants.

This is the 42nd year the Wolf Foundation will award the Wolf Prize "to outstanding scientists and artists from around the world … for achievements in the interest of mankind and friendly relations among peoples," according to the foundation's website. Wolf Prizes are given in art, agriculture, physics, medicine and mathematics. A New York Times article noted that the Wolf Prize is thought of as one of the predictors of a future Nobel Prize.

Doudna

Charpentier

Society for Glycobiology presents awards

Gerald Hart, **Robert J. Linhardt** and **Manfred Wuhrer** were among the researchers recently honored by the Society for Glycobiology.

Hart is president of the American Society for Biochemistry and Molecular Biology and a Georgia Research Alliance eminent scholar at the University of Georgia. He received the President's Innovator Award, given each year since 2015, which honors the contributions of one scientist who has had a significant impact.

For Hart, that impact was not only creating a new field in glycobiology, the dynamic and inducible modification of nuclear and cytosolic proteins via O-GlcNAc, but also shepherding its growth and providing "exemplary service to the glycobiology and life science community," the society's website states.

Linhardt, a professor at Rensselaer Polytechnic Institute, was honored with the Karl Meyer Lectureship Award. Established in 1990, the award is given to well-established scientists who have made widely recognized major contributions to the field of glycobiology.

Linhardt has contributed to the understanding of glycosaminoglycans and heparins. He was a co-discoverer of polyanhydrides for drug delivery, which resulted in a wafer to treat brain cancer, and he also helped introduce low-molecular-weight heparins into the market.

Wuhrer, head of the Center for Proteomics and Metabolomics at Leiden University Medical Center in the Netherlands, received the Molecular & Cellular Proteomics/ASBMB Lectureship Award. Established in 2013, the award honors scientists who have been at the forefront of the emerging field of glycomics and glycoproteomics.

Wuhrer's recent research has focused on analyzing the glycans of human proteins, with particular attention to immunoglobulins. His work on technology centers on higher throughput mass spectrometry glycomics workflows, which his lab applies to unravel protein glycosylation signatures of various human diseases including autoimmune diseases, infectious diseases, metabolic disorders and cancer.

Also honored were **Nancy Dahms**, who received the Rosalind Kornfeld Award for Lifetime Achievement in Glycobiology (reported last month in ASBMB Today), and **Jochen Zimmer**, who received the Oxford University Press Glycobiology Significant Achievement Award.

These awards were presented at the Society for Glycobiology's annual meeting, held in Phoenix in November.


Hart


Linhardt


Wuhrer

National Academy of Inventors names fellows


Brown


Goldstein

Three ASBMB members joined the ranks of the National Academy of Inventors in December as part of a class of 168 new fellows.

The academy was launched in 2010 to promote entrepreneurship within academia. According to the NAI website, its fellows program recognizes professors who have made or contributed to "outstanding inventions that have made a tangible impact on quality of life, economic development and the welfare of society."

These ASBMB members are among the 2019 NAI fellows:

Michael Brown and **Joseph Goldstein** of the University of Texas Southwestern, longtime colleagues and collaborators, are known for discovering the low density lipoprotein, or LDL, receptor and the SREBP transcription factor family, among other important contributions to the field of lipid metabolism. The two, who shared a Nobel Prize in 1985, hold 29 patents jointly.


Hruby

Victor Hruby of the University of Arizona studies the design and synthesis of biologically active peptides and peptide mimics with biological activity. He holds 27 patents for peptide hormone mimetics.

The NAI has more than 4,000 members and fellows at more than 250 institutions worldwide.

Belfort wins honorary degree


Belfort

The University of Cape Town has conferred an honorary doctorate of science on **Marlene Belfort**, a distinguished professor in the departments of biological sciences and biomedical sciences at the State University of New York at Albany.

Belfort received a bachelor's degree from UCT in 1965 followed by doctoral and postdoctoral work at the University of California, Irvine, and the Hebrew University of Jerusalem.

Her lab at SUNY Albany explores the dynamics of elements that interrupt genes, introns and inteins, studying their structure, function and regulation and their applications in biotechnology and infectious disease. Her achievements include the self-splicing of introns in bacteriophage T4 and a detailed analysis of the splicing mechanism. Her recent work has led to development of a model for the mechanism of intron evolution that is applicable to prokaryotes and may shed light on vertebrate genes.

Belfort has mentored younger scientists, technicians, undergraduates, postgraduates and even high school students. Within the global scientific community, she is known for her support of women in science.

Belfort received her honorary doctorate in December.

Honors for Hall and research partner


Hall

Biochemist **Michael Hall** has won two awards with David Sabatini for their roles in the discovery of mTOR, the mammalian target of rapamycin: the BBVA Foundation Frontiers of Knowledge Award in biology and biomedicine and the Royal Swedish Academy of Sciences' Sjöberg Prize.

Hall, a professor of biochemistry in the Biozentrum Center for Molecular Life Sciences at the University of Basel, Switzerland, discovered the target of rapamycin in yeast in 1991. Several years later, Sabatini, then a graduate student, discovered its mammalian homolog.

Before Hall's lab demonstrated that yeast's TOR complexes link nutrient availability to protein translation and the growth phase of the cell cycle, researchers did not know that growth was actively regulated. Later work from the lab linked mTOR activity to nucleotide synthesis and cytoskeletal organization.

This stronger understanding of mTOR signaling has had clinical implications. The kinase is overactivated in many cancers and has been linked to diseases such as diabetes. Rapamycin, the original mTOR inhibitor, is used as an anti-cancer agent, an immunosuppressant for organ transplantation and a coating for coronary stents to block new growth. Researchers believe reduced mTOR signaling is involved in the longer lifespans of mice fed restricted diets, leading to hopes that mTOR inhibitors might limit the effects of aging-related diseases.

Hall and Sabatini received the Frontiers of Knowledge award in January; it includes a commemorative sculpture and a €400,000 cash prize split among the winners in each category. The Sjöberg Prize, awarded in early February, consists of $1 million, divided between the awardees. Hall also received a Lasker Award in 2017.

Evensen wins Marshall


Evensen

Claire Evensen, president of the American Society for Biochemistry and Molecular Biology Student Chapter at the University of Wisconsin–Madison, is one of 46 students to receive a 2020 Marshall Scholarship.

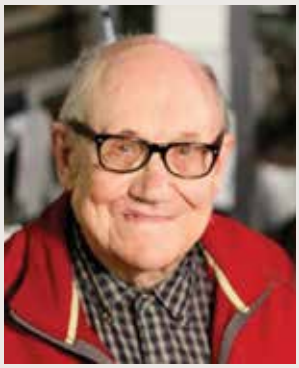
Evensen is set to graduate this spring with a bachelor's degree in biochemistry and mathematics. For three years, she has researched the biophysics of transcription initiation with Thomas Record, the John D. Ferry professor of biochemistry. She earned several campus research grants to support her work and presented her research at national conferences. She is a Goldwater scholar, an Astronaut scholar and a finalist for a Rhodes scholarship.

As president of her ASBMB Student Chapter, Evensen has organized a regional conference on networking and research presentation. In March, undergraduates from across the region are expected to attend the Molecules in the Midwest conference at UW–Madison.

Established in 1953 to honor the ideals of the Marshall Plan, the Marshall Scholarship Program gives high-achieving young Americans the opportunity to study at the graduate level at any university in the United Kingdom. Up to 50 scholarships are awarded each year.

Evensen plans to join a master's degree program in mathematical modeling and scientific computing at the University of Oxford.

Kenneth Standing



Kenneth G. Standing, a pioneer in time-of-flight mass spectrometry and its applications to study biological macromolecules, died March 21, 2019. He was 93.

Born and raised in Winnipeg, Canada, Standing earned an undergraduate degree at the University of Manitoba and completed his M.A. and Ph.D. in nuclear physics under Rubby Sherr at Princeton University. He joined the University of Manitoba faculty in 1953; there he designed, built and commissioned a cyclotron particle accelerator.

In the late 1970s, Standing changed the focus of his research to TOFMS, an essential component of the proteomics field. He collaborated with biologists to solve a range of problems; during the SARS outbreak in 2002 and 2003, his group provided sequence information for much of the virus' protein structure before the genome was sequenced. He retired as a professor in 1995 but continued his research as an emeritus professor well into his 80s.

Standing's many awards and accolades included the American Chemical Society Field and Franklin Award for outstanding achievement in mass spectrometry and the Encana Principal Award from the Ernest C. Manning Foundation, known as Canada's Nobel Prize. He was elected as a fellow of the American Physical Society and of the Royal Society of Canada. In 2009, the University of Manitoba awarded him its highest honor, the honorary degree of doctor of science.

Standing is survived by his children and their spouses: Mike and Brenda Janz; Tim; Liz and Clarence Jackson; and Jon and Andrea Jackson. He also is survived by his grandchildren, Willem, Tannin, Rachel, Luke and Corin.

Judith Saffran

Judith Saffran, a cancer researcher and a quiet pioneer in women's postgraduate education, died Jan. 14 in Queens, New York. She was 96.

Born Judith Cohen in Montreal in 1923, she attended McGill University, earning a bachelor's degree in chemistry in 1944 and a Ph.D. in biochemistry in 1948. She married Murray Saffran, a fellow McGill student, in 1947 and did postdoctoral research at Montreal's Jewish General Hospital. She taught an advanced biochemistry lab class at McGill for several years.

The Saffrans moved to the U.S. in 1969 and settled in Ohio, where Judith worked as a researcher first at Toledo Hospital and later at what was then the Medical College of Ohio (now the University of Toledo College of Medicine and Life Sciences). Murray founded the department of biochemistry at the college and was a pioneer in the research of stress hormones. He died in 2004.

Judith Saffran and her colleagues examined the binding and metabolic activity of the hormone progesterone, which is crucial to a wide array of biological activity such as neuronal development, steroid production and breast development. In its synthetic

Harold W. Gardner

Harold W. Gardner, a biochemical researcher and environmental activist who lived most recently in Carlisle, Pennsylvania, died Nov 6. He was 84.

After service as a U.S. Navy courier, Gardner earned a Ph.D. in biochemistry at Pennsylvania State University. He worked as a researcher at the Pineapple Research Institute in Honolulu, at the University of California, Los Angeles, and at the Agricultural Research Service (an agency of the U.S. Department of Agriculture) in Peoria, Illinois. His focuses included lipid chemistry, enzymology, free radical chemistry, fungal products and plant ecology. He published more than 120 papers and was an associate editor for the journal Lipids.

Gardner worked with the Sierra Club on projects to preserve water quality in the Illinois and Mississippi rivers. After his retire-

forms, progesterone is prescribed in therapies including menopausal hormonal therapy and gender-affirming therapy. It also is involved in the pathophysiology of breast cancer. To help elucidate this function, Saffran investigated the hormone's activity in cultures of uterine cells derived from rats and guinea pigs. She also explored the regulatory effect of hormone on the production of other endogenous steroids. She retired from the Medical College of Ohio in 1997.

Saffran, who was descended from a Russian Jewish family, volunteered in the 1990s with the Toledo chapter of ORT, an international charity founded in 19th century Russia that describes itself as a "global educational network driven by Jewish values." She moved to New York in 2014 to be closer to her daughter, who was a professor of biochemistry at Queens College.

Few women of Saffran's generation had doctoral degrees. "She was a pioneer in women's higher education and in women's work as scientists," her son David Saffran told the Toledo Blade. "She was also humble. She never thought she was special, and she never bragged about her education and her status as a scientist."

Saffran is survived by her daughter, Wilma Saffran; sons, David, Arthur and Richard Saffran; nine grandchildren; and five great-grandchildren.

ment, he focused on tallgrass prairie restoration in Illinois, writing a book and numerous papers on native plants. He later owned a 70-acre nature preserve in Pennsylvania and advised the Penn State Arboretum on their prairie project.

He is survived by his wife, Cheryl Pauli; two daughters, Kelly Gardner and Denali Brooke; three sons, Scott Gardner, Michael Gardner and Bryce Gardner; and five grandchildren.

Albert S. Mildvan

Albert Samuel Mildvan, an emeritus professor of biological chemistry and chemistry at the Johns Hopkins University School of Medicine, died Oct. 24 in Baltimore after a prolonged illness. He was 87.

Born in Philadelphia, Mildvan earned a bachelor's degree in chemistry and mathematics from the University of Pennsylvania in 1953 and an M.D. from Hopkins in 1957. After postdocs at the National Institutes of Health and Cambridge University, he did an advanced postdoctoral fellowship with Mildred Cohn at the University of Pennsylvania, where he developed expertise in nuclear magnetic resonance and electron paramagnetic resonance, spectroscopic techniques that became the backbone of his research career. He was on the faculty of the University of Pennsylvania before returning to Baltimore in 1981 to join the Hopkins faculty.

The author of more than 270 publications covering a range of protein biochemistry and enzymology, Mildvan studied the mechanism of enzyme action and its relevance to neoplastic, cardiovascular and metabolic disease. He discovered the first Mn^{2+} metalloenzyme, pyruvate carboxylase, and made key contributions to the interpretation of the effects of site-directed mutagenesis.

Mildvan served on the editorial board of the Journal of Biological Chemistry from 1979 to 1991, and in 1988 he received the American Society for Biochemistry and Molecular Biology's Herbert Sober Prize recognizing outstanding biochemical and molecular biological research.

He is survived by his wife, Patricia June Tarr Mildvan; children Heather Mildvan Pytel, Pamela Mildvan Cummins and Margo Susan Mildvan; sons-in-law Theodore R. Cummins and Eric T. Arnold; sister Donna Mildvan; and grandchildren Hannah and Benjamin Cummins and Clement Pytel.

IN MEMORIAM

Robert L. Herrmann

Biochemist Robert L. Herrmann died Dec. 12 at the age of 91.

Herrmann was born in 1928 in New York City and grew up in Queens. His pursuit of an undergraduate degree in chemistry at Purdue University was interrupted by two years of service in the Navy on the U.S.S. Shenandoah, after which he married his childhood sweetheart, Betty Ann Cook. He then returned to Purdue, finished his degree and enrolled as a graduate student at Michigan State University. In 1956, he accepted a Damon Runyon fellowship at the Massachusetts Institute of Technology.

