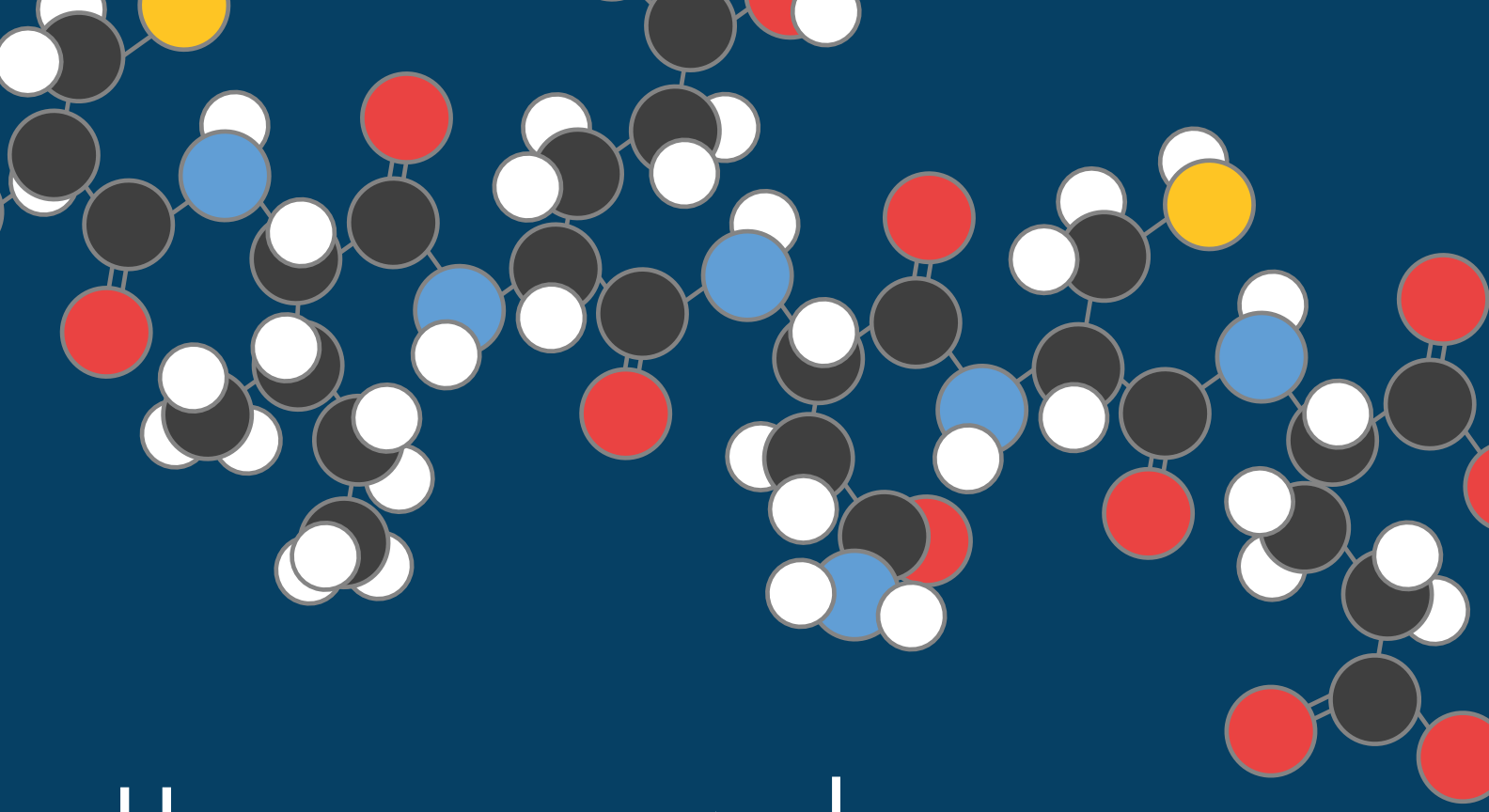
Vol. 18 / No. 10 / November 2019

ASBMB TODAY

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

Giant gene thieves



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ASBMB
American Society for Biochemistry and Molecular Biology

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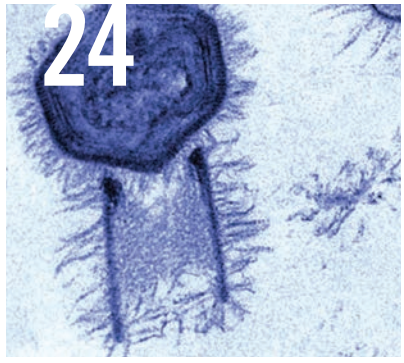

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ASBMB
American Society for Biochemistry and Molecular Biology
www.asbmb.org/asbmbtoday
PRINT ISSN 2372-0409

It's about time

By Comfort Dorn

Our concept of time is dictated, at least in part, by how we spend our days.

For those who work in academia, the year is shaped by the cycle of semesters and vacations that make up a school calendar, and days might include set hours for teaching, study, writing and research.

When I was home taking care of infant children, I lived very much in the moment, and many moments dragged interminably. My sleep-deprived brain seldom could look beyond the next feeding or diaper change. Toilet training and teething were processes that took months but seemed to go on for years. Yet when my children went off to elementary school, it had all passed in a flash.

For a couple of years, I had a job as an administrator in an Episcopal church. Many of my tasks, such as newsletters and bulletins, had weekly or monthly deadlines, but hovering overhead was the great cycle of the liturgical year with its ancient rituals. The feast of Pentecost might fall in May, but January wasn't too early to start planning.

When I worked at a daily newspaper, we had a 24-hour cycle that reset every night as soon as the next day's issue landed in the press room. We all liked working on long-term projects, but every day we had to feed the beast — and that was the schedule that drove us. The advent of 24-hour online news only made the pace more frantic.

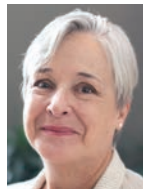
As managing editor of this magazine, I have gone back to looking many months into the future. We spend a fair bit of time planning our feature stories and special issues, and we also need to keep in mind the calendar of the American Society for Biochemistry and Molecular Biology — the hub of which is the annual meeting.

Here at ASBMB central, we constantly think and talk about the society's biggest event; the next annual meeting is forever looming, even the day after the last one ends. We aim to include annual meeting information in almost every issue of ASBMB Today — because it's that important.

This month, we profile the 12 fascinating people who have been named recipients of the ASBMB's annual awards and will speak at the 2020 annual meeting in San Diego. In the past, we've profiled award winners right before the meeting; here, we're trying something new. The 2020 meeting may be five months away, but once you've read about these researchers — their lives and their science — I think you'll want to register right away.

Depending on the pace of your life right now, those five months could just fly by.

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



Member Update

By ASBMB Today staff

Gingras, Ueffing win HUPO awards


Gingras


Ueffing

Anne-Claude Gingras and **Marius Ueffing** were among those presented with awards at the Human Proteome Organization's annual meeting in Adelaide, Australia, in September.