In 1957, Herrmann joined the American Scientific Affiliation, or ASA, a Christian religious organization of scientists, and remained active in the group for many decades. There, he met the investor and philanthropist Sir John Templeton, with whom he collaborated in writing several books, including Templeton's biography. Herrmann was a founding member of the John Templeton Foundation, which supports research at the intersection of science and religion.

After completing his postdoctoral fellowship, Herrmann took a faculty position at Boston University, where he taught biochemistry for 17 years. Following a stint teaching biochemistry at Oral Roberts University in Tulsa, Herrmann moved back to New England in 1981 to serve as executive director of the ASA, a position he held until his retirement in 1994.

Herrmann is survived by his wife, Elizabeth Herrmann; sister, Carol; children, Stephen, Karen, Holly and Anders; and eight grandchildren.

Ervin Erdös

Ervin G. Erdös, who survived a German concentration camp to become a distinguished professor and medical researcher in the U.S., died Nov. 17 at the age of 97.

Erdös was born into a Jewish family in 1922 in Budapest, where his father worked as an engineer until Hungary joined the Axis nations after Hitler's rise to power. He was conscripted to a forced labor brigade, and after Germany invaded Hungary in 1944, he and his father were sent to the Sachsenhausen concentration camp in Germany, where they witnessed many atrocities.

After the camp was liberated, Erdös returned to Budapest and enrolled in medical school. In 1950, he fled the Communist regime and completed his medical degree in Munich. He then worked in a German laboratory, where he began studying how

Hans Kornberg

Boston University biochemist Sir Hans Kornberg died Dec. 16. He was 91.

Born in 1928 to a Jewish family in Germany, Kornberg fled to the United Kingdom in 1939, staying with an uncle in Yorkshire. After finishing grammar school, he gravitated toward chemistry and became a junior laboratory technician for Hans Krebs, who discovered the eponymous metabolic cycle, at the University of Sheffield. Kornberg worked in Krebs' lab through his time at the university, where he earned a bachelor's degree in chemistry in 1949 and a Ph.D. in biochemistry in 1953.

After postdoctoral stints in the U.S. and U.K. and lecturing at the University of Oxford at Krebs' behest, Kornberg was appointed as the first chair in biochemistry at the University of Leicester in 1960. In 1975, he moved to the University of Cambridge, where he was appointed the Sir William Dunn chair of biochemistry. He also served as the master of Christ's College and then deputy vice chancellor until his mandatory retirement in 1995. He then took a job at Boston University, where he continued his research and taught upper-level biochemistry.

Kornberg's seven-decade research career focused on the regulation of carbohydrate transport in microorganisms. He authored

enzymes and peptides aid in the control of blood pressure.

Erdös moved to the U.S. in 1954. He worked first at Carnegie Mellon University and then moved to Oklahoma City, where he served as head of pharmacology at the University of Oklahoma Medical School from 1963 to 1973. From there, he moved to the University of Texas Southwest Medical Center in Dallas, where he became a professor of pharmacology and ran a research laboratory. In 1985, he moved to Chicago and served as a distinguished professor at the University of Illinois at Chicago.

Erdös was recognized for his work on angiotensin I converting enzyme, or ACE. He discovered that ACE exerted a dual effect on blood pressure by controlling two oppositely acting peptides.

He is survived by his wife, Sara Rabito; sons Peter and Philip and their wives; and four granddaughters. He was preceded in death by his son Martin Erdös.

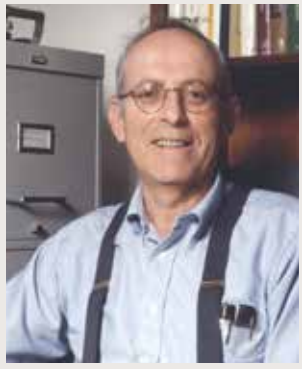
Read "An exploration of bioactive peptides: My collaboration with Ervin G. Erdös" by Rajko Igic at jbc.org.

more than 250 papers and notably elucidated the glyoxylate cycle, which is used by plants and other nonanimals to enable the biosynthesis of biomass from 2-carbon compounds, as well as the concept of anaplerosis, an important mechanism for ensuring carbon oxidation by the Krebs cycle.

He was made a fellow of the Royal Society in 1965 and knighted in 1978. He was a fellow of the American Academy of Microbiology and a foreign associate member of the National Academy of Sciences and the American Academy of Arts and Sciences.

Kornberg met Monica King at Oxford; they married in 1956 and had four children. King died in 1989, and Kornberg remarried in 1991; his wedding with Donna Haber was the first Jewish wedding to take place on the Cambridge campus. He is survived by Haber; his daughters, Julia and Rachel; his twin sons, Jonathan and Simon; and grandchildren and great-grandchildren.

Irwin Fridovich



Irwin Fridovich, a professor emeritus at Duke University and past president of the American Society for Biochemistry and Molecular Biology who also served on the Journal of Biological Chemistry editorial board and on the ASBMB Today editorial advisory board, died Nov. 2. He was 90 years old.

Born in 1929 in Brooklyn, New York, Fridovich attended the Bronx High School of Science and the City College of New York before earning a Ph.D. in biochemistry at the Duke University Medical Center.

Duke invited him to become a faculty member, and he remained at the university for more than 60 years. In his long and distinguished career, he published more than 500 scientific articles and discovered superoxide dismutase, or SOD, essentially founding the field of free radical biology. A November 1969 paper about SOD, written by Fridovich and then–grad student Joe M. McCord and published in the Journal of Biological Chemistry, has been cited more than 9,300 times.

Fridovich served as president of several professional societies, including the ASBMB in 1982, and earned several lifetime achievement awards. He was a member of the National Academy of Sciences and the American Academy of Arts and Sciences. In 1997, he shared the Elliott Cresson Medal from the Franklin Institute with McCord. He was appointed the James B. Duke professor of biochemistry in 1976.

He continued to go to Duke every weekday until about four months before his death to read the latest scientific journals and to enjoy weekly lunches with friends and colleagues.

Fridovich was married for 59 years to the former Mollie Finkel. He is survived by his daughters, Sharon F. Freedman and Judith L. Fridovich-Keil; brother, David Fridovich; two grandchildren and

Marilyn Farquhar (1928 – 2019)

By John Bergeron & J. David Castle

The passing of Marilyn Farquhar on Nov. 23 brought to a close a long and inspiring career in cell biology. She rightly ranks among the pioneers in her field and especially as a role model for women in science.

We met Marilyn more than 50 years ago at the Rockefeller University when she was a visiting professor in George Palade's lab. Marilyn had worked previously with Palade, and their early and classic insights into the organization of epithelial junctions, published in the period 1963-65, remain a staple in medical and cell biology textbooks to this day.

Here were characterized, in detailed resolution, tight junctions, intermediate junctions, and desmosomes, along with basement membranes that Marilyn was later to study in detail, especially in the kidney glomerulus. These are the defining feature of all epithelia in our bodies.

At Rockefeller in 1969, Marilyn was part of an amazing group of colleagues that included David Sabatini, Günter Blobel, Phil Siekevitz, Jim Jamieson and David Luck. Marilyn and George had close interactions with Christian De Duve and his group, located in the same building at Rockefeller. Collectively, the pioneers' focus was on deciphering mechanistically the workings of the cell, especially its membrane-bounded organelles, which often were being seen and studied for the first time.

Marilyn came for her sabbatical at Rockefeller from her lab in the department of experimental pathology at the University of California, San Francisco. Shortly after she arrived, a paper from her work at UCSF was published that conceptually unified and showed in intricate detail the structures that captivated the Palade and De Duve labs.

ROCKEFELLER UNIVERSITY PRESS

Marilyn Farquhar was an electron microscopy pioneer and a treasured mentor to generations of cell biologists.

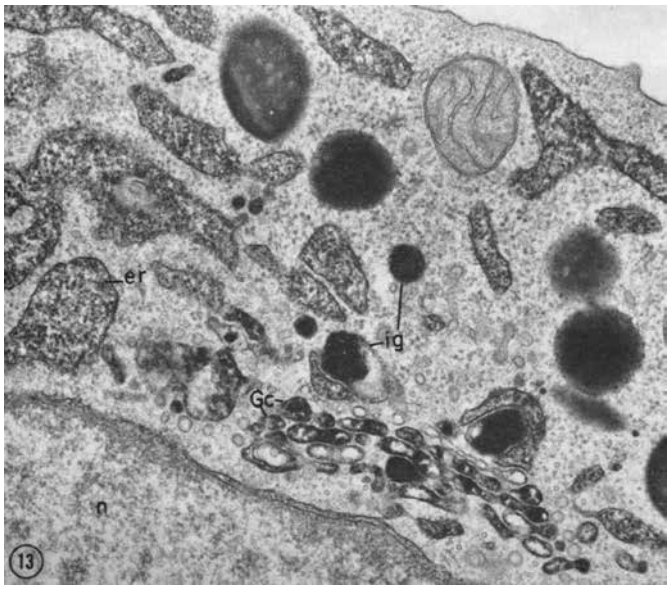
She was clearly among the standard setters in a department and institution loaded with scientific talent. Furthermore, because she was both friendly and easily approachable, she enriched the scientific environment of numerous students and colleagues and a host of collaborators.

She married George Palade in 1970, and her sabbatical at Rockefeller turned into an extended transcontinental migration. Together, they moved to Yale School of Medicine in 1973, where she became the Sterling professor of cell biology. At Yale, she was a major force in shaping the new section of cell biology that ultimately became the department of cell biology. As she continued to make contributions in discovery research,

ROCKEFELLER UNIVERSITY PRESS

This image from a 1965 paper in the Journal of Cell Biology by Marilyn Farquhar and George Palade shows a desmosome linking the plasma membranes of cells located in the granular (SG) and cornified layers of amphibian skin. Magnification x 135,000.

ROCKEFELLER UNIVERSITY PRESS



This image from a 1970 paper in the Journal of Cell Biology by Dorothy Bainton and Marilyn Farquhar shows concentration of myelocyte peroxidase within the secretory pathway of a rabbit eosinophil beginning in the endoplasmic reticulum (labeled er) and progressing through the Golgi (Gc) and maturing secretory granules (ig). Parallel observations for acid phosphatase and arylsulfatase pointed to the lysosome-like nature of these granules. Magnification x 43,000.

she also developed a modern cell biology course that became a valued component of the medical school curriculum.

At Rockefeller and at Yale, Marilyn and George were close friends and colleagues of visiting Romanian scientists Nicolae and Maya Simionescu, and they strongly encouraged Nicolae and Maya, who were pioneers in bringing modern cell biology to Romania. Marilyn and George were honored guests at the inauguration of the Institute of Cell Biology and Pathology in Bucharest, celebrated in 1979 with an international symposium featuring giants in the field, all of whom were Marilyn's close friends and colleagues.

Marilyn was always proud that she was California born and raised. She earned her undergraduate and graduate degrees at the University of California, Berkeley, and then moved to the Rockefeller University in New York City for postdoctoral training with George Palade before joining the faculty at UCSF. In 1990, she returned to California as the founding chair of the department of cellular and molecular medicine of the University of California, San Diego, Medical School.

We continue to appreciate Marilyn's early contributions to understanding the developmental regulation of leukocyte granulogenesis and granule turnover in endocrine cells by lysosomal degradation. She made numerous contributions to unraveling the intricacies of the Golgi apparatus, including biogenesis, sorting and recycling. Her discoveries on the biogenesis of glomerular basement membranes included the classic definition of the role of associated proteoglycans in regulating glomerular filtration. She and her colleagues clarified the organization, trafficking, signaling and pathological roles of podocalyxin and megalin in renal podocytes and proximal tubule cells.

As time progressed, Marilyn became a major force in exploring the roles of G protein-coupled receptors, growth factor receptors and associated regulatory complexes in intracellular membrane trafficking. As with the work of all great scientists, the approaches employed by Marilyn's laboratory evolved with the times. She maintained her creative use of electron microscopy as a signature

COURTESY OF MAYA SIMIONESCU

This photo taken in 1979 at the inaugural symposium of ICBP Bucharest shows, in the front row, from left to right, Werner Franke, Maya Simionescu, Gunter Blobel, Marilyn Farquhar, George Palade, Christian De Duve, Nicolae Simionescu and David Sabatini.

experimental tool throughout her career.

Marilyn's achievements were recognized with many awards and honors including election to both the National Academy of Sciences and the American Academy of Arts and Sciences. She received the American Society for Cell Biology's E.B. Wilson Medal and the American Society of Nephrology's Homer W. Smith Award. She was particularly gratified by the Federation of American Societies for Experimental Biology Award for Excellence in Science that she received in 2006 at the American Society for Biochemistry and Molecular Biology Annual Meeting in San Francisco.

Marilyn followed the accomplishments of her trainees and colleagues, including us, with eager interest and always with encouragement. We remember her ready smile and cheerful disposition. Her memory provides enduring inspiration to all of us who had the good fortune to follow the beauty and impact of her discoveries.

The authors thank Maya Simionescu (ICBP, Bucharest); Susan Ferro-Novick (University of California, San Diego); Stuart Kornfeld (Washington University, St. Louis); Colin Hopkins (Imperial College, London); Bill Brown (Cornell University); Pietro De Camilli (Yale University); David Sabatini (New York University) and Kathleen Dickson (McGill University) for their comments and suggestions.

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A deeper insight into phospholipid biosynthesis in Gram-positive bacteria

By Diego E. Sastre & Marcelo E. Guerin

Gram-positive bacteria can cause serious and sometimes fatal inflammatory diseases including pharyngitis, pneumonia, myocarditis, meningitis, and septicemia. These bacteria synthesize phosphatidic acid, the central precursor of membrane phospholipids, using an unusual acyl-phosphate intermediate in a three-step pathway mediated by three phospholipid synthesis enzymes: PlsX, PlsY and PlsC.

PlsX is a peripheral membrane transacylase that catalyzes the conversion of acyl-acyl carrier protein to acyl-phosphate and helps coordinate fatty acid and phospholipid biosynthesis. PlsX binds and inserts directly to lipid bilayers, a process mediated by an amphipathic four alpha-helical bundle subdomain that protrudes from the main core of the enzyme.

In disentangling this binding and insertion of PlsX, our lab has found that PlsX membrane binding is mediated by phospholipid charge, whereas unsaturation of fatty acids and membrane fluidity influence membrane insertion. Superficial access to the membrane is not sufficient to ensure efficient delivery of the acyl-phosphate from PlsX to the acyltransferase partner PlsY, which depends on proper and stable insertion of PlsX in the membrane. Such substrate channeling can make this metabolic pathway more efficient and prevents the release of unstable intermediates, protecting them from decomposition and/or diffusion through the aqueous cytoplasm.

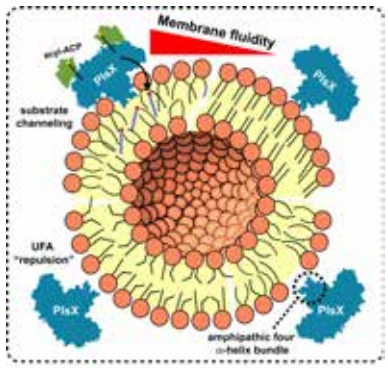
In a recent paper in the **Journal of Biological Chemistry**, we propose a model in which membrane fluidity governs the membrane insertion of PlsX, which is required for the proper acyl-phosphate delivery to PlsY.

Our model breaks a paradigm in membrane biology: The membrane fluidity and unsaturated fatty acids, or UFAs, do not seem to hold hands. At higher membrane fluidity, PlsX inserts deeper into the membrane, but increased UFA content reduces PlsX binding and insertion.

How can PlsX sense the UFAs, and why do UFAs repel PlsX binding and insertion? We suspect the repulsion effect might be part of a mechanism to downregulate the total phospholipid synthesis observed at low growth temperature.

In membrane insertion, peripheral proteins can cluster as transient oligomers when interacting with lipid bilayers. This crowding would be intensified with increased protein radius and depth of penetration into the hydrophobic region of the membrane. PlsX mostly is distributed homogenously at the bacterial cell membrane, but PlsX foci also are transiently and randomly observed, which could represent physiological oligomeric states related to the regulation of PlsX activity.

We propose that PlsX inserts deeper into more fluid membranes (containing little or no unsaturated fatty acid content), causing oligomers, in the form of foci at the membrane. Thus, modulating membrane insertion could regulate the substrate channeling as well as the protein crowding, regulating the phospholipid biosynthesis.



DIEGO SASTRE

This schematic representation shows binding/insertion of PlsX to lipid bilayers.

These results highlight the relevance of spatial organization for metabolic pathway functioning and tell us more about how membrane composition and protein mobility can modulate this biosynthesis route. PlsX and PlsY are present in pathogenic bacteria and absent in eukaryotes, so the results offer exciting possibilities for inhibitor design to fight antibiotic-resistant bacteria.

DOI: 10.1074/jbc.RA119.011122.

Diego E. Sastre was recently hired as an assistant research scientist in the Sundberg lab in the department of biochemistry at the Emory University School of Medicine.

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Scrutinizing pigs' greatest threat

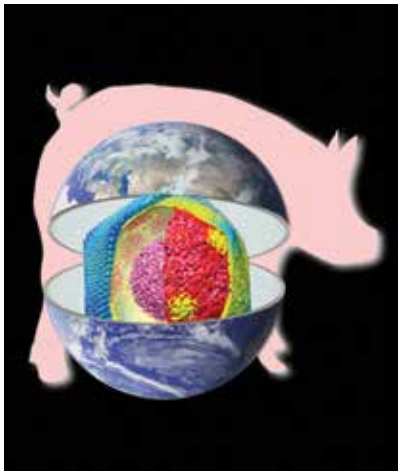
By John Arnst

African swine fever virus is harmless to humans, but the virus — endemic to warthogs, bushpigs and soft ticks in sub-Saharan Africa — causes a hemorrhagic fever in domestic swine and has devastated pig population across China and southeast Asia.

The virus' unique multi-layered architecture may be blocking vaccine development. Nicola G. A. Abrescia, German Andrés and their colleagues recently peered between those membranes to capture the structure of ASFV's virion. They described its architecture in the **Journal of Biological Chemistry**.

"What was striking is that actually you have four layers: two envelopes and two protein capsids for this virus," said Abrescia, a structural biologist at the Center for Cooperative Research in Biosciences near Bilbao, Spain. "So you have this outer envelope which is acquired when the virus goes out of a cell, but below this envelope you have another set of icosahedral capsids and in between a membrane bilayer, all of them enclosing the genome-containing nucleoid."

In previous studies, Andrés — a senior researcher at the Centro de Biología Molecular Severo Ochoa's Electron Microscopy Unit in Madrid — found that both the extracellular and intracellular forms of ASFV are infectious. This suggested that the outer membrane might not be necessary for infectivity, as the virus sheds its coat while entering into a host cell. The researchers hope a better understanding of ASFV's structure might contribute to more efficient vaccine design.



D. CHARRO, G. ANDRÉS, N.G. ABRESCIA

African swine fever, which ravaged domestic and feral pig populations in Spain and Portugal in the 1980s, was eliminated from the Iberian Peninsula by 1995. Today, the Georgia 2007 strain, which originated in sub-Saharan Africa but emerged in the Republic of Georgia in 2007, poses a monumental threat to the pork industries of Central and East Asia.

One challenge: ASFV is big — a giant virus, in fact, almost twice the size of influenza virions and thicker than the typical layer of ice in which particles are suspended for cryo-electron microscopy. This complicates sample preparation. Most microscopes' field of view can capture only a few virus particles, challenging efficient data collection. And despite its size, ASFV's outer membrane isn't resilient outside of a host.

"The outer lipid envelope is relatively fragile," Abrescia said, "so you have to set up a very good purification protocol which doesn't destroy so much of the virus's envelope."

The researchers went to co-author Rebecca Dillard's lab at the University of Leiden in the Netherlands to collect images of a thousand viral particles with a Titan/Krios transmission electron microscope. The virus' size also causes its capsids to span more than one focal plane, contributing to image blur, so Abrescia and Andrés biochemically deconstructed the virus in solution, and then purified and resolved the fold of the individual protein composing the outer capsid.

Abrescia's team isn't alone in pursuing the structure of ASFV. Just before their JBC paper appeared online, a group at the Chinese Academy of Sciences in Beijing described the pathogen's structure at greater resolution in the journal Science, and later a third group at the University of Science and Technology of China published another cryo-EM analysis in the journal Cell Host & Microbe. A fourth group earlier described the structure of ASFV's major capsid protein p72 in the journal Cell Research.

Despite these successes, the inner capsid remains a challenge. "Even the high-resolution structures that our Chinese colleagues have obtained do not fully explain the inner capsid," Abrescia said. "Indeed, it has remained something that requires more exploration."

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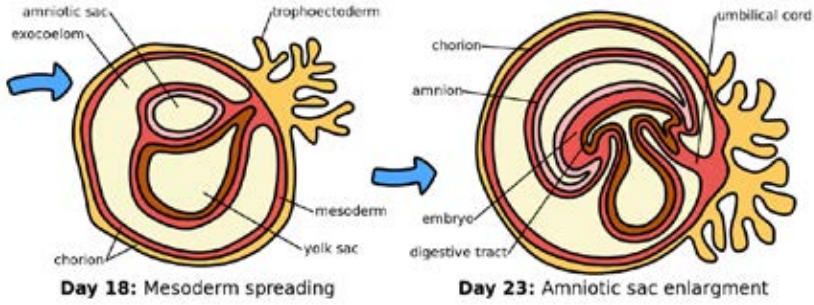
Progesterone from an unexpected source may affect miscarriage risk

By Laurel Oldach



ZEPHYRIS/WIKIMEDIA COMMONS

These illustrations show the fingerlike projections called villi that attach the surface of the nascent placenta to the uterine lining during early pregnancy.

About 20% of confirmed pregnancies end in miscarriage, most often in the first trimester, for reasons ranging from infection to chromosomal abnormality. But some women have recurrent miscarriages, a painful process that points to underlying issues. Clinical studies have been uneven, but some evidence shows that for women with a history of recurrent miscarriage, taking progesterone early in a pregnancy might moderately improve these women's chances of carrying a pregnancy to term.

A recent study in the **Journal of Lipid Research** sheds light on a new facet of progesterone signaling between maternal and embryonic tissue. The work hints at a preliminary link between disruptions to this signaling and recurrent miscarriage.

Progesterone plays an important role in embedding the placenta into the endometrium, the lining of the uterus. The hormone is key for thickening the endometrium, reorganizing blood flow to supply the uterus with oxygen and nutrients, and suppressing the maternal immune system.

Progesterone is made in the ovary as a normal part of the menstrual cycle, and at first, this continues after fertilization. About six weeks into pregnancy, the placenta takes over making progesterone, a critical handoff. (The placenta also makes other hormones, including human chorionic gonadotropin, which is detected in a pregnancy test.) Placental progesterone comes mostly from surface tissue organized into fingerlike projections that integrate into the endometrium and absorb nutrients. Some cells leave those projections and migrate into the endometrium, where they help to direct the reorganization of arteries.

Using cells from terminated pregnancies, Austrian researchers led by Sigrid Vondra and supervised by Jürgen Pollheimer and Clemens Röhrl compared the cells that stay on the placenta's surface with those that migrate into the endometrium. They discovered that the enzymes responsible for progesterone production differ between those two cell types early in pregnancy.

As a steroid hormone, progesterone is derived from cholesterol. Although the overall production of progesterone appears to be about the same in migratory and surface cells, migratory cells accumulate more cholesterol and express more of a key enzyme for converting cholesterol to progesterone. Among women who have had recurrent miscarriages, that enzyme is lower in migratory cells from the placenta than it is among women with healthy pregnancies. In contrast, levels of the enzyme don't differ between healthy and miscarried pregnancies in cells from the surface of the placenta.

The team's findings suggest that production of progesterone by the migratory cells may have a specific and necessary role in early pregnancy and that disruption to that process could be linked to miscarriage.

"If we can identify the exact mechanisms and cells that are affected," Vondra said, "that would lead us one step closer to understanding the big picture of what causes recurrent miscarriages and possibly to being able to intervene and allow these women to have successful pregnancies."

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Finding neoantigens faster — advances in the study of the immunopeptidome

By Laurel Oldach

The immune system may seem quiescent until an infection prods it to leap into action. In fact, it maintains active surveillance to distinguish what belongs in the body from what does not. As part of this surveillance, T cells prowl through tissues, seeking signs of something amiss. Special constitutively active mechanisms report to T cells on cell contents that otherwise would be hidden.

David Gfeller leads the computational cancer biology group at the University of Lausanne in Switzerland, where his lab works to characterize immune infiltrations at the cell level. "In order to detect cells that are infected or malignant, something intracellular has to be presented at the cell surface," Gfeller said.

That presentation is the job of human leukocyte antigens, or HLAs, a subset of which display peptides pulled from chopped-up intracellular proteins. The repertoire of peptides they present, which varies according to HLA alleles, protein expression patterns across tissues and other factors, is called the immunopeptidome; it determines what antigens T cells can recognize and respond to.

Understanding how peptides are selected to become part of the immunopeptidome is key to harnessing adaptive immunity. For example, an effective vaccine must use a peptide that HLA proteins will take up and display. When antigen presentation goes amiss — if T cells mistakenly recognize ordinary components of the cell as dangerous invaders or overlook new mutant antigens — diseases like autoimmunity and cancer can result.

Two papers in **Molecular & Cellular Proteomics** highlight recent advances in the study of the immunopeptidome.

Excitement over immunopeptidomics

The first tumor-specific HLA-binding peptide was identified in 1997. But immunopeptidomics really took off in 2014, when researchers discovered that cancer treatments to boost T cell activity, overcoming immunosuppression induced by tumors, depend on T cell recognition of tumor-specific antigens. Predicting the composition of the immunopeptidome and how it differs between healthy and cancerous tissue became part of a medical frontier with enormous potential: cancer immunotherapy.

Such is the history reviewed by Juan Antonio Vizcaíno, a proteomics team leader at the European Bioinformatics Institute, and colleagues in a perspective in MCP. The authors summarize technical advances in immmunopeptidomics and findings that have linked HLA alleles with human diseases. They also look ahead to a time when immunopeptidome-wide association studies may make it possible to predict an individual's susceptibility to autoimmunity, infection or cancer — and they discuss the possible challenges in the way.

Immunopeptidomics experiments remain technically challenging. Several fieldwide initiatives aim to pool data on the peptides presented by HLA proteins in various tissues and disease states, among them the Immune Epitope Database and the Human Immuno-Peptidome Project. Based on this hard-won knowledge about the binding preferences of HLA proteins, researchers have generated algorithms to predict which peptides HLA proteins may display, enabling computational study of the immunopeptidome. But these algorithms still fall short in predicting display of post-translationally modified peptides.