Gingras, a principal investigator at the Lunenfeld–Tanenbaum Research Institute at Mount Sinai Hospital in Toronto, a professor at the University of Toronto and a deputy editor of the journal Molecular & Cellular Proteomics, was one of two scientists recognized with the HUPO Discovery in Proteomics Award. The award highlights single discoveries in the field of proteomics and honored Gingras' development of tools and methods for interactomics. Gingras is known for systems biology research focused on signal transduction networks, with applications in diseases from cancer to diabetes.

Ueffing, a professor at the University of Tuebingen in Germany, received the HUPO Clinical and Translational Proteomics Award. His research has demonstrated that Parkinson's disease risk factor LRRK2 contributes to the disease by perturbing vesicular trafficking in neurons. His team also has studied retinal degeneration and genetic ciliopathies, contributing to new diagnostic approaches for these diseases.

Stubbe honored with Priestly Medal


Stubbe

JoAnne Stubbe, Novartis professor emerita of chemistry and biology at the Massachusetts Institute of Technology, has been named the 2020 Priestly Medal winner by the American Chemical Society.

The award, the society's highest honor, recognizes lifetime achievement. It is named for Joseph Priestly, the chemist who discovered oxygen and several other gases.

Stubbe has spent her career investigating the mechanisms of ribonucleotide reductases — enzymes that play an essential role in DNA replication and repair. She is being recognized for "pioneering studies of enzymatic radical chemistry, long-range proton-coupled electron transfer, DNA cleavage by anti-cancer drugs, enzymatic formation of polyesters and purine biosynthesis," according to the ACS.

A member of the National Academy of Sciences since 1992, Stubbe has received numerous accolades for her work, including the Humboldt Research Award, the Welch Award and the National Medal of Science.

Trejo named assistant vice chancellor


Trejo

Joann Trejo, a professor of pharmacology at the University of California, San Diego, School of Medicine, was appointed assistant vice chancellor for health sciences faculty affairs in June.

Trejo, who has been on the faculty at UCSD since 2008, studies the role of G protein–coupled receptor signaling in vascular inflammation and cancer.

She has served on the council of the American Society for Biochemistry and Molecular Biology and the Board of Scientific Advisors for the National Cancer Institute. Her work on equity and inclusion was recognized in 2016 with a UC San Diego Inclusive Excellence Award.

As vice chancellor, Trejo is responsible for developing strategies for enhancing success, recruitment and retention of an engaged diverse faculty and for comprehensive faculty development at UCSD.

Justement elected FASEB president


Justement

Louis Justement, a professor of microbiology at the University of Alabama at Birmingham, has been elected president of the Federation of American Societies for Experimental Biology.

Justement served as chair of the FASEB Science Policy Committee's Training and Career Opportunities Subcommittee from 2008 to 2018 and FASEB vice president for science policy from 2018 to 2019.

At UAB, Justement's research involves analyzing the molecular and functional roles of the adaptor protein HSH2 and the transmembrane receptor TLT2 as well as the virulence factors produced by Mycobacterium tuber-

culosis. He is also the director of the university's Graduate Biomedical Sciences Immunology Graduate Theme and the Undergraduate Immunology Program.

He will become president in July 2020 after serving for a year as president-elect.

Maquat joins Expansion Therapeutics board


Maquat

Lynne Maquat, J. Lowell Orbison endowed chair and professor in the biochemistry and biophysics department at the University of Rochester School of Medicine, joined the scientific advisory board of the biotech startup company Expansion Therapeutics in June.

Maquat, who directs Rochester's Center for RNA Biology, is best known for her research on nonsense-mediated mRNA decay. She is a fellow of the National Academy of Sciences, the National Academy of Medicine, and the American Academy of Arts and Sciences as well as a past recipient of both the American Society for Biochemistry and Molecular Biology's William C. Rose Award and the Federation of American Societies for Experimental Biology's Excellence in Science Award.

Expansion Therapeutics develops small molecules that bind RNA based on its tertiary structure. The company's goal is to use such molecules to treat genetic disorders caused by nucleotide repeat expansions, such as the muscle-wasting disease myotonic dystrophy.

Showalter promoted to full professor


Showalter

Scott Showalter, a structural biologist at Pennsylvania State University, has been promoted from associate to full professor.

Showalter has been at Penn State since 2008. Prior to starting as an assistant professor, he was a postdoctoral fellow at Florida State University and the National High Magnetic Field Laboratory.

Showalter's group uses biophysical techniques such as calorimetry and nuclear magnetic resonance spectroscopy to investigate protein structures and interactions, with particular emphasis on RNA polymerase and RNA-binding proteins.

In his 11 years as a junior professor at Penn State, Showalter has received numerous awards and grants, including Agilent's new investigator award in NMR spectroscopy and a National Science Foundation CAREER award. He as an editorial board member for the Journal of Biological Chemistry.

Benning named distinguished professor


Benning

Christoph Benning, director of the Michigan State University Department of Energy Plant Research Laboratory, was promoted in July to university distinguished professor, MSU's highest honor for its professors.

Benning studies the biosynthesis and dynamics of lipids in plants, particularly in the chloroplast. His group uses biochemical and synthetic biology approaches to understand how the thylakoid, a subsection of the chloroplast, maintains a specialized lipid membrane in which the proteins responsible for photosynthesis are embedded. The group also studies lipid-derived plant metabolites, such as terpenoids.

Born and raised in Germany, Benning earned his Ph.D. at MSU in 1991 and returned there as a professor after a stint as an independent young investigator at a German research institute. He became the director of the MSU–DOE plant research lab in 2015.

Beggs wins Lasker essay prize


Beggs

Grace Beggs, a graduate student in the biochemistry department at Duke University, was one of three winners of the Lasker Essay Contest this year.

In her essay titled "Game on: Smartphone technology for science education," Beggs argues in favor of an augmented-reality smartphone app to promote molecular biology education through play. You can read her essay at the Lasker Foundation's website.

In the Brennan lab at Duke, Beggs, a fifth-year Ph.D. candidate, works on multidrug binding proteins involved in antibiotic resistance in strains of public-health importance, such as Neisseria gonorrheae and E. coli.

University of Alberta honors Kay


Kay

Cyril M. Kay, professor emeritus of biochemistry at the University of Alberta, received an honorary doctorate of science at the university's June convocation.

Kay, who has served on the faculty of the University of Alberta since 1958 and has belonged to the American Society for Biochemistry and Molecular Biology since 1961, is best known for his studies of protein structure and function. Those investigations, 28 of which Kay published in the Journal of Biological Chemistry over the years, covered

a wide biochemical range, including conformational changes in myosin proteins; functional changes induced by post-translational modifications; calcium-regulated interaction in the endoplasmic reticulum; and proteins with antifreeze, antimicrobial and lipid-binding characteristics.

Kay was the founding co-director of the Medical Research Council of Canada Group in Protein Structure and Function, which became internationally respected in the protein world. For 10 years he was the vice president for research of the Alberta Cancer Board. He is a fellow of the Royal Society of Canada and an officer of the Order of Canada.

Hunter delivers IUBMB Jubilee lecture


Hunter

Tony Hunter was the International Union of Biochemistry and Molecular Biology's Jubilee lecturer at the IUBMB September meeting on inhibitors of protein kinases in Warsaw, Poland.