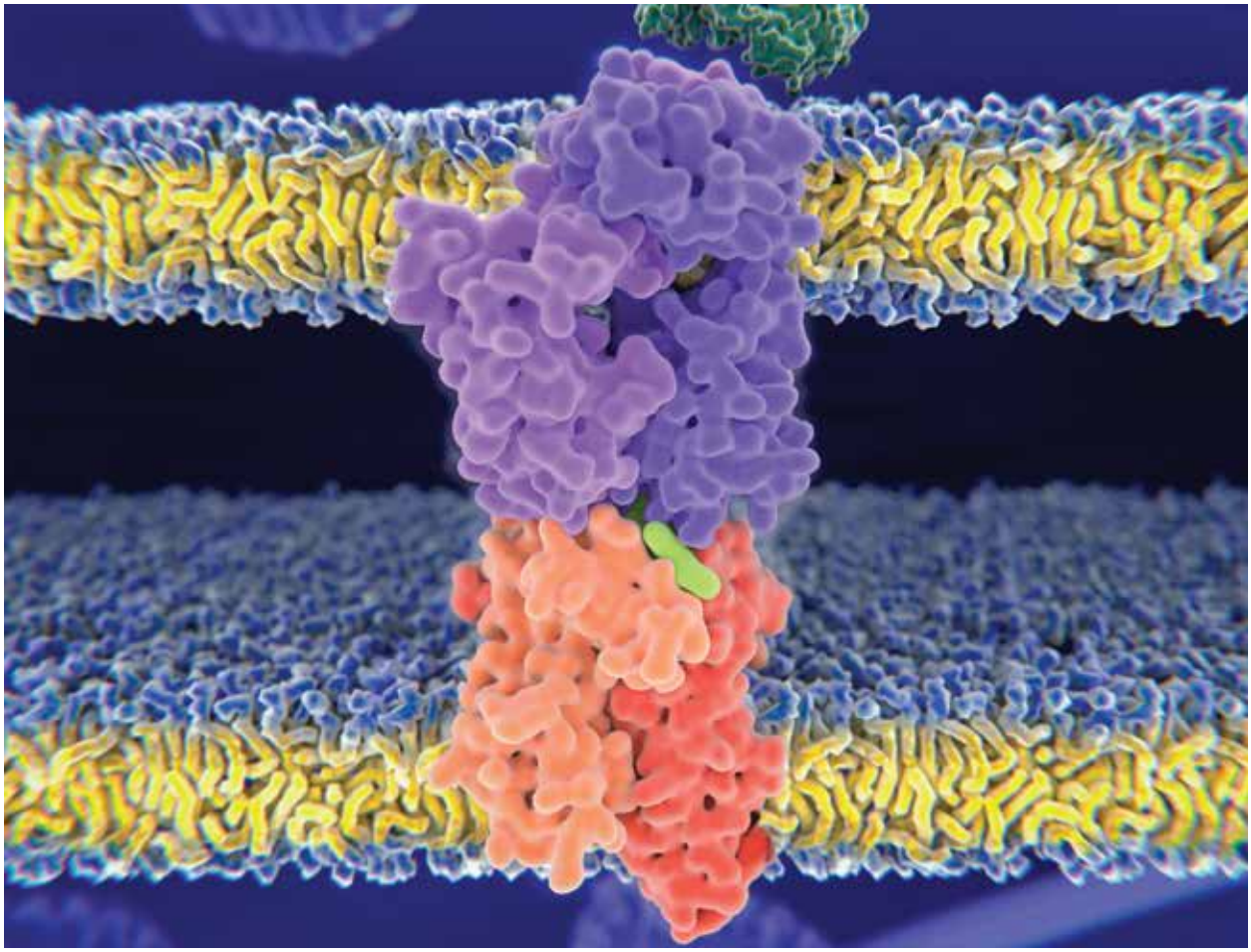
Phosphorylated immunopeptides

In addition to genetic changes, many cancers undergo major changes to signaling pathways — for example, 46% of cancer samples in a recent study carried alterations in the MAP kinase pathway. Quantifying how those signaling changes might be reflected at the cell surface is a matter of conjecture.

Michal Bassani–Sternberg, an investigator at the Ludwig Institute for Cancer Research in Lausanne, studies cancer-specific HLA ligands. "We cannot yet extract or purify phosphorylated HLA-binding peptides to a really good depth of coverage as opposed to the depth of unmodified peptides," she said.

Until recently, this technical limitation hampered efforts to understand whether unusual phosphopeptides might be unique tumor markers in some cases of cancer.

Now, doctoral student Marthe Solleder and collaborators in



An HLA protein (orange) is shown presenting a T cell receptor (violet) with a peptide antigen (green). Researchers are working to find out more about how peptides are selected for presentation.

Bassani–Sternberg's and Gfeller's labs have come up with a new bioinformatics tool for predicting phosphorylated HLA ligand peptides. They report the work in MCP.

"We collected a huge data set of peptides displayed at the cell surface that were measured by mass spectrometry," Bassani–Sternberg said, "and we searched the spectra for modified peptides that contain a phosphate group."

Working mostly with previously collected spectra from immunopeptidomics experiments, the team reanalyzed immunopeptidome data, uncovering phosphorylated HLA-binding peptides that previously had been overlooked. This let them make inferences about HLA proteins' phosphopeptide binding preferences.

"For example, of the three types of HLA class I molecules, one called HLA-C is especially apt to bind to phosphorylated peptides," Solleder said.

The algorithm may be useful for expanding the known range of targets displayed on cancer cells. Bassani–Sternberg said, "If we know where the mutations are in the genome of a patient, we can apply these prediction algorithms to predict which of the mutations is likely to be presented as a ligand on the HLAs of the patient. Similarly, we can now predict which of the known phosphorylated sites the proteins are likely to be presented as HLA ligands."

The researchers have shared all their data and computational tools. They hope the extra information about phosphorylated peptides may help others find novel antigens. In the long term, such insights may help guide tumor-targeting treatments.

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DOI: 10.1074/mcp.TIR119.001641

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From the journals

By Jack Lee & Anand Rao

Stress-free pathways to pathological TDP-43

Amyotrophic lateral sclerosis, or ALS, and frontotemporal dementia, or FTD, are devastating neurological conditions characterized by progressive degeneration of nerve cells. There is growing evidence that the two diseases are closely related — with overlapping genetic, neuropathological and clinical presentations. Among the similarities is hyperubiquitylated TAR DNA-binding protein of 43 kDa, or TDP-43, which is insoluble and aggregates in ALS and subtypes of FTD. While the origin of pathological TDP-43 aggregation remains unknown, some research has suggested that stress granules play a key role.

In a study published in the **Journal of Biological Chemistry**, Friederike Hans and colleagues at the University of Tübingen used time-course experiments conducted in cells to show that TDP-43 ubiquitylation occurs even when stress granule formation has been inhibited. Their findings demonstrate a novel pathway by which TDP-43 is modified and becomes insoluble, expanding our knowledge of the pathological manifestations of this protein.
DOI: 10.1074/jbc.RA119.010617

Breast cancer cells acquire lipids by endocytosis

Researchers long have thought that breast cancer tumor cells synthesize lipids as they multiply; more recent studies show that cancer cells also can take up lipids. In a recent paper published in the **Journal of Lipid Research**, Leslie Lupien of the Norris Cotton Cancer Center and researchers in the U.S. and Belgium identified a new pathway for lipid uptake. Experiments in multiple breast cancer cell lines showed that very low-density lipoprotein, or VLDL, is taken up via receptor-mediated endocytosis through interactions with surface-bound lipoprotein lipase, or LPL, and the VLDL receptor. The researchers propose that LPL may be binding free VLDL and concentrating it at the cell surface, thereby promoting VLDL uptake by the VLDL receptor. These findings have therapeutic implications and add to an increasing body of evidence that targeting fatty acid synthesis alone may not be effective in certain tumor types.
DOI: 10.1194/jlr.RA119000327

Using co-elution to study protein interactions

Studying how the vast network of proteins and molecules in a cell interact, a discipline known as interactomics, is crucial to researchers' fundamental understanding of biological processes and for the development of new medicines and biotechnology. Among the technical strategies for mapping the interactome, co-elution is a global protein interaction mapping method. However, strategies vary across studies that utilize co-elution, depending on experimental considerations.

In a review in the journal **Molecular & Cellular Proteomic**s, Daniela Salas and colleagues at the University of British Columbia delineate co-elution methods used to map protein–protein interaction networks and discuss important considerations in designing co-elution studies, such as the choice of separation method and how to analyze co-elution profiling studies. The researchers also discuss the benefits of co-elution versus other mapping methods, including the time and resources required to perform the protein mapping and the number of protein interactions that can be explored.
DOI: 10.1074/mcp.R119.001743

What are bacterial cell walls made of?

Gram-negative bacteria exist in nearly all life-supporting environments on Earth. Many Gram-negative bacteria, such as Pseudomonas aeruginosa, Neiseseria gonorrhoeae and Chlamydia trachomatis, cause disease in plants and animals, including humans. Understanding the composition of the bacterial cell wall helps scientists to design more effective antibiotics.

Peptidoglycans, or PGs, are polymers composed of sugars and amino acids that form a critical component of bacterial cell walls. In Gram-negative bacteria, PGs are assembled in the cytoplasm and exported to the periplasm, where they undergo important functional modifications and are thought to be relatively consistent in composition across species. In a paper published in **the Journal of Biological Chemistry**, Erin Anderson and colleagues at the University of Guelph in Ontario present an optimized mass spectrom-

continued on p. 20

Chemical activator of GPR120 affects fat taste detection

In addition to sweet, sour, salty, bitter and umami, there might be a sixth taste: fat. Researchers have identified two receptor proteins, CD36 and GPR120, that are involved in detecting fat taste in both humans and mice. Mice that don't express any GPR120 protein, for example, have less preference for fatty acids than normal mice.

Studies also have shown an association between fat taste sensitivity and obesity. In both mice and humans, GPR120 deficiency led to increased obesity. Thus, obesity might be modulated by tricking the body into thinking it is consuming fat when it's taking in a small molecule that binds a fat taste receptor.

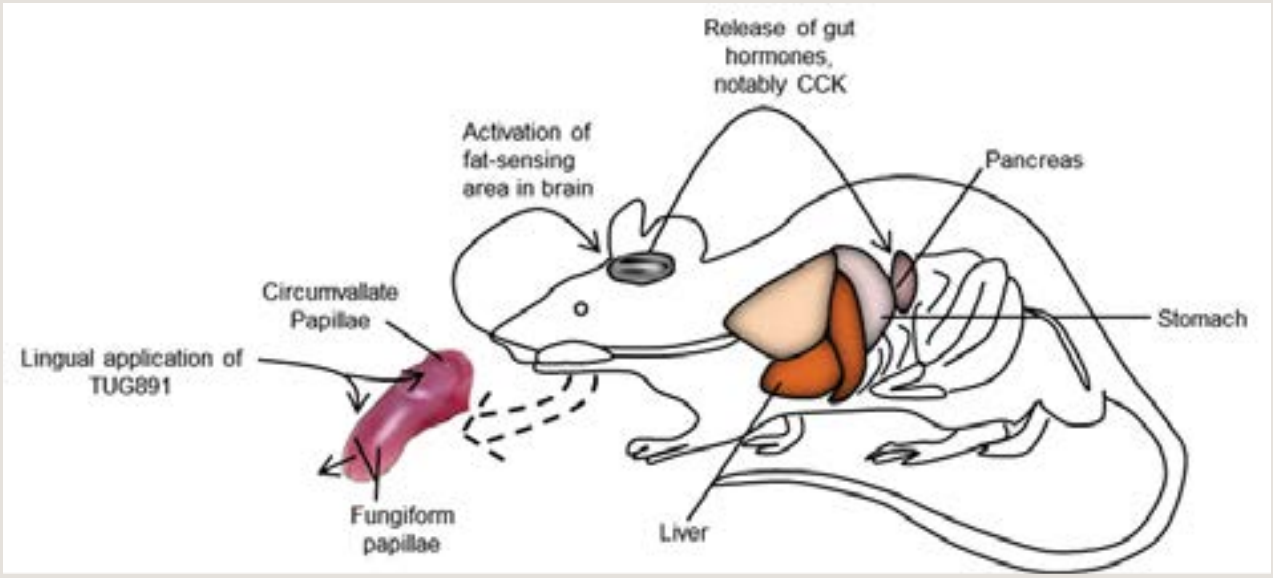
In a recent paper in the **Journal of Lipid Research**, Babar Murtaza from the University of Burgundy in Dijon and colleagues report that they tested whether a small molecule that binds GPR120 could be used for such a treatment. TUG891 previously had been shown to reduce obesity in mice.

In studies using mouse and human taste bud cells, the researchers found that adding TUG891 or linoleic acid, a fatty acid, could promote calcium signaling through GPR120. They also tested whether TUG891 could activate the tongue–brain–gut loop by applying TUG891 or linoleic acid directly to the tongues of sedated animals. In both cases, pancreatic and bile duct secretions increased, as did blood circulation of the gut hormone cholecystokinin. The treatment also had an anti-inflammatory effect: The concentration of adiponectin, an anti-inflammatory cytokine secreted by fat tissue, in the blood increased, while levels of inflammatory cytokines decreased.

In behavioral tests, the researchers found that mice typically preferred drinking a solution of water, linoleic acid and a stabilizer over a solution of water and the stabilizer alone. Adding TUG891 to the linoleic acid solution removed any preference. These findings suggest that TUG891 may be helpful in human treatments to decrease consumption of fats and reduce obesity.

DOI: jlr.RA119000142

—Jack Lee



BABAR MURTAZA

In the researchers' model of how TUG891 might be working, after the chemical is detected on a mouse's tongue, resulting activation of a fat-sensing area in the brain leads to the release of gut hormones.

continued from p. 18

etry–based strategy for assessing PG composition and making inferences about enzymatic activity. Using this approach, the researchers identified 160 unique muropeptides in P. aeruginosa, demonstrating that its PG composition is more diverse than previously thought. Their findings, which provide an important contribution to our understanding of this bacterium, will benefit development of more effective antibiotics.
DOI: 10.1074/mcp.RA119.001700

Triple therapy to treat atherosclerosis

Atherosclerosis is the leading cause of cardiovascular disease. Statins can help lower the low-density lipoprotein cholesterol that causes plaque, but treatment typically leads to only a modest reduction in plaque volume. In a recent paper in the **Journal of Lipid Research**, Marianne Pouwer of the Netherlands Organization of Applied Scientific Research in Leiden and a team of researchers in the U.S. and the Netherlands identified a combination of drugs that not only slowed plaque progression but also reversed it and improved plaque composition.

The researchers fed mice a high-cholesterol, high-fat diet and treated them with atorvastatin in combination with monoclonal antibodies alirocumab and/or evinacumab. The mice treated with the statin and one antibody had lower cholesterol and slower plaque progression compared to mice that received no treatment. Mice treated with a combination of all three drugs had plaques that were not only smaller but had less macrophage content and were less likely to rupture. These findings indicate that high-intensity treatment with multiple drugs could be a promising approach in humans as well.
DOI: 10.1194/jlr.RA119000419

Confident identification of citrullinated peptides

Citrulline is an amino acid not encoded in the genome. It is generated by a post-translational modification to the amino acid arginine, a process known as citrullination. In recent years, scientists concerned with the immune system have been paying attention to citrullination because of its role in inducing anti-citrullinated proteins/peptide antibodies, which results in an autoimmune reaction where the host's immune system attacks its healthy tissue. The bacteria Porphyromonas gingivalis generates citrullinated epitopes in the periodontium, which contributes to chronic periodontitis and recently has been linked to rheumatoid arthritis.

Using a new two-dimensional heptafluorobutyric acid–based separation system combined with liquid chromatography–mass spectrometry, Daniel Larsen and colleagues at the University of Southern Denmark analyzed the outer membrane vesicles and other related elements of P. gingivalis to identify 79 citrullinated proteins with 161 citrullination sites. These results were reported in a paper published in the **journal Molecular & Cellular Proteomic**s. This work establishes a method for identifying citrullinated proteins that will advance development of treatments for human autoimmune and inflammatory diseases.
DOI: 10.1074/mcp.RA119.001700

Plant protein parodies and human immunity

When certain ligands bind chemokine receptors, such as CXCR4, a response is triggered that regulates host immunity and stimulates immune cell migration. Human macrophage migration inhibitory factor, or MIF, is a structurally unique protein capable of binding its cognate receptor CD74 and chemokine receptors. MIF has been implicated in autoimmunity, cancer and inflammatory diseases, and researchers have found it to be essentially unchanged throughout evolution in organisms ranging from mammals to unicellular parasites.

In a paper published in the **Journal of Biological Chemistry**, Ludwig-Maximilians-Universität researcher Dzmitry Sinitski and collaborators recognized that MIF has significant sequence homology with a family of plant proteins known as MIF/d-dopachrome tautomerase–like proteins, also known as MDL proteins. Using spectroscopy, the researchers characterized MDL proteins in the plant Arabidopsis thaliana and found similar protein structure to human MIF. Cell migration experiments showed that plant MDL proteins were able to stimulate CXCR4 signaling and act as a chemoattractant for primary human monocytes and T cells. These findings demonstrate that proteins in plants that are homologous to human proteins and cytokines can stimulate signaling cascades, which may suggest new ways plant proteins affect human biological processes.

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The curious case of Benja-mouse Button: SIRT6 and aging

In this digital age, we see no shortage of product advertisements that promise to make us feel young again. According to a recent Statista report, the global anti-aging market was estimated to be worth approximately $50 billion in 2018 and is projected to grow in coming years. While it's no surprise that many manufacturers make exaggerated claims of their products' efficacy, one method is scientifically supported: calorie restriction.

Calorie restriction has been suggested as a strategy to increase life span and reduce aging-related disorders including heart failure and inflammatory disease. Studies have demonstrated that limiting calories can lessen fibrosis, the formation of scarlike tissue on organs such as the heart and lungs, in a variety of cardiovascular disease models.

SIRT6, an enzyme linked to aging, is activated during calorie restriction, but researchers lack a complete mechanistic understanding of how SIRT6 may be involved in the aging process. Sangeeta Maity and colleagues at the Indian Institute of Science in Bengaluru sought to close this gap in knowledge, and the results of their study were published in the **Journal of Biology Chemistry**.

Using Western blot analyses and luciferase activity assays, the researchers demonstrated that signaling by TGF-beta, a well-known driver of fibrosis, was activated in SIRT6-deficient cardiac cells. Subsequent experiments showed age-dependent multiorgan fibrosis in mice engineered to be SIRT6-deficient, confirming the findings in cells. Their results suggest that under normal circumstances, SIRT6 represses the transcriptional activity that hyperactivates TGF-beta. However, SIRT6 activity decreases with age, resulting in increased TGF-beta activity, leading to fibrosis. These results improve our understanding of the molecular players involved in aging and identify potential therapeutic targets to treat aging-related disease and illness

DOI: 10.1074/jbc.RA119.009432

"The magic isn't the squid… The magic is the protein."

THE BIOPHOTONIC SECRETS OF A BRILLIANT ANIMAL

By Laurel Oldach

Just offshore from Redondo Beach in Los Angeles, there's an underwater canyon. According to local scuba enthusiasts, once a year it becomes a highway to an invertebrate orgy in the shallows.

Underwater photographer–videographer Brent Durand and others in the Los Angeles scuba diving community keep an eye out each December for signs of the squid run, when the footlong animals emerge en masse from the canyon into the shallow water near shore to mate.

"The squid are just filling the entire water column," Durand said. In some places near the bottom, divers find themselves "surrounded by a wall of squid so dense that if you reach to grab one of your gauges, you might have a squid between your hand and the gauge.

"You have to be OK with squid being pressed against your face."

Squids are intensely visual animals, and the swarm is attracted by the divers' lights. According to Durand, it is easy to tell whether another dive group has passed through recently by how many are already amassed when he descends to the bottom. For him, while the throngs are impressive, the moments when he's near fewer animals can be even more compelling.

"On the outside of the mating aggregation, you can really quiet down," Durand said. Sometimes a single squid "will hover in front of you, and you feel like you're almost connecting, checking each other out."

At those moments, watching the squid's rapidly changing color displays, a diver may glimpse something unique to the California market squid and a few of its cousins: their tunable iridescence. The phenomenon is a remarkable feat of optics not known to happen in other biological contexts. New research in the Journal of Biological Chemistry sheds some light onto the biochemistry that makes it work.

How is iridescence generated?

Most cephalopods can change color swiftly through a small palette of pigmentary yellows, reds and browns — an ability that makes them stars of many "now you see me, now you don't" camouflage videos. This is controlled by chromatophores, cells with a sac of pigment that expand or contract with muscle activity. In a small family of shallow-water squid species that includes the California market squid, the Caribbean reef squid, and a few other flashy cousins, the palette is nearly unlimited.

On these squids' mantles, when the chromatophores are retracted, they reveal splashes of color arranged in a pattern that looks a bit like leopard skin. Each bright splotch is made up of a few dozen to a few hundred cells called iridocytes. Unlike chromatophores, iridocytes use structural color. Pigment produces a color by absorbing certain wavelengths and reflecting others that eventually

Caribbean reef squids, like this colorful specimen, are members of the loliginid family.

reach the observer's eye. But structural color depends on a different optical phenomenon, which occurs when light reflects from a regular, repeated structure.

Dan Morse

It's a phenomenon called Bragg reflection. Dan Morse, a distinguished professor at the University of California, Santa Barbara, explained: "An example is the rainbow of reflection that you can see from the surface of a CD disk. The distance between the grooves determines the color, the wavelength, at which constructive reflection occurs."

Squid iridocytes have just such a structure. "The iridophore cells contain a stack of membrane-enclosed sandwiches of protein that are very thin, something like a stack of Frisbees within the cell," Morse said. "The light scattering is coming from the interfaces between the membrane and the external space."

Whether light is passing through layers of plastic and air, as in the CD, or of cell contents and extracellular fluid, as in the squid, whenever a large number of alternating layers with different refractive indices are repeated at the

BRENT DURAND

A male market squid (left) clasps a female (right) during the squid run off of Redondo Beach. The camera's illumination lights up multicolored iridophores on the female's mantle. Underwater photography "turns the regular scuba divers into citizen scientists," Brent Durand said. "As a photographer and videographer, you start paying more attention to the details, and trying to capture footage of them."

same distance apart, some light can be reflected off each layer. For light whose wavelength is about four times the distance between layers, those reflections will be in phase, allowing constructive interference between rays. Other wavelengths will not get this brightness boost.

In most animals with structural coloration, such as iridescent beetles, bright butterflies or even certain types of cuttlefish and octopus, the reflectors' dimensions are fixed, keeping the reflection at one wavelength — or, in the case of iridescence, a few wavelengths that differ according to the observer's angle. But squids in the loliginid family can alter the structure of the tiny features inside iridophores, changing the color that results — or even whether iridescent patches appear on their milky skin at all.

Dynamic iridescence depends on the brain

For a long time, researchers were stumped about how squids could turn their iridescence on and off.


Roger Hanlon

A colleague and friendly collaborator/competitor of Morse, Roger Hanlon of the Marine Biological Laboratory in Woods Hole, Massachusetts (now an affiliate of the University of Chicago), was part of a team that reported in the late 1980s and early 1990s that iridophores' change from colorless to iridescent came with a change in thickness of the protein-dense plates within iridocytes and could be stimulated by applying the neurotransmitter acetylcholine.

Among neuroscientists who study vertebrates, acetylcholine is most familiar for its role in the neuromuscular junction (though cholinergic cells also are found throughout the brain). It is responsible for the signaling between neurons in the peripheral nervous system and the muscle cells that do those neurons' bidding.

The same light-scattering properties that make iridophores so bright also made them difficult to study using light microscopy. Scientists could not see whether neurons were forming synapses at iridophores; stimulating various nerves did not seem to cause the iridescence to change. And as cephalopod researchers had learned in one physiological system after another, to expect squid systems to behave just like human systems was to be disappointed by eons of divergent evolution.

"These goofy animals are built so differently (from us)," Hanlon said. "They're doing things that aren't by the book — and they're sure not by the vertebrate books."

So he considered it possible that, like a starfish's tube feet, iridophores might be responding to acetylcholine that diffused in from another tissue. But there were problems with that hypothesis, too — mostly the speed at which iridophores change compared with sluggish starfish.

As the squids get visual information, Hanlon said, "The animal has to integrate that information 'upstairs' and it has to make all the motor output — that being the millions chromatophores and iridophores — they have to be turned on, and it all happens in about one to one and a half seconds."

It was a puzzle until, in 2012, Hanlon's lab reported that the delivery of acetylcholine to control color was, indeed, neuronal. In a follow-up paper, they worked out the unusual neuroanatomy that had so confused their previous investigations.

Protein phase separation drives color change

In the meantime, the researchers had made some progress on how acetylcholine could alter the spacing of light reflectors within iridophores. The accordionlike ruffled-membrane stacks are packed with a protein called reflectin. A 2009 collaboration between Morse and Hanlon's labs had found that reflectin is phosphorylated upon acetylcholine stimulation. Morse's recent research shows exactly how that phosphorylation drives color change.

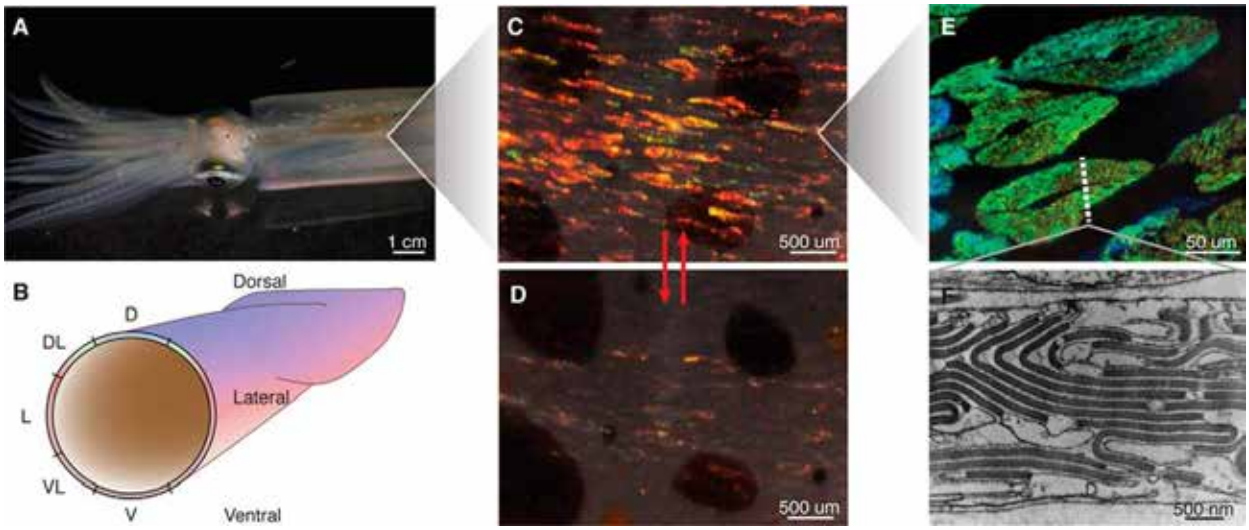
"This very complex, multistep process is largely contained in (reflectin)," Morse said.

Morse's lab showed in 2013 that the distance between the stacks was determined by water efflux. At rest, an intact iridocyte's membrane-folded plates are swollen with water. Using deuterated water, the researchers showed that the cell will expel that water after treatment with acetylcholine.

"Dehydration shrinks the thickness and spacing of the membrane-enclosed layers, changing the wavelength that's reflected," Morse said. The more water is expelled, the shorter the distance between stacks and the shorter the wavelength that will be reflected best.

Since 2013, research from Morse's lab, chronicled in a series of papers in the Journal of Biological Chemistry, gradually has elaborated a biochemical mechanism linking water expulsion with acetylcholine signaling. The color change is driven by inducible phase separation that happens after reflectin is phosphorylated.

Reflectin proteins are conserved among many cephalopod species. There are four isoforms in the California



DEMARTINI ET AL. JBC 2015

In a figure from a JBC paper, Morse and his colleagues zoomed in on the iridescent patches of a female California market squid's mantle, illustrating the cells' anatomy with both light microscopy and transmission electron microscopy.

market squid. The relectin that fills and determines the distance between alternating layers in the iridocyte has an alternating structure of its own. Between conserved domains, it has linker regions rich in arginine and aromatic amino residues. These domains have a strong net positive charge and do not lend themselves to secondary structure.

According to Morse, reflectin's two types of domains have opposing activities. "The cationic linkers are like compression-resisting shock absorbers. Because of electrostatic repulsion, they want to stretch out and keep the protein in an extended, unstructured form. The alternating domains are like the spring on our screen doors: They want to compress, but they're held in check by the repulsion of the linkers."

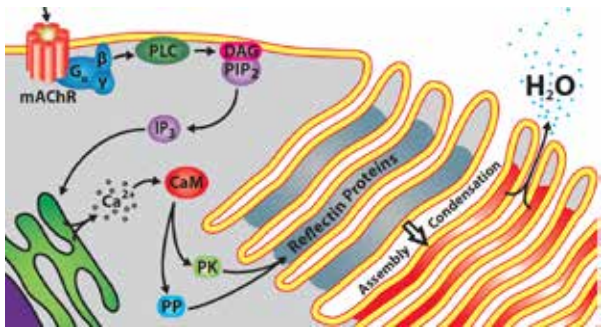
When acetylcholine is released, it activates a tyrosine kinase — the enzyme's exact identity is not yet known — that phosphorylates the linker regions. Adding negatively charged phosphates neutralizes the positive charge of those domains, reducing their repulsion and letting reflectin assemblies begin to form. With more phosphorylation, the positive charge eventually is neutralized, allowing formation of larger complexes.

"As the reflectin particles become fewer and bigger, osmotic pressure within the stacks drives more and more liquid out," Morse said. "Now, the contents are very dense by this time … which means that the opacity increases. But the color of that reflectance is set by the dimensions separating the membrane layers."