IUBMB Jubilee awards support travel to small symposia by prominent scientists to deliver plenary lectures.

Hunter, a professor at the Salk Institute and the University of California, San Diego, studies cellular growth control. He is known best for the discovery in the late 1970s of tyrosine kinases, which started the study of those proteins. His work, which uncovered a new type of protein regulation and enabled development of a new class of cancer drugs, has been recognized widely with prizes and awards, most recently the 2018 Tang Prize, for which he'll give an award lecture at the Experimental Biology meeting in April in San Diego.

Barbour moves to UNC Chapel Hill


Barbour

Suzanne Barbour, who until recently was a professor of biochemistry and biophysics and the dean of the graduate school at the University of Georgia, moved to the University of North Carolina at Chapel Hill in September to become the dean of that university's graduate school.

Barbour, whose research background is in phospholipase signaling, had overseen UGA's hundreds of graduate programs since 2015. She has been an active member of the American Society for Biochemistry and Molecular Biology's Education and Professional Development Committee for more than a decade and recently was elected to the society's governing council. She also serves as a coach for the Academy for Future Science Faculty.

IN MEMORIAM

Raymond W. Ruddon Jr.

Raymond W. Ruddon Jr., a professor emeritus of pharmacology at the University of Michigan, died April 26. He was 82.

Ruddon's research helped determine a mechanism of cancer-cell resistance for the anticancer drug nitrogen mustard and characterize the biosynthesis and secretion of the cancer diagnostic marker human chorionic gonadotropin, or hCG. His lab was the first to determine the intracellular folding pathways of hCG.

Born in Detroit in 1936, Ruddon earned a bachelor's degree from the University of Detroit in 1958 and then a Ph.D. in 1964 and M.D. in 1967 from the University of Michigan. He joined the University of Michigan faculty as an instructor in 1964 and was named a professor in 1974.

Ruddon interrupted his academic career twice, first to work at the National Institutes of Health's National Cancer Institute for five years and later to serve for seven years as a corporate vice president at Johnson & Johnson. He was also a professor at the University of Nebraska for seven years. At Michigan, he chaired the pharmacology department, was associate director of the cancer center and served as senior associate dean at the medical school. He authored more than 100 scientific papers and five books, including the widely used oncology text, Cancer Biology.

For many years, Ruddon kept a foot mannequin wearing a white sock on his desk, a reminder of advice he received and shared in response to researchers asking what experiments they should do next. The answer: "Whatever snaps your socks."

IN MEMORIAM

Edward J. Massaro

Edward J. Massaro, a toxicologist, died June 1, a few days before his 85th birthday, in Cary, North Carolina.

Massaro, a native of Passaic, New Jersey, studied mercury poisoning in fish, wrote textbooks on biochemistry and toxicology, and according to his family was "the coolest biochemistry professor at the University of Buffalo" when he taught there from 1968 to 1978 at what is now the Jacobs School of Medicine and Biomedical Sciences. The Buffalo News reports that during that time, he spoke out against industrial ash and mercury pollution and participated in the first observation of Earth Day.

Later in his career, Massaro worked at Mason Research Institute in Worcester, Massachussetts; the department of veterinary sciences at Pennsylvania State University, where he studied the effects of micronutrient deficiencies and lead exposure; and the Environmental Protection Agency's National Health and Environmental Effects Research Lab in North Carolina, where as a senior scientist he researched teratogenic compounds. He continued to conduct and publish on toxicology research until he retired in 2015.

Massaro was elected a fellow of the American Association for the Advancement of Science in 1986. In 1992, he received the EPA's Scientific and Technological Achievement Award.

He is survived by his wife of 41 years, Arlene Massaro, M.D., and their four children, 11 grandchildren and four great-grandchildren.

Seymour S. Cohen

The American Society for Biochemistry and Molecular Biology recently learned that **Seymour S. Cohen** of Woods Hole, Massachusetts, died in December. He was 101.

Cohen, a New York native, earned his Ph.D. in biochemistry from Columbia University in 1941 and studied virology both for the U.S. Army during World War II, when he helped to develop a new vaccine for typhus, and later when he returned to academia. He held faculty positions at a number of institutions, including the University of Pennsylvania, the University of Colorado Medical School in Denver and the State University of New York at Stony Brook.

Cohen won the Eli Lilly Prize in 1951 for his work on bacteriophage biochemistry and for describing how radiolabeled viruses spread between cells. He was involved in the development of early chemotherapeutic compounds, including 5-fluorouracil, which is still in use to prevent DNA replication in skin cancer; for that development, Cohen was named a lifetime professor of the American Cancer Society. Among his many other honors were membership in the American Academy of Arts and Sciences and the National Academy of Sciences. He is said to have been nominated for the Nobel Prize several times.

At age 98, he was elected to serve as a member of a National Academies panel that put together a national strategy for the elimination of hepatitis B and C. That report was published in 2017.

Cohen is survived by his two children and their spouses, five grandchildren, and five great-grandchildren.

NEW MEMBERS

Paulina Alatriste, University of Kentucky

Scott Aoki, Indiana University School of Medicine

Jessie Arneson, Washington State University

Zerubabbel Asfaw, Franklin and Marshall College

Stephan Azatian, Texas Tech University

Arun Balasubramaniam, National Central University

Katherine Bearden, University of Florida

Ian Belger, Wayne State University

Alana Belkevich, State University of New York Upstate Medical University

Sandrine Belouzard, Centre national de la recherche scientifique

Elayne Benson, Presbyterian College

Gifty Blankson, Maryville University

Rider Bodkin, Presbyterian College

Kayla Bramlett, Presbyterian College

Brandon Buck, Florida State University

Amber Buhagiar, Yale University

Amatullah Burhani, Wayne State University

Tannor Byrd, Presbyterian College

Albert Campbell, Kennesaw State University

Elizabeth Cervantes, Texas Wesleyan University

Aaron Chamberlain, Object Pharma, Inc.