While acetylcholine activates the kinase in question, Morse said that the phosphatase seems to be constitutively active. "The result is that the signal that activates iridescence is ephemeral. From moment to moment, there's a pulse of neuronal signal in response to whatever the animal sees. The brain fires this neuron; acetylcholine is released and diffuses to these cells, activating the color change; but then the phosphates quickly are removed. That means the system produces a color in response to a neuronal signal and then can be reset very quickly.

"You can see the tissue return to colorless if you provide no further stimulus. But if stimulus is continuing and changing, then the color can continuously change."

Morse's work has garnered attention for his meticulous attention to the biophysics of reflectin's response to signaling. Hanlon said, "I think Dan's avenue of inquiry,



COURTESY OF DANIEL MORSE

A schematic cartoon illustrates the change in iridophores' reflective platelets after acetylcholine treatment.

looking more and more carefully at very specific mechanisms of subtle changes in nanostructure and in how the reflectin protein changes its conformation is really going to be important to understand the system."

Engineering materials based on reflectin

As reflectin has come into focus, researchers have begun considering ways to use the protein, which Morse often calls a "marvelous molecular machine," to inspire bioengineering efforts.

"Because of its domains' opposing physical activities, the protein works as a sensor that can measure signals and produce a proportional calibrated output," Morse said. "Can we transport this very precisely calibrated transduction … into other signal-dependent, proportionally switching reconfigurable materials? If so, we could design reconfigurable materials that might be used for many applications."

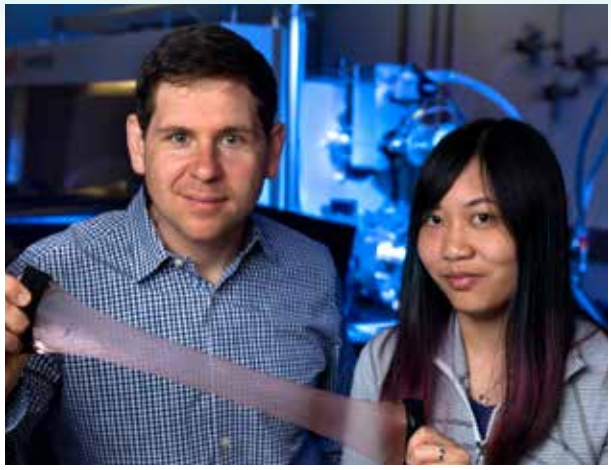
For example, he said, the ability to control the viscosity of bulk quantities of protein might be used to solve problems in protein manufacturing for pharmaceutical or industrial purposes.

Meanwhile, researchers led by materials scientist Alon Gorodetsky at the University of California, Irvine, are working on developing stimulus-responsive biomaterials inspired by reflectin.

"The first day I was starting my independent position, I walked into a room where Roger Hanlon was giving a talk about cephalopods' camouflage ability," Gorodetsky said. "It was just mindblowing. I said, 'OK, I'm dropping half the research that I was planning on doing and switching to reflectin.'"

According to Gorodetsky, reflectin's combination of properties is unique. "I can't think of another protein that has this high refractive index and excellent electrical properties, can be processed so easily, and is also very stable."

It's stable enough, in fact, that his lab developed a tape coated in a thin film of reflectin that changes infrared reflectivity after being stretched. On the other hand, it is so responsive to many stimuli — pH, ionic strength, humidity, charge — that it is not an ideal material for reusable technologies. Instead, Gorodetsky said, his lab now uses the protein as inspiration to derive materials that improve upon its qualities.



STEVE ZYLIUS/UCI

Alon Gorodetsky, a professor at UCI, and graduate student Erica Leung made composite material inspired by squid skin. It combines layers transparent to infrared light with adjustable layers that reflect infrared light, and it is responsive to stretching.

Back in the world of basic science, Morse is also curious about whether the reversible assembly of reflectin could shed light someday on other types of protein assembly — such as the formation of amyloid plaques in the brain that occurs early in Alzheimer's disease. "Both classes of proteins, the amyloids and the reflectins, have extended domains of positively charged amino acids that appear to form liquid–liquid phase separated droplet intermediates," Morse said. "It raises the question: Why is this process reversible, harmless and even advantageous in the case of reflectin, but irreversible and pathological in the case of Alzheimer's?"

Plenty also remains to be learned about reflectin's function in the squid. Gorodetsky said that one of the most interesting questions is how different reflectin isoforms, which have high sequence identity, create different optical effects in different cells.

Ask Morse about his favorite aspects of his work, and the answer is the same. "Its elucidation of this complex molecular machine embodied in the reflectin protein. The magic isn't the squid. The magic isn't the photonics. The magic is the protein machine and its mechanism of action."

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Colorful, yet colorblind

Researchers don't know exactly why squid use tunable iridescence. According to Lydia Mäthger, a scientist at the Marine Biological Laboratory in Woods Hole, Massachusetts, "There isn't anything that really proves that any of this is used for communication between the squid."

But, Mäthger added, it is difficult to study ocean animals' behavior and very difficult to prove a hypothesis about intraspecific signaling. "Say you did film something that was definitely a signal. Then the question still is, did the neighboring squid that looked at it perceive it as a signal? And what does it mean?"

In her first paper as a graduate student, published in 2001, Mäthger investigated how iridescence might look underwater. She recalls her adviser telling her to imagine the squid 30 meters below the surface and think about how their skin might appear at that depth.

Using data collected by divers, Mäthger did just that. At the depths the squid frequent, sunlight is filtered to blue-green by the water above, so it is unlikely that the animals enjoy the color displays they are famous for. That's doubly certain since cephalopods express just one photoreceptor, well suited to blue-green light, and cannot differentiate between wavelengths as humans do.

"When one of these iridophores reflects red under white light," Mäthger explained, "for the squid, red is just a very dim green. If an iridophore reflects green, that'll be a really bright green at the depths at which they occur."

Another feature of marine light is that nearly all of it comes straight down. That enabled Mäthger to predict exactly how an activated iridescent patch would appear to an observer above, below or alongside the animal. Her results suggested that the iridescence may help both with camouflage and schooling. To an observer looking straight down from above, the squid will be scarcely visible. To an observer at the same depth, it will appear about four times as bright as the background.

Subsequent research has suggested other potential explanations for tunable iridescence. Among male loliginid squid, a flash of iridescence is part of aggressive displays. Among females, some researchers have argued that when two stripes of iridescence flanking a white stripe show up, that may be a signal that they are not receptive to mating. However, no one has proved the function of any visual signal conclusively.

Still, Mäthger said, given the small size of the field and the squids' reliance on light, "It would be kind of silly to assume, only because it's not been proved scientifically, that they don't use it."

— Laurel Oldach

Deep water filters white light from the sun to blue-green. Here, a Caribbean reef squid swims in the brighter shallows.

Lydia Mäthger

"Start simple. It always gets more complicated."

A conversation with Paul Dawson

By Laurel Oldach

Be fearless. Find a good question, and think through what you would need to answer that question. And start simple, because it always gets more complicated as you move forward."

Yellow bile, one of the four humors of ancient and medieval physiology, once was believed to cause irritability. Scientists since have determined that its biological function is solubilizing fat from food so it can be absorbed into the intestinal epithelia. Bile acids, amphipathic molecules produced in the liver, are the key to this process. In the gut, they form micelles with fats, sterols and fat-soluble vitamins that then are absorbed.

Paul Dawson knows more about bile than the average person. Dawson has studied how bile acids are absorbed and recycled — or left in the gut to be eliminated — for most of his career. His lab identified transporter proteins at the far end of the small intestine that are responsible for picking up bile acids after they've shed their lipid payload and returning them to the hepatic portal vein.

These days, Dawson's work focuses on inhibitors of bile acid transport, especially of the protein apical sodium-dependent bile acid transporter, or ASBT. Because bile acids are made from cholesterol in the liver, researchers hypothesize that drugs that block their reabsorption might help to clear excessive cholesterol in fatty liver disease. Dawson's lab has shown that bile acid uptake inhibitors can block the development of fatty liver disease in mice.

Dawson, a professor at Emory University School of Medicine and an associate editor of the Journal of Lipid Research, talked to ASBMB Today about his work. The conversation has been condensed and edited.

I understand that you run your lab jointly with a colleague who is a physician?

I've been camped in a clinical department for most of my faculty career. It's been a very good experience: My clinical colleagues like to hear about the basic science, and I've certainly learned from their experience with patients.

I've known Saul Karpen for many years. When I came to Emory, we realized that there would be benefits to working together. We focus on our own research interests, but there are other areas where the synergy is really powerful. Since Saul is a practicing pediatric hepatologist and investigator, we work on basic science questions about observations that he makes in the clinic. Our offices are right next to one another, and people in our labs all work together as one larger group to answer scientific questions. I think that's not uncommon now in academia.

Paul Dawson is shown in his office at Emory University, where he and a colleague who is a practicing physician work together to address research questions.

Tell me about your training.

I went to Stony Brook University thinking I was going to work with someone who was doing nerve regeneration. As graduate students, we often think we know what we're interested in, but we're pretty undifferentiated. My first rotation was with an amazing mentor named David Williams, who was applying cutting-edge molecular biology techniques to study cholesterol metabolism and apolipoproteins. I was so excited by that work I abandoned my idea of working in the other lab and threw myself into learning all I could about cholesterol metabolism.

In the summer, Michael Brown would visit Long Island with his wife, Alice, and children. (Note: Brown and Joe Goldstein are longtime collaborators at the University of Texas Southwestern.) I remember Mike Brown visiting my advisor to talk about what was going on in cholesterol metabolism. This is just prior to Brown and Goldstein winning their Nobel Prize; they were doing amazing work on the LDL receptor and control of cholesterol homeostasis.

I had a chance to meet with Brown when I was getting ready to graduate, which emboldened me to apply to their lab for a postdoc. It was a nerve-wracking period, because I didn't hear anything for a while, and then they won the Nobel Prize. I thought, "Well, I don't know if I'm going to make it into their lab or not." I was amazed when literally two weeks after they won the prize, I got an acceptance letter. I still have it. It was a real turning point in my career.

I took over a project from Thomas Südhof, who was leaving the lab to do his Nobel Prize–winning work on synaptic transmission. Helen Hobbs was in the lab, and Tim Osborne — really great scientists, early in their careers. I learned so much vicariously by talking to others around me. Brown and Goldstein were wonderful mentors — demanding, but appropriately so. It was an amazing time in their lab.

When I was finishing, Larry Rudel recruited me to Wake Forest School of Medi-

MARATHONFOTO, COURTESY OF PAUL DAWSON

Paul Dawson in motion during the Toronto half-marathon in May 2019. He and his wife, Anu Rao, often plan their travels around races.

cine. Larry built a vibrant ecosystem for lipid investigators. He was in a sense a Johnny Appleseed, training investigators and then sending them out around the country. There's a whole generation of lipid researchers that passed through the Section on Lipid Sciences he put together.

What research questions did you work on at Wake Forest?

When I was getting ready to leave my postdoctoral lab, in discussions with colleagues, I recognized an interesting niche: The transporters responsible for moving bile acids hadn't been identified. These are important control points that establish the fate of bile acids, either enterohepatic cycling or elimination from the body, and could potentially contribute to the pathophysiology of a variety of diseases. When I moved to Wake Forest and started my lab, the question was, "How do bile acids — which are charged molecules and prevented from just passively diffusing across a membrane — get from the lumen of the gut into the portal circulation?"

I came up in that generation when it was possible to start out focusing on something very basic with translational implications and spend much of your career trying to work that out. Looking back now, it wasn't exactly as charted, but we were able to do the things I wanted. We identified a sodium cotransporter called ASBT that's responsible for absorbing bile acids from the intestine, and a binding protein that helps move bile acids within the cell. We also discovered that mutations in ASBT cause primary bile acid malabsorption and congenital diarrhea.

> "I came up in that generation when it was possible to start out focusing on something very basic with translational implications and spend much of your career trying to work that out."

Then the question was, "If a bile acid gets in on one side of the (epithelial) cell, how does it get out the other side?" That took longer to figure out, but we were ultimately able to show that another transporter, organic solute transporter alpha-beta, moves the bile acid across the basolateral side into blood. If it's mutated in patients, this transporter also causes congenital diarrhea. It was very satisfying establishing that this is the basic permeation pathway for how bile acids traverse the intestinal epithelial cell.

You moved to Emory a few years ago. Has your research focus stayed the same?

I'm interested in how preventing the return of bile acids to the liver can potentially produce benefit there. The transporter on the apical membrane turned out to be an interesting drug target for small-molecule inhibitors. We've worked with industry over the years, and they ultimately developed nonabsorbable inhibitors that can block bile acid uptake. Now there's a whole group of these therapeutics in clinical development. I was interested in helping to evaluate them critically and, if they're promising, to move them forward into patients. Coming here was an opportunity for me to work with Saul Karpen and other clinical investigators on that.

You mentioned working with pharmaceutical researchers. What was that like?

Early on in the development of the inhibitors for ASBT, Wake Forest patented the use of cells for screening and then licensed them to various companies. I helped them

set up the screens used to identify some of the high-affinity small-molecule inhibitors that were developed.

It took more than a decade from the identification of the transporter to the development of the inhibitors and their use in patients. When we were first cloning it in the lab, if someone had said to me, "Years down the road, these cloned transporters will be used in screens that will lead to a drug that will end up in a patient," I'm not sure I would have believed them. But that's ultimately what happened.

What's it like getting a glimpse into pharmaceutical research?

It's refreshing. You learn so much from the way these colleagues think about how to address questions. In the lab, we sometimes take a meandering approach, which can be valuable; but sometimes we've meandered off a little too far in one direction or the other before we came back to the center and figured out where we were going.

There are times when the efficiency that I've seen from people in industry would be useful, especially for students. At the end of the day, they need to produce a body of work that will be publishable and provide all the research skills that they need to move on with their training and careers.

So how do you balance following your curiosity with productivity?

Typically, students start out with a couple of potential projects. After a certain period of time, we say, "Okay, set that one on the back burner and shift your attention to this one. You're making good progress here, and this is a project that can carry you to the finish line."

We looked for the basolateral bile acid transporter, which gets the bile acid out of the enterocyte, for about eight years. Students would work on that project, trying various strategies, and then, if it looked like it wasn't going to work, they moved on to something safer so they could move forward in their careers.

When did you first become involved with the Journal of Lipid Research? What have you most enjoyed about joining its leadership team?

The JLR had always been one of my go-to journals to follow what's going on in the lipid field. I joined the editorial board in 2011. Then in 2019, Nick Davidson and Kerry-Anne Rye (the JLR's editors-in-chief) invited me to be an associate editor. I have enjoyed working with the editors, other AEs and staff as the group works to chart the future for the JLR.

Is there advice for research that you find yourself giving again and again?

That idea of being fearless; in Brown and Goldstein's lab, they really instilled that concept. Find a good question, and think through what you would need to answer that question. And start simple, because it always gets more complicated as you move forward.

Also, talk a lot with other people in the lab and other students and postdocs and faculty. A lot of science is tacit; you read the methods section of a paper, and a lot of nuances aren't there. But if you have a chance to talk to somebody in the next lab, you can learn so much from them.

What are you most interested in outside the lab?

My wife, Anu Rao, and I — she's a scientist too — are both runners. We'll get up early in the morning and go for a run with friends; it's a really good way to start the day and helps clear our heads.

If we're at a meeting, we'll look to see if there's a race nearby. If we go on a trip, we try to plan it along with a race — typically something not so long, like a half-marathon, so that it's manageable. We'd always wanted to visit Iceland, so we went there in August when there was a half-marathon in Reykjavik.

Running is something you can do on most mornings. You can just go out the door, run and come back and feel pretty good as you get started on your day.

"When we were first cloning [ASBT] in the lab, if someone had said to me, 'Years down the road, these cloned transporters will be used in screens that will lead to a drug that will end up in a patient,' I'm not sure I would have believed them. But that's ultimately what happened."

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

Dear ASBMB Today reader,

As you probably know by now, the American Society for Biochemistry and Molecular Biology and the other host societies have canceled the 2020 Experimental Biology meeting due to concerns about spread of COVID-19.

We learned of this decision just as we were sending the March issue of ASBMB Today to the printer. Although they will not be presenting at the meeting this year, we thought you would enjoy reading about these three scientists and their work. We hope you will have an opportunity to hear their talks in the future.

Sincerely,
Comfort Dorn, managing editor

MCP to host proteomics session

By Saddiq Zahari

The editorial leadership team of the journal **Molecular & Cellular Proteomics** has chosen three investigators to present their current research during a symposium at the 2020 American Society for Biochemistry and Molecular Biology Annual Meeting in San Diego.

"These are mid-career scientists leading and gaining penetrating discoveries of the workings of biological systems through the tools of molecular proteomics," said Al Burlingame, MCP editor-in-chief and chair of the session.

The session, titled "Exciting Biological Insights Revealed by Proteomics," will be held at 3:15 p.m. on Monday, April 6. Read more about the speakers and their research in the following pages.

The speakers

Anne-Claude Gingras is a senior investigator at the Lunenfeld–Tenenbaum Research Institute in Toronto. Her group employs mass spectrometry and a proximity-dependent biotinylation technique called BioID to study protein–protein interaction and spatial localization.

Matthias Selbach is a professor at the Max Delbrück Center for Molecular Medicine in Germany. His group uses mass spectrometry–based quantitative proteomics to investigate proteome dynamics and cellular signaling on a global scale.


Anne-Claude Gingras


Matthias Selbach


Benjamin Garcia

Benjamin Garcia is a presidential professor of biochemistry and biophysics at the University of Pennsylvania. His group studies histone post-translational modifications and systems epigenetics using novel methodologies in mass spectrometry.

Saddiq Zahari (szahari@asbmb.org) is the manager of compliance for Molecular & Cellular Proteomics. Follow him on Twitter @saddiqzahari.

MOLECULAR & CELLULAR PROTEOMICS SESSION

Gingras studies proteomics' implications for research

By Adriana Bankston

When Anne-Claude Gingras was working on her Ph.D. in Nahum Sonenberg's lab at McGill University, she focused on the regulation of the protein synthesis machinery by phosphorylation. Her thesis described the role of the mechanistic target of rapamycin complex in phosphorylating a translational inhibitor.

Curious about the unexplored protein phosphatase components of phosphoregulation, Gingras realized that then-emerging proteomics technologies would be key to solving this puzzle. She moved to Seattle to study mass spectrometry with Ruedi Aebersold, and there she improved methods for protein–protein interaction detection. She started her own research group in late 2005.

Gingras now runs a signal transduction, systems biology and proteomics lab at the Lunenfeld–Tanenbaum Research Institute in Toronto. Her team works to improve experimental and computational approaches for interaction proteomics. Misregulation of protein phosphorylation is implicated in numerous diseases, including cancer and diabetes, so she applies these techniques to identify and understand new components of signaling pathways related to these pathologies. More recently, she began systematically applying the proximity-dependent biotinylation approach BioID to study the composition and organization of membraneless organelles and, ultimately, of human cells.

Her group's success in defining new biological complexes and pathways implicated in disease heavily relies on the contributions of talented students, fellows and research assistants with diverse expertise in biochemistry, cell biology, mass spectrometry and bioinformatics, as well as a large network of key scientific collaborators.

Her Ph.D. and postdoc advisors shaped not only her scientific directions but also how she interacts with other scientists, Gingras said. She is committed to sharing data, methods, reagents and protocols and to helping other scientists realize their objectives. Her motto, she said, is "Science works much faster when you help one another."

Anne-Claude Gingras

Tools for studying proteomics changes in organelles

To determine where proteins are in a cell, Anne-Claude Gingras' group uses mass spectrometry as a high-resolution discovery-based microscope. They employ a technique known as BioID that reports on the proximity of a protein to another used as bait.

Her student Christopher Go created 200 stable cell lines that each express one organelle marker as a probe and performed proximity-dependent biotinylation to identify the composition of each organelle. Research associate James Knight then developed computational tools to analyze and visualize the data. This revealed new addresses for many unexplored proteins and showed proteins that are at contact interfaces between organelles.

Using this work as a reference map, the Gingras lab is creating sensors to report on proteomic changes in an organelle after perturbations such as drug treatment, various growth conditions and genetic modulation with CRISPR. In profiling the surface of the lysosome, postdoctoral fellow Geoffrey Hesketh found a new pathway that activates the mechanistic target of rapamycin complex by extracellular protein through the process of macropinocytosis. This work has implications for disease in which macropinocytosis is activated, such as Ras-dependent cancers.

Adriana Bankston (abankston81@gmail.com) is a principal legislative analyst at the University of California's Office of Federal Governmental Relations in Washington, D.C. Follow her on Twitter @AdrianaBankston.

MOLECULAR & CELLULAR PROTEOMICS SESSION

Selbach seeks the science behind the magic

By Kerri Beth Boggs

When Matthias Selbach was a child, he loved science and magic tricks. His father gave him a book of science experiments that he could do with household items. He spent many afternoons testing tricks like the inverted water glass. With just an index card, he magically could keep a glass of water from spilling when he turned it upside down. The results fascinated him, but he wanted to understand what made the experiments work.

"For me, science was a bit like a magic trick," he said. "There is some truth behind it that may not be obvious at first. Once you understand the explanation, you can share it with others and excite them about it."

That curious instinct was the foundation for Selbach's future career. He earned his Ph.D. in a cell biology lab at the Max Planck Institute for Infection Biology in Berlin. However, he felt constricted by the classical, hypothesis-driven methods he used in his Ph.D. work. He wanted a system for asking broad scientific questions that he could answer on a global scale.

During his postdoc with Matthias Mann, Selbach immersed himself in the world of proteomics. In this field, he asked fundamental biological questions that he could address with mass spectrometry technology to yield big-picture data sets.

Selbach is now a professor at the Max Delbrück Center for Molecular Medicine in Berlin, where he and his team use proteomics to analyze protein synthesis and decay as well as protein–protein interactions. He is particularly interested in the interface between biology and mass spectrometry technology.

"This technology is like a Swiss Army knife for biomedical research," he said. "It's extremely versatile, and you can always find new ways to apply it to biological questions."

Matthias Selbach

Investigating the dynamic proteome

Proteins are the key actors in most biological processes, and Matthias Selbach's lab studies the dynamic proteome to interpret how genomic information yields specific phenotypes.

In his recent work, Selbach aimed to understand how bird flu affects the proteome of human cells. Although bird flu usually does not spread efficiently from human to human, specific strains could trigger pandemics. Scientists hypothesize that the 1918 H1N1 flu virus that killed millions of people worldwide originated in birds.

Selbach's team infected human lung cells with bird or human flu virus and analyzed changes in the proteome using mass spectrometry. They found that the viral matrix protein M1 was produced in higher quantities in the cells infected with human flu virus. The M1 protein is required for exporting newly synthesized viral RNA from the nucleus and assembling infectious progeny for release. Their findings provide a molecular basis for understanding the species barrier for flu virus.

The influenza virus study, recently published in the journal Nature Communications, is just one example of how Selbach uses proteomics to analyze the underlying causes of human disease. His lab also studies how disease-associated mutations and cell signaling events affect protein-protein interactions. They use high-throughput techniques to identify mechanisms linked to strong disease phenotypes. Selbach hopes these methods eventually will lead to earlier patient diagnosis and advances in personalized treatment.

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

Garcia uses mass spectrometry to unravel the human epigenome

By Nivedita Uday Hegdekar

When Benjamin Garcia was introduced to mass spectrometry as an undergrad in Carlito Lebrilla's lab at the University of California, Davis, he thought it was an "interesting and useful analytical technique," he said. Little did he guess the central role it would play throughout his research career.

"Lebrilla was an amazing mentor," Garcia said. "Despite my limited knowledge in analytical chemistry, he treated me like a… regular member of the group. I enjoyed the scientific discovery process and decided to apply to graduate school."

His timing could not have been better. In the early 2000s, the human genome just had been sequenced, and Garcia became interested in investigating the various proteins encoded by genes.

"Proteomics research was in its infancy, and MS opened up a lot of opportunities to explore the area," he said. His interest led him to pursue doctoral research with Don Hunt at the University of Virginia.

Under the guidance of Hunt, whom he described as "brilliant and visionary," Garcia studied tandem mass spectrometry of complex biological mixtures. By the time he earned his Ph.D. in chemistry in 2005, he was fully immersed in the field of proteomics.

"And after that, there was no looking back," he said with a laugh.

Garcia has established himself as a leader in mass spectrometry and proteomics. He serves on the editorial boards of several scientific journals, including **Molecular & Cellular Proteomics**, and has received numerous awards, including the Presidential Early Career Award for Scientists and Engineers.

Excited by the progress being made in large-scale omics, Garcia said he hopes scientists can apply their knowledge to eventually "reprogram a diseased epigenome" in various diseases.

Besides his regular responsibilities as a professor at the University of Pennsylvania, Garcia develops programs that support diversity and underrepresented minority scientists at the university. As the leader of a large and productive research group, he believes mentorship is a key aspect of scientific discovery.

"As a PI, the most enriching experience has been training and mentoring researchers from different walks of life," he said.

Benjamin Garcia

Advanced MS approaches elucidate 'diseased' epigenome

Benjamin Garcia's research group has developed novel methodologies for MS analysis of histones for application in post-translational modifications and systems epigenetics. Their most recent approach shows promise in the analysis of isolated histones from human clinical samples. Advantages over standard proteomics experiments include its quicker sample run time and improved quantification.

The group has used MS for high-throughput global profiling of histone post-translational modifications to better understand several cellular mechanisms and diseases. For example, they recently unraveled how recurrent loss-of-function alterations in polycomb-repressive complex 2, a histone-modifying complex, drive the formation of cancer cells in malignant peripheral nerve sheath tumors, an aggressive sarcoma.

The group's findings will help identify several epigenetic targets. The long-term goal is to treat diseases with histone-modifying enzymes or targeted small-molecule inhibitors.

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

Discover Common Bonds

Congratulations to the 2020 ASBMB Leadership Award winners!

Anita Corbett
Emory University
ASBMB Mid-Career Leadership Award

Natalie Jura
University of California, San Francisco
Early-Career Leadership Award

Thank you for your dedication to advancing the careers of women in biochemistry and molecular biology!

Learn more about the ASBMB Leadership Awards in the career resources section at asbmb.org.

Use the mic!

By Rajini Rao

The glowing introduction is done. There follows a smattering of anticipatory applause. You stride confidently to the podium and wave away the microphone, saying, "I'll speak loudly; can everyone hear me?" A few heads in the front row nod in assent, and you launch into your talk.

Don't be this person. Use the microphone.

You may be surprised to learn that up to 20% of the population has some degree of hearing loss, making it the third most common physical condition, after arthritis and heart disease, according to the Hearing Loss Association of America. Deafness gets progressively worse with age, affecting approximately one in three people between the ages of 65 and 74. More women, relative to men, find it hard to hear lower frequencies.

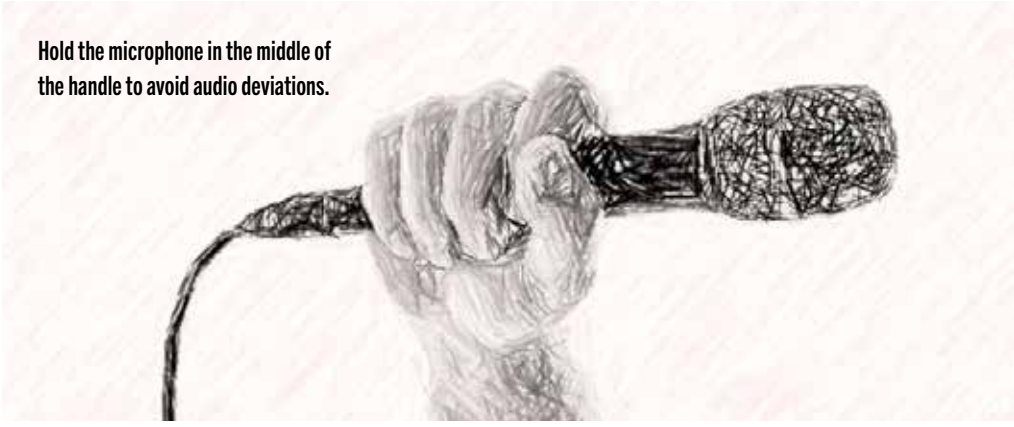
When you decline to use the microphone, you are projecting your ableism, not your voice, by assuming that able-bodied people are the norm. If not, you reason, why wouldn't they speak up? But people with disabilities often are exhausted from the constant need to self-advocate. Perhaps they don't wish to bring attention to themselves.