Edmond Chan, Queens University

Guanqun Gavin Chen, University of Alberta

Rong Chen, Wake Forest School of Medicine

Jennifer Chesko, Genesis Biotechnology Group: Medical Diagnostic Laboratories

Eva Chi, University of New Mexico

Lorencia Chigweshe, Wesleyan University

Ekram Ahmed Chowdhury, Texas Tech University Health Sciences Center

Scott Clark, Western Texas College

Evan Collins, Yale University

Mae Covacevich, Texas Wesleyan University

Jaclyn Daigle, Thermofisher Scientific

Elizabeth Duchow, Univeristy of Wisconsin–Madison

Amanda Dwikarina, University of Missouri

Christabel Ebuzoeme, Texas Southern University

Inayah Entzminger, City University of New York Graduate Center

Maria A Feliz Norberto, Lehman College

Mona Fendereski, University of Southern Mississippi

Daniel Ginsburg, Immaculata University

Victoria Godieva, Florida International University

Stephen Gonzalez, California State University, Fullerton

Christian Goossen, Rochester Institute of Technology

Alla Grishok, Boston University School of Medicine

Vaibhavi Gujar, Southern Illinois University Carbondale

Chandan Gurung, University of Southern Mississippi

Nesma Hassan, Cairo University

Tyler Higginbotham, Virginia Tech

Richard Holz, Colorado School of Mines

Liliana Jaraczewski, Presbyterian College

Kayla Karnes, Texas Wesleyan University

Andy Karplus, Oregon State University

Anahita Keer, Texas Wesleyan University

Kofi Khamit-Kush, Clark Atlanta University

Moon Kim, Inha University

Kobie Kirven, Presbyterian College

Crystal Kotan, University of Nevada, Las Vegas

Neetij Krishnan, St. Olaf College

Andrew Kyzer, Presbyterian College

Jamila Labee, Presbyterian College

Madison Ladines, Presbyterian College

Andrew Lane, University of Kentucky

Miranda Leek, Oregon State University

Javier Leo, University of New Mexico

Jonathan Licht, University of Florida

Mlana Lore, Eckerd College

Martin Martin, University of California, Los Angeles School of Medicine

Bryan Mata, Texas Tech University

Timothy Meredith, Pennsylvania State University

Robin Mockett, University of South Alabama

Efehi Nehikhare, Lanzhou University of Technology, China

Angelo Nicolaci, H. Lee Moffitt Cancer Center & Research Institute

Holiness Olasore, University of Lagos

Jesus Olmos, Texas Wesleyan University

Gabriela Ortiz-Soto, Universidad Central del Caribe School of Medicine

Joseph Osinubi, University of Delaware

Jason Pajski, University of Mount Olive

Sophia Pantazelos, Providence College

John Pascal, Université de Montréal

Sophia Pirinea, Providence College

Nava Poudyal, Clemson University

Tanadje' Price, Presbyterian College

Jonathan Pruneda, Oregon Health & Science University

Pablo Ranea Robles, Icahn School of Medicine at Mount Sinai

Hernandez Ricardo, Presbyterian College

Prateeksha Rout, Rutgers University–New Brunswick

Kristian Ruiz, Houston Baptist University

Nolan Ryan, University of Wisconsin–Parkside

Chase Sanders, University of Kentucky

Russell Sapio, Graduate School of Biomedical Sciences, Rowan University

Sarah Seeherman, Lake Erie College of Osteopathic Medicine

Theophilus Tandoh, Mississippi College

Xuemei Tong, Shanghai Jiao Tong University School of Medicine

Tina Tootle, University of Iowa

Gea-Ny Tseng, Virginia Commonwealth University

Jennifer Tuokkola, Ohio State University

Tomas Vaisar, University of Washington

Zhiyong Wang, Carnegie Institution for Science

Blake West, Presbyterian College

Shay Wigginton, GENEWIZ

Hong Wu, St Jude Children's Research Hospital

Martin Wühr, Princeton University

Shouling Xu, Carnegie Institution at Stanford

Valentin Yakubenko, East Tennessee State University, Quillen College of Medicine

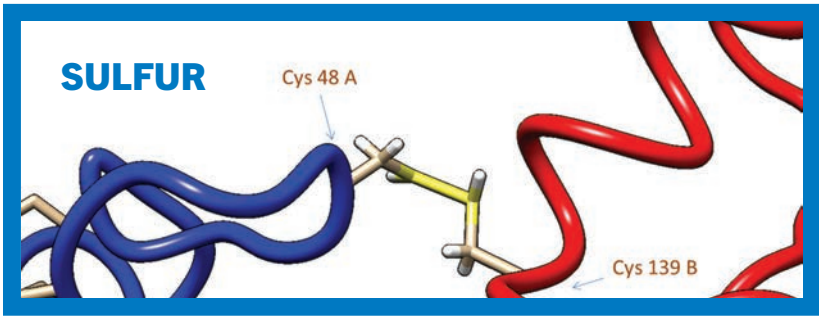
SEND US YOUR NEWS

Have you recently been promoted or honored? Do you have good news to share with fellow ASBMB members? Email it to us at asbmbtoday@asbmb.org — and don't forget to include a photo!

For November, it's that smell of sulfur

By Quira Zeidan

We mark the 150th anniversary of Dimitri Mendeleev's periodic table of chemical elements this year by highlighting elements with fundamental roles in biochemistry and molecular biology. So far, we've covered hydrogen, iron, sodium, potassium, chlorine, copper, calcium, phosphorus, carbon, nitrogen, oxygen, manganese and magnesium.



MIKEJL921/WIKIMEDIA COMMON

Depiction of the intermolecular disulfide bridge between cysteine residues 48 A and 139 B on opposite chains of the human phenylethanolamine N-methyltransferase dimer.

In November, families all over the U.S. celebrate Thanksgiving by eating roasted turkey. During digestion, the proteins in that turkey (and other foods) break down into smaller amino acids that are used by the body's cells to synthesize its own proteins.

Methionine and cysteine — two of the 20 amino acids normally present in the proteins we consume — are our major dietary source of the element sulfur. The organic compound methysulfonylmethane, or MSM, present in vegetables, legumes, herbs and animal products, is another important natural precursor of sulfur.

With chemical symbol S and atomic number 16, sulfur is a reactive nonmetallic element with oxidation states ranging from -2 to +6. Depending on the environment, sulfur compounds may accept or donate electrons. Sulfur reacts with almost all other elements — except for noble gases — and commonly forms polycationic compounds.

Sulfur is created inside massive stars as the product of the nuclear fusion between silicon and helium. By mass, sulfur is the 10th most common element in the universe — present even in many types of meteorites — and the fifth most common element in the Earth. Natural events such as volcanic eruptions, hot spring vents and tidal flats emit abundant sulfur that later accumulates either as pure elemental crystals or as sulfate and sulfide minerals and rocks.

In most ecosystems, the weathering of ore minerals releases stored sulfur that reacts with the oxygen in the air to produce sulfate particles. Sulfate is assimilated by plants and microorganisms and converted into essential biomolecules such as vitamins and proteins, subsequently moving up the food chain. Sulfur is released back onto the land either by decomposition of organic matter or in rainfall. Terrestrial sulfur drains into water systems, where it cycles through marine communities or deposits in deep ocean sediments.

Some anaerobic bacteria in human gut flora can oxidize organic compounds or molecular hydrogen as an energy source and use sulfate instead of oxygen as the final electron acceptor during respiration. These sulfate-reducing prokaryotes often produce hydrogen sulfide, which causes intestinal gases and flatulence in humans.

In stark contrast, some microorganisms, such as green and purple sulfur bacteria, can use reduced sulfur compounds, and even elemental sulfur, as an energy source to produce sugars by chemosynthesis, using oxygen as the final electron acceptor. Giant tube worms that live on the Pacific Ocean floor rely on these bacteria to feed on seawater sulfide.

Plants and bacteria use environmental sulfate for the synthesis of the nonessential amino acid cysteine. Mammals also can synthesize cysteine from the glycolytic intermediate 3-phosphoglycerate, but they use methionine — an essential amino acid that must be ingested — as the supplier of the sulfur atom. Neighboring cysteine residues in peptide chains can form covalent disulfide bonds that contribute to protein flexibility and control protein structure and assembly.

Quira Zeidan (qzeidan@asbmb.org) is the ASBMB's education and public outreach coordinator. Follow her on Twitter @quirazeidan.

Bacterial invasion may explain recurrent urinary tract infections

By Courtney Chandler

Urinary tract infections, better known as UTIs, are the most common bacterial infection in women of all ages, and an estimated 50% of women will experience a UTI at least once during their lives.

Postmenopausal women are especially susceptible and many suffer from repeated infections. Recent research suggests that this recurrence may partially be explained by where the infecting bacteria go — namely, into the walls of the bladder.

Kim Orth, a professor at the University of Texas Southwestern Medical Center, and Nicole DeNisco, an assistant professor at the University of Texas, Dallas, along with colleagues at UT Southwestern found bacteria in bladder-wall biopsy samples of postmenopausal women. The presence of these bacteria within the tissue seemed to initiate local adaptive immune responses, which may contribute to the pathology of recurrent UTIs, or RUTIs.

Orth and DeNisco partnered with urologist Philippe Zimmern to study the host-pathogen interactions involved in RUTI using urine from postmenopausal women as well as the bladder-wall samples. They expected to find bacterial species associated with bladder and urinary tract infections, such as Escherichia coli. Instead, they saw that more diverse species of bacteria were able to invade the bladder's surface, which is called the urothelium.

"These results were very surprising as we expected to see E. coli associated with all of the patients," Orth said. "Instead, we found a number of different types of bacteria that correlated with diseased tissue."

When they examined and analyzed the tissue further, the research team found both swelling and an increased presence of antibody-secreting B-cell lymphocytes, a key component of the adaptive immune response; normally, in the absence of infection, antibody-secreting

B-cell lymphocytes are at low levels. Scientists long have thought that this response may contribute to RUTI; these findings support that theory and provide better insight into the disease mechanism.

Women with RUTIs spend billions of dollars annually on medical care, and the pain and discomfort associated with the infection can lead to reduced quality of life. Antibiotics are the standard prescribed treatment, but doctors are seeing a rise in antibiotic-resistant RUTIs, which are especially difficult to treat. Yet research on the underlying cause can be challenging. Most studies are done on mice, which have limited lifespans and don't accurately represent postmenopausal women. Orth, DeNisco and Zimmern's study of postmenopausal patient samples is, therefore, important.

"Solid data about what causes the disease from patients that have RUTI, rather than making assumptions, is in itself a major breakthrough," Orth said.

Future research can build on Orth, DeNisco and Zimmern's findings to learn how different treatments affect RUTIs both for patient outcome and at the molecular level at the site of infection itself. They have planned future studies on how to remove the invading bacteria from the bladder and target the local immune response effectively. The results could help guide medical treatment plans to reduce the recurrence of UTIs in postmenopausal women.

Courtney Chandler (courtneyec19@gmail.com) is a postdoctoral researcher at Johns Hopkins University and a careers columnist for the ASBMB. Follow her on Twitter @CourtneyEChan.

Snug as a bug in the mud

How anaerobic bacteria make unsaturated fatty acids

By Martin J. Spiering

Lipids are ubiquitous molecules, serving as structural building blocks for membranes, messengers in cell signaling or compounds for energy storage. Their versatility relies in part on the presence of one or more double bonds in the long lipid carbon chains. The more double bonds a lipid has, the more unsaturated it is; and the more unsaturated lipids there are in a membrane, the more flexible the membrane tends to be.

To make unsaturated fatty acids, cells growing in the presence of molecular oxygen have an advantage; they can use this powerful oxidant to insert a double bond into a fatty acid chain via a dehydrogenation reaction. But what about organisms that cannot grow in the presence of molecular oxygen?

This question piqued the curiosity of Harvard professor Konrad Bloch, who had a long-standing interest in oxygen as a biosynthetic reagent and knew that molecular oxygen is toxic to some microorganisms. During a summer course in the 1950s taught by the eminent microbiologist Cornelius van Niel, Bloch became acquainted with obligately anaerobic bacteria that thrive only in the absence of oxygen.

Howard Goldfine, an emeritus professor of microbiology at the University of Pennsylvania, worked with Bloch on bacterial fatty acid biosynthesis. He said Van Niel's course caused Bloch "to wonder what goes on in anaerobes, because obviously, they couldn't use molecular oxygen."

To answer this, Bloch studied fatty acid biosynthesis in two species of the anaerobic bacteria clostridia.

"Clostridia are present anywhere where there's no oxygen," Goldfine said. "If you look in mud several inches below the surface, you'll find clostridia, and they're happily growing."

In 1961, Bloch, Goldfine and colleagues published two papers in the **Journal of Biological Chemistry** on unsaturated fatty acid biosynthesis in clostridia. The papers, now recognized as JBC Classics, reported that the clostridia species produce unsaturated fatty acids via a route distinct from that in aerobic cells.

Goldfine's association with Bloch began through their shared interest in anaerobic metabolism. Goldfine was working on anaerobic bacteria in Earl Stadtman's lab at the National Heart Institute of the National Institutes of Health.

"(Bloch) was coming down to NIH for a study section, and he asked if we could have lunch together, and then he asked, would I be interested in coming to visit his lab?" Goldfine said.

Goldfine knew Bloch's work on cholesterol and fatty acids, for which Bloch was to win the Nobel Prize in physiology or medicine with Feodor Lynen in 1964. Goldfine jumped at the opportunity and stayed for three years in the Bloch lab.

"I was really very, very fortunate to have had the opportunity to work with Bloch, because he was a man of really great depth and understanding," Goldfine said. "It was a turning point in my career."

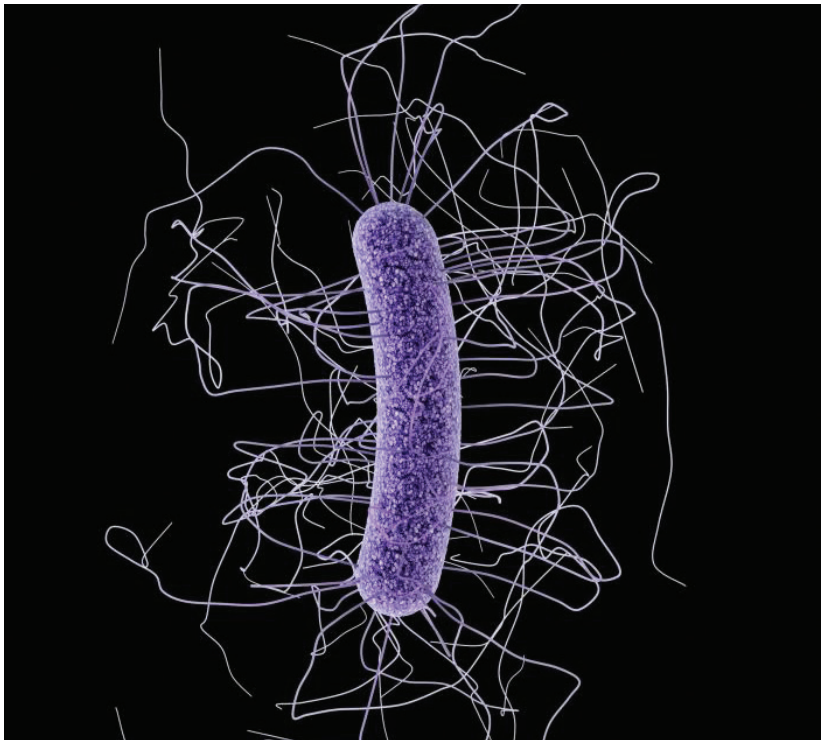
Goldfine's expertise soon was tested: Removing all oxygen from the experimental system to study unsaturated fatty acids in anaerobic organisms posed a challenge. He first tried to grow the clostridia in a helium atmosphere in a vacuum desiccator, "but that didn't completely remove oxygen, because there could be a trace of oxygen in the helium," he said.