When your audience cannot hear you, they cannot fully participate. Rather than engage with your data or your ideas, they struggle to make out the words. When you use a microphone, this cognitive burden is gone, and now everyone can focus on your splendid research! It's a win-win for all.

Here are some tips on using the microphone effectively.

- Listen to your own voice projecting through the speakers, and adjust accordingly.
- When using a lapel mic, check what side of the screen you'll be standing on and wear the mic on the side you'll turn toward when you look at the screen; wear it high enough to accommodate your turned head, and remove chains or badge ribbons that may interfere.
- A hand-held mic must be kept at a steady distance from your mouth at all times.

RAJINI RAO



Hold the microphone in the middle of the handle to avoid audio deviations.

- A podium mic should be adjusted for your height.

Investing just a few minutes to set yourself up for an effective broadcast could make or break your success as a speaker.

Other practices that will ensure inclusion:

- Additional microphones for questions from the audience are good, but if there aren't any, be sure to repeat the questions using your microphone.
- The judicious use of labels and headings on your slides, large enough to be seen at the back of the room, adds another layer of comprehension.
- If you are a moderator or session chair, it's your job to ensure that multiple people aren't talking at the same time and making it harder to tune in on any one voice.

For more tips and firsthand insights on how to give a hearing-friendly and inclusive talk, watch "Like the mic," a short video distributed by Rooted in Rights and the Hearing Loss Association of America.

The next time you come up to the podium to give a talk, don't say, "I don't need the microphone." You may not, but someone in your audience does.

Rajini Rao (rrao@jhmi.edu) is professor of physiology at the Johns Hopkins University School of Medicine and chair of the ASBMB Today editorial advisory board. Follow her on Twitter @madamscientist.

What can your ombuds office do for you?

By Bill Sullivan

If you become embroiled in a conflict at an academic institution, you should know you are not alone. Whether the issue is between students, between faculty members, or between a student and a faculty member, if your campus has an ombuds office, trained professionals are available to help. The primary function of this office is to assist its visitors in determining how they might best address their concerns about conflict, allegations of mistreatment, and/or a lack of professionalism in an impartial, safe and confidential matter.

To learn more about ombuds, I spoke to Marly Bradley and Joe DiMicco, who have been ombudspersons at the Indiana University School of Medicine for two years and three years, respectively. In that time, more than 300 people have sought their help in dealing with a wide array of concerns. Our conversation has been edited and condensed for ASBMB Today.

What does an ombuds office do?

The first and most important thing we do is listen, listen, listen. The ombuds may serve as a sounding board. We try to help our visitors identify and choose potential actions they might take to address their issues. The concerns that bring visitors to the office might include perceived unfairness in grading or evaluation, a toxic or uncomfortable work environment, a difficult relationship with a particular individual — in fact, if it's a conflict you can imagine, we've probably heard some version of it in the confidence of our office. The ombuds often can identify campus resources for resolving or addressing a problematic issue. We also can serve as mediators or engage in shuttle diplomacy between parties in conflict.

While our first function is to assist the visitor, we also can bring systemic problems to the attention of administration and leadership. Examples include widespread dissatisfaction in a particular academic unit or department, a flawed administrative process leading to simmering resentment and/or dysfunction, or a gap in existing policies and procedures that needs attention. Often, these issues are brought to light only because of the unique position and features of our office, most notably confidentiality. We meet regularly with the dean and can reach out to other offices at any time. However, we share information only if we have the visitor's permission.

Who does the ombuds office serve on campus?

Although originally formed primarily to address the issue of medical student mistreatment, the office serves all teachers (faculty) and learners (medical students, residents, fellows, grad students and postdocs) on all nine campuses across the state. Our office is on the Indianapolis campus, but we visit the other campuses regularly. While we prefer to meet face to face, we are open to speaking by phone, Zoom, Skype or whatever else is mutually convenient.

When should a person talk to an ombudsperson?

Honestly, there is never a wrong time to speak with us. We are an excellent and noncommittal point of first contact. If a visitor needs help from another office, we gladly will refer them or help set up a meeting. Nothing is hurt by reaching out to us first, as we are a confidential resource. If someone is struggling with a perceived lapse in professionalism, mistreatment or unfairness, if they need to talk and are not sure where to go, we are always happy to help however we can. If a person is unsure who to talk to, or whether they want to talk at all, we are completely confidential and available. After clarifying their issue and situation in a meeting with us, many visitors decide to go no further. In that case, no record of that meeting exists. We keep no formal records with identifying information, and we shred any notes we take during a meeting at the close of our interaction.

Are there things people should not expect from their ombuds office?

A visitor should not expect a personal advocate, although we can and do advocate for fairness. A visitor should not expect us to fix their problems; our goal is to help visitors help themselves.

What information do you consider confidential? Is there anything that is not kept confidential?

Our most important operating principle is confidentiality. Everything is confidential. We will not disclose the details of our meeting, or even the fact that we have met, unless the visitor gives us explicit permission to do so. We often discuss cases

between ourselves (again, with the visitor's permission), as the confidentiality is held within our office.

There are a few exceptions to this absolute confidentiality. If we see clear evidence that the visitor or someone else is in danger of physical harm, Indiana University requires that we report this to an appropriate office or authority. Also, the university requires that we report clear evidence of sexual harassment or of discrimination on the basis of race, religion, nationality, gender or sexual preference.

What is the history behind the ombuds office?

The term ombuds derives from the Swedish word for advocate, and many people are familiar with ombudspersons in settings where they would serve in this capacity (e.g., student ombuds in an undergraduate college or university setting or patient ombuds in many hospitals). However, ours is properly termed an organizational ombuds office, meaning that one of our operating principles is neutrality. That is, we remain neutral in conflicts between individuals while working to help our visitors to resolve, defuse or mitigate these conflicts. (We can and do step out of this neutral stance to advocate for justice and fair treatment if the situation so dictates.)

Our office was born out of the need for a confidential resource for conflict resolution and support, and to encourage the reporting of mistreatment or breaches of professionalism. From the beginning, the dean tasked the office with being available and responsive to teachers and learners alike.

What inspired you to become an ombudsperson?

Marly Bradley: It was a natural fit. I've always been inclined to serve in areas of advocacy, and while ours is a neutral office, we do advocate for fairness. I chaired the university's teacher–learner advocacy committee for almost 10 years, and this seemed like an ideal opportunity to continue my service in an expanded role. Our two-person office was an added draw. I have a clinical background, and my partner ombuds has a research background. Our experiences over a combined 60 years provide unique insight into the issues that most of our visitors face.

Joe DiMicco: After I retired from my 30-plus years on the faculty at the end of 2011, I missed my connections with students and my former colleagues. In 2016, the university approached me about the plan to start an ombuds office at the school of medicine and invited me to apply. The administration thought that my many years of experience would afford valuable insight into the history and culture of the institution and that my position as an emeritus professor would afford me freedom and independence. I originally planned to stay for five years, but the sense of purpose I achieve in working with visitors and my terrific working relationship with Marly Bradley have me thinking that I'll likely stick around a bit longer.

To learn more, check out the International Ombudsman Association website, ombudsassociation.org.

Bill Sullivan (wjsulliv@iu.edu) is a professor at Indiana University School of Medicine and the author of several books. He is a member of the ASBMB Today editorial advisory board. Follow him on Twitter @wjsullivan.

OMBUDSPERSON AT THE ASBMB ANNUAL MEETING

The American Society for Biochemistry and Molecular Biology and the other host societies of the Experimental Biology conference have appointed an ombudsperson to serve as an independent, neutral off-the-record/confidential resource for meeting attendees.

EB prohibits all forms of discrimination and harassment and has enlisted the ombudsperson to support the conference's code of conduct and anti-harassment policy.

The ombudsperson will assist individuals and, without breaching confidentiality, inform the EB management team of concerns raised at the conference and insights or observations about systemic issues. The ombudsperson will be available by phone or email April 2–8.

Questions? Email management@experimentalbiology.org

CLASSIFIEDS

Assistant Professor of Biochemistry
West Virginia University

The Division of Plant and Soil Sciences at West Virginia University invites applications for a full-time, 9-month, tenure-track position of Assistant Professor of Biochemistry (50% teaching, 50% research). West Virginia University is the state's flagship land grant institution, currently enrolls nearly 32,000 students, and is an R1 research university as defined by the Carnegie Foundation. The Davis College of Agriculture, Natural Resources, and Design has 110 faculty and 150 full-time staff, enrolls 1,700 undergraduate and 280 graduate students across a full spectrum of degree programs (28) housed in five academic divisions. The Division of Plant and Soil Sciences is a diverse unit consisting of about 25 faculty and equivalent positions in agronomy, soil science, entomology, genetics, horticulture, environmental microbiology, and plant pathology. The Division houses four undergraduate academic majors and partners with other academic units to offer an intercollegiate major in Biochemistry. The Division also offers Masters and PhD degrees. The position is located on West Virginia University's Evansdale campus in Morgantown, West Virginia. The successful applicant will be housed in a new, state-of-the-art facility and have access to a competitive start-up package.

https://careers.asbmb.org/job/assistant-professor-of-biochemistry/53049193/

Teaching Assistant Professor
West Virginia University

The Department of Biochemistry at West Virginia University, Morgantown, WV invites applications for a faculty position of Teaching Assistant Professor, Scientist Educator Track. This fulltime, non–tenure track position will have a major commitment to teaching medical, dental, and other health sciences students in the fields of biochemistry, molecular biology, and cell biology. In addition, the candidate will contribute to course and programmatic administration, educational innovation, and scholarship in the Department.

https://careers.asbmb.org/job/teaching-assistant-professor/53048278/

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

Upcoming ASBMB events and deadlines

MARCH

Endometriosis Awareness Month

13 Deadline for advance registration for 2020 ASBMB Annual Meeting

16 Deadline for ASBMB Networking Event Proposals

APRIL

World Parkinson's Awareness Month

4–7 2020 ASBMB Annual Meeting held in conjunction with Experimental Biology

25 **World Malaria Day**

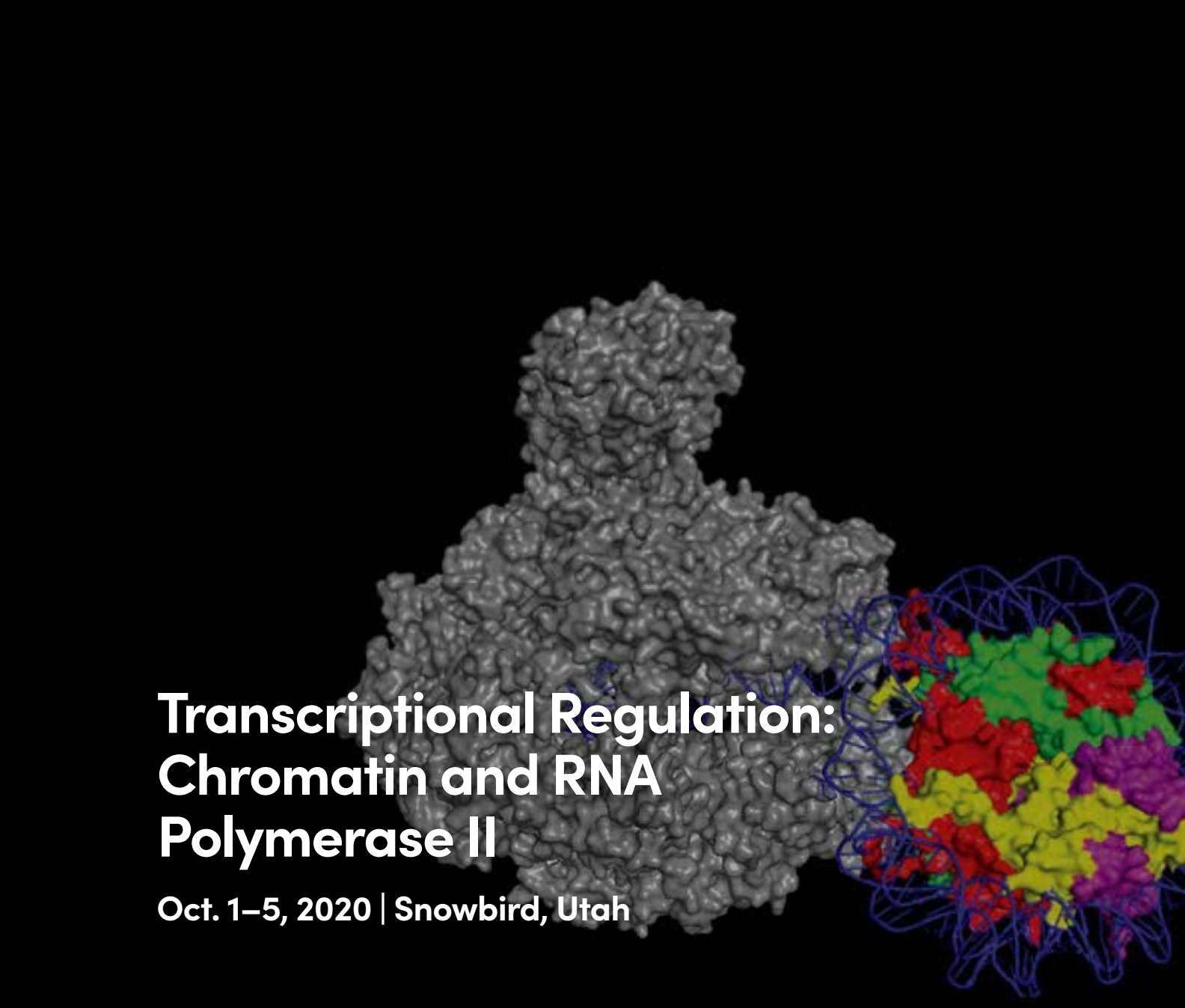
MAY

1 Deadline for Promoting Research Opportunities for Latin American Biochemists (PROLAB) applications

12–18 **National Women"s Health Week**

20 **World Autoimmune Inflammatory Arthritis Day**

ASBMB



Transcriptional Regulation: Chromatin and RNA Polymerase II

Oct. 1–5, 2020 | Snowbird, Utah

Submit your abstract by July 15.

ASBMB