So Goldfine resorted to a chemical trick and skillful lab acrobatics. He poured a 5% potassium carbonate solution into the desiccator base, above which he placed the flasks holding the bacteria along with a beaker containing pyrogallic acid. After sealing the desiccator, Goldfine gingerly tilted it to tip the pyrogallol into the potassium carbonate solution. The resulting mixture removed any traces of oxygen from the helium-filled desiccator.

The researchers relied on Bloch's expertise in radiocarbon labeling and detection. After feeding 14C-labeled lipid precursor acetate to the bacterial cultures, Bloch and Goldfine extracted the lipids from the cells, used gas chromatography to separate fatty acids, identified them with standards and assessed them for 14C labeling in a scintillation counter.

In the first study, Goldfine and Bloch reported incorporation of two-thirds of the 14C-labeled acetate into

CENTERS FOR DISEASE CONTROL AND PREVENTION



Anaerobic bacteria such as clostridia (Clostridium difficile is shown here) can produce unsaturated long-chain fatty acids in the absence of molecular oxygen.

Konrad Bloch

Howard Goldfine

saturated lipids and one-third into monounsaturated lipids, showing that bacteria can produce unsaturated fatty acids in the absence of molecular oxygen.

But how could the anaerobic clostridia create double bonds in fatty acids?

To answer this question, Goldfine and Bloch fed a series of 14C-labeled saturated fatty acids ranging in length from 8 to 18 carbons to the cells. They found that the clostridia do not make unsaturated fatty acids by desaturating bonds in their saturated counterparts. Instead, the clostridia produce a single double bond during elongation of the short (8–10 carbons long) saturated fatty acids, resulting in long-chain monounsaturated fatty acids.

Bloch and colleagues then noticed that the unsaturated fatty acids differed in where the double bond was located in the lipid chain, resulting in different fatty acid isomers.

To find out how these isomers were made, as described in the second JBC paper, Bloch, Goldfine and another member of the lab, Günter Scheuerbrandt, fed 14C-labeled octanoic and decanoic acids to a clostridium and again measured 14C incorporation into fatty acids. They tweaked their procedure to include exposure to a strong oxidant that breaks lipid double bonds, enabling them to home in on the mechanism that creates the different fatty acid isomers.

"I distinctly remember Paul Baronowsky — he was a graduate student at the time — standing at the blackboard at the end of the lab writing that pathway," Goldfine said. "'This is how you get the double bond here. And if you do it with another precursor, you get the double bond there.' He drew it all out beautifully."

Their experiments clearly showed that the individual isomers don't arise from interconversions among them and established which short-chain fatty acids are the precursors to the various long-chain fatty acid isomers.

Thus, innovative rejiggering of lab equipment, foundational biochemistry methods and several incisive blackboard sketches helped uncover how anaerobes make unsaturated fatty acids.

The results of Bloch's lab stood the test of time. "The pathway that is in the second JBC (Classics) paper has held up for 60 years," Goldfine said. "It's pretty astonishing."

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Researchers clock DNA's recovery time

By Jonathan Griffin

In the time it takes for an Amazon Prime delivery to arrive, cells damaged by chemotherapy can fix their most important DNA almost completely. That's true in mouse livers mice at least, according to a new study.

Researchers found that DNA damaged by the chemotherapy drug cisplatin is mostly good as new in noncancerous tissue within two circadian cycles, or two days. The results, published in the **Journal of Biological Chemistry**, could inform strategies for administering chemotherapy at times that maximize tumor damage while minimizing side effects.

NATIONAL HUMAN GENOME RESEARCH INSTITUTE

Circadian rhythmicity of metabolic processes has a significant impact on physiology and behavior.

Side effects of cisplatin include kidney, liver and peripheral nerve injury. Cisplatin kills cells, cancerous or not, by damaging their DNA, so Nobel laureate Aziz Sancar and his team aimed to uncover the pattern of DNA repair in healthy cells. In normal cells, the circadian clock drives the rhythm of DNA repair, but not in tumors.

"Most cancers do not have a functional clock and so, basically any time that it's good for the normal tissue, you can hit the cancer," said Sancar, a professor at the University of North Carolina School of Medicine.

In an earlier study, Sancar's team looked at DNA repair across a mouse genome, uncovering two mechanisms of circadian-controlled DNA repair.

They found that for some genes, transcription — during which damaged DNA is recognized and patched up — was controlled by the circadian clock. The pattern was specific to each gene, with repair peaking at different times of day. For the remaining DNA that is not transcribed or expressed, repair was less efficient but also clock-controlled, and maximum repair occurred between 4 p.m. and 6 p.m., Sancar said.

In this previous experiment, they examined DNA two hours after injecting cisplatin, but in their new work in JBC, Sancar's team wanted to study recovery on a more clinically relevant time scale.

Patients get cisplatin intravenously at weekly, 10-day or two week intervals, allowing recovery time between doses, Sancar explained. "And so we wanted to know what happens over those long periods."

Using a technique developed in their lab, the team captured and sequenced fragments of damaged DNA from mice injected with cisplatin. Over 70 days, they produced maps displaying where and when DNA was fixed at the resolution of a single nucleotide.

The DNA of transcribed genes was just about fully mended in two circadian cycles, Sancar said. Most repair in the first 48 hours was to these genes.

The remaining damage in nontranscribed DNA is not harmful in normal cells that aren't replicating, Sancar said. But for cancer cells, which divide uncontrollably, this damage could lead to cell death.

Before this information is considered in the clinic, further experiments are needed, Sancar said.

Sancar is working with oncologists, evaluating new cisplatin regimens in mice implanted with human tumors to find a treatment that reduces toxicity in normal tissue while hitting cancer hard.

DOI: 10.1074/jbc.RA119.009579

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Lack of sleep affects fat metabolism

By Laurel Oldach

We all tend to be a little short on sleep during the work week. A new study adds to the mounting evidence of how harmful insufficient sleep can be. In the **Journal of Lipid Research**, researchers at Pennsylvania State University report that just a few days of sleep deprivation can make people feel less full after eating and cause them to metabolize the fat in food differently.

Researchers have known for some time that sleep disruption has harmful effects on metabolism. Orfeu Buxton, a professor at Penn State and a senior author of the new study, contributed to much of the earlier research demonstrating that long-term sleep restriction puts people at a higher risk of obesity and diabetes. However, Buxton said, most of those studies focused on glucose metabolism, which is important for diabetes, while relatively few assessed digestion of lipids from food.

Kelly Ness, now a postdoctoral fellow at the University of Washington, ran the study when she was a graduate student in Buxton's lab. After spending a week getting plenty of sleep at home, 15 healthy men in their 20s checked into the sleep lab for 10 nights, she said. After three nights spent establishing a baseline, the participants spent no more than five hours in bed for the next five nights. The researchers designed the schedule to resemble a work week.

During the study, Ness said, she and other researchers collected data, but they also spent time "interacting with the subjects, playing games with them, talking with them — helping to keep them awake and engaged and positive."

To find out how this schedule affected metabolism, the researchers gave the participants a standardized high-fat dinner, a bowl of chili mac, once early in the study and again after four nights of sleep restriction.

"It was very palatable — none of our subjects had trouble finishing it — but very calorically dense," Ness said.

Most participants felt less satisfied after eating the rich meal while sleep deprived than when they had eaten it well rested.

Then researchers compared blood samples from the participants. They found that sleep restriction affected the postprandial lipid response, leading to faster clearance of lipids from the blood after a meal. That could predispose people to put on weight.

"The lipids weren't evaporating — they were being stored," Buxton said.

The simulated work week ended with a simulated Friday and Saturday night when participants could spend 10 hours in bed catching up on missed shut-eye. After the first night, they ate one last bowl of chili mac. Although their metabolic handling of fat from food was slightly better after a night of recovery sleep, they didn't recover to the baseline healthy level.

This study was highly controlled, which makes it an imperfect model for the real world, Ness said. It focused on healthy young people, who are usually at a lower risk of cardiovascular disease, and all the participants were men. The researchers wondered whether giving more recovery time would change the magnitude of recovery they observed.

Nonetheless, Buxton said, the study gives worthwhile insight into how we handle fat digestion.

"This study's importance relies on its translational relevance. A high-fat meal in the evening, at dinnertime — and real food, not something infused into the vein? That's a typical exposure. That's very American."

DOI: 10.1194/jlr.P094375

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This protein makes antibody drugs work

By Laurel Oldach

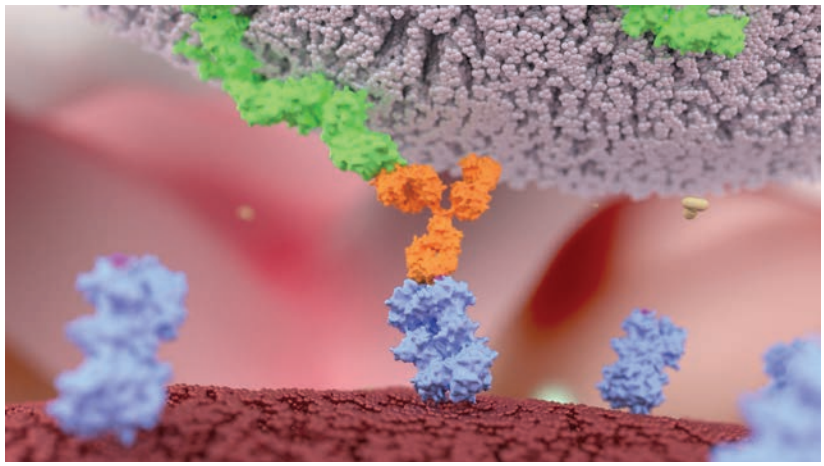
Hundreds of therapeutic antibody drugs target cell-surface molecules in cancers and other diseases. But different patients respond differently to antibody therapy, and doctors struggle to predict who will benefit most.

Except for a few used to ferry drugs or toxins to a specific cell population, most antibodies work by recruiting the immune system. When natural killer cells, the body's tiny assassins, recognize antibodies coating a target cell, the NK cells latch onto the target and kill it.

Kashyap Patel, a gradstudent at Iowa State University, studies the receptor CD16a, receptor protein on natural killer cells that recognizes and binds to antibodies. Patel and his advisor, Adam Barb, now a professor at the University of Georgia, were interested in changes to CD16a that might underlie binding changes.

"CD16a in our bodies is different than the CD16a that's used to test monoclonal antibodies," Patel said. Whereas the recombinant version used in laboratories has limited posttranslational modifications, the human version is glycosylated at five different sites. Glycosylation, which happens in the endoplasmic reticulum, can add complex branched structures to a protein; those modifications can alter proteins' binding characteristics and could in principle make CD16a more or less likely to bind to antibodies.

Scientists know that a genetic polymorphism near one N-glycosylation site in CD16a can influence how well antibody treatment works.



An artist's rendering shows CD16 receptors on a natural killer cell (blue) binding to the constant region of an antibody (orange) that also is bound to a target molecule.

It isn't clear whether that polymorphism affects glycans directly or whether genetic changes that do affect glycans affect CD16a-antibody binding. Studying the variations in glycan structure at each site is difficult, because isolating enough CD16a from a single person to analyze poses a technical challenge.

In a recent article in the journal **Molecular & Cellular Proteomics**, Patel, Barb and colleagues report that they studied post-translational modifications to CD16a in glycopeptide samples harvested from the natural killer cells of individual plasma donors. Then they used glycomics tools to determine the structures of the glycans.

"We weren't expecting the variability we saw," Patel said. At five sites in CD16a, the team found substantial variability in the structure of glycans — both among the donors and within each individual.

The researchers don't know yet what to make of the glycan variability, because the donor pool was small and few studies of this type have been done. However, now that the protocol for studying glycan composition from a single person is worked out, Barb's lab hopes to determine whether changes to that composition affect the immune system's response to antibody therapy.

When Patel started this project, he didn't know much about protein glycosylation, but he said he intends to keep studying it as a postdoctoral fellow.

"Once you see a protein with N-glycans on it, you cannot unsee it. You can't ignore it."

DOI: 10.1074/mcp.RA119.001607

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From the journals

By John Arnst, Isha Dey, Jonathan Griffin & Dawn Hayward

A link between stress and depression

Chronic stress affects the electrophysiology of neurons in various regions of the brain including the medial prefrontal cortex, or mPFC, increasing risk for depression. The mechanisms underpinning these alterations are not understood fully, however. In a recent paper in the **Journal of Biological Chemistry**, Chenghui Song and colleagues at Scripps Research write that they studied chronically stressed mice to uncover the downstream effectors of GPR158 — a receptor enriched in the mPFC. They found that a complex between GPR158 and RGS7, which is a negative regulator of GPCR signaling, limited potassium current from mPFC neurons in stressed mice, leading to suppressed neuronal excitability. The authors suggest this freshly uncovered mechanism could support the development of new therapies for stress-induced depression.
DOI: 10.1074/jbc.RA119.00753

Using stem cells in veterinary therapy

Stem cells can regenerate themselves and differentiate into various cell types. In recent years, adult stem cells have become important candidates for therapy both in human diseases and in veterinary science, exemplified by the use of bone marrow-derived mesenchymal stem cells, or BMMSCs, to repair locomotor disorders in hard tissues such as bone and cartilage in dogs and cats. However, BMMSCs also can affect the immune system by triggering the release of cell proliferation factors. Thus, researchers need comprehensive understanding of the diversity of BMMSCs in dog breeds to speculate on their biological function.

In a collaborative study published in the journal **Molecular & Cellular Proteomics**, Filip Humenik and a team of researchers from France and Slovakia used a multi-omics approach to characterize BMMSCs from adult dogs of six breeds and assessed their ability to differentiate into bone, cartilage and fat cells. Conditioned medium derived from these cells showed an angiogenic response in a chicken embryo model, meaning it promoted the formation of new blood vessels from existing blood vessels, which is beneficial for regenerating tissue, but critical for cancer development. This work reinforces the need for more clinical studies before considering MSCs for veterinary treatment.
DOI: 10.1074/mcp.RA119.001507

How liver response changes with age

The glutamine- and asparagine-depleting enzyme asparaginase is used as a treatment for blood cancers, but its clinical success is hindered by side effects including hepatotoxicity. To uncover how age could affect the liver's response to asparaginase, Inna Nikonorova of Rutgers University and colleagues examined livers from mice of varying ages treated with the enzyme. While juvenile mouse livers experienced steatosis and iron accumulation, adult livers exhibited upregulated serine, glycine and one-carbon metabolism and increased inflammation. These results, recently published in the **Journal of Biological Chemistry**, suggest that adult and juvenile livers employ different strategies to maintain homeostasis.
DOI: 10.1074/jbc.RA119.009864

A new enemy for drug-resistant cancer cells

Two drugs constitute medicine's first line of defense against acute myelogenous leukemia: daunorubicin and cytarabine, or Dnr and Ara-C. AML cancer cells quickly grow resistant to these drugs, however, and often require further treatment. Past research has shown that Dnr raises the levels of ceramides, lipids that contribute to apoptosis, in treated cancer cells. Researchers at the East Carolina Diabetes and Obesity Institute recently generated Dnr- and Ara-C-resistant AML cell lines to further investigate ceramide's role. Their work was published in the **Journal of Lipid Research**.

Ceramide is broken down to sphingosine, another lipid that can be catabolized further. Li-Pin Kao and researchers in the Cabot lab found that in drug-resistant cell lines, ceramide levels were low and breakdown products were high, indicating cancer cells rewired normal cells' pathway to evade apoptosis. The enzymes involved in ceramide breakdown had higher activity in resistant cell lines, and ceramide addition no longer affected cancer cells.

Treatment with inhibitors that

Demystifying mitochondrial morphology in fatty livers

For an ailment nonchalantly dubbed "the unnamed disease" in 1980, nonalcoholic fatty liver disease has become disconcertingly prevalent. NAFLD is now the most common cause of chronic liver disease, affecting between 80 and 100 million people in the United States and close to one billion people worldwide. True to its name, the disease is characterized by a buildup of lipids in the liver; over time, the excess fat can cause inflammation, scarring and, ultimately, organ failure.

Over the past four decades, researchers have been unable to clarify the role of mitochondria in NAFLD — the organelles have been found both to overproduce glucose and to shut down in different patients, changing shape all the while.

To understand whether a change in mitochondrial morphology causes dysfunction or vice versa, researchers at the University of Geneva engineered a mouse lacking in prohibitin-2, a protein in the organelle's inner membrane that plays a role in cell proliferation, apoptosis and mitochondrial dynamics, or coordinated cycles of fission and fusion.

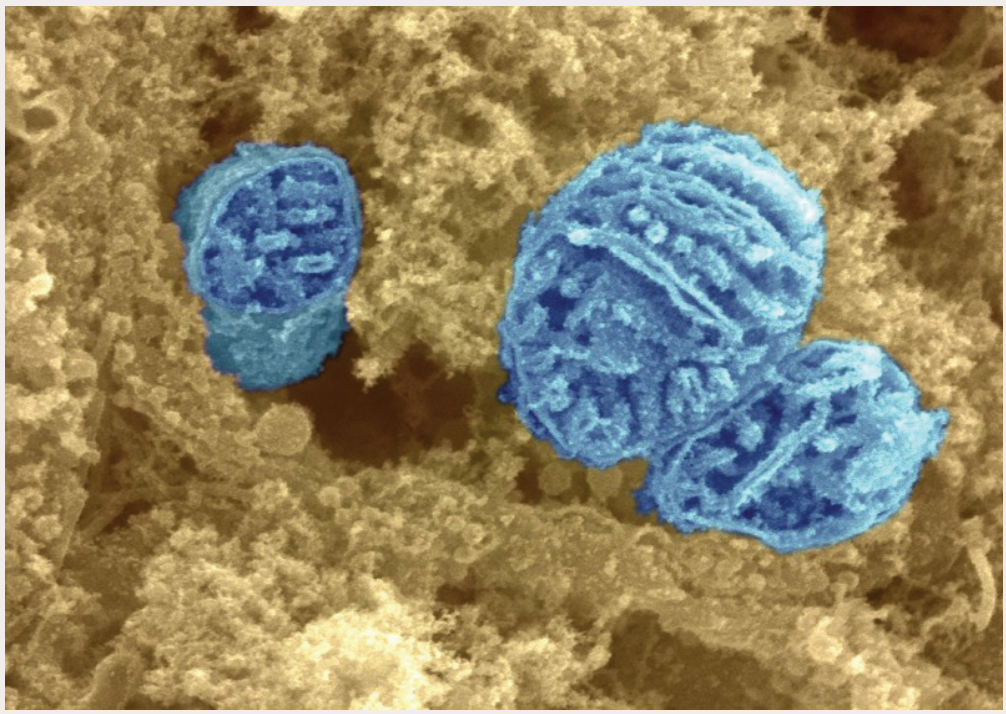
In a paper published in the **Journal of Biological Chemistry,** Lingzi Li and colleagues found that knocking out Phb2, which normally forms large ring-shaped complexes with its sibling molecule Phb1, caused the mitochondria to fragment and stop producing glucose. The absence of Phb2 also led to excessive cleavage of OPA1, a protein essential to mitochondrial dynamics.

When the researchers then used adenovirus to express a cleavage-resistant long version of OPA1, L-OPA1 delta, they found that hepatic mitochondria returned to a normal shape due to a stabilization in dynamics but did not regain their previous function of glucose production. When they then expressed L-OPA1 delta in mice that didn't have Phb2 knocked out, they found it caused excessive mitochondrial respiration and glucose production. Together, their results suggest that cycles of mitochondrial fusion and fission, regulated by prohibitin, play a role in controlling glucose production.

DOI: 10.1074/jbc.RA119.007601

— John Arnst

DAVID FURNESS/WELLCOME COLLECTION



Mitochondria often lose their normal rodlike or spherical shapes in the livers of people with nonalcoholic fatty liver disease.

prevent ceramide breakdown proved beneficial; the researchers saw higher ceramide levels and higher cancer cell apoptosis rates. Higher mitochondrial respiration rates in resistant cell lines were reversed as well. Resistant cancer cells tend to rely on oxidative phosphorylation, which produces more ATP than glycolysis. This dual inhibitor effect on ceramide levels and mitochondrial respiration could help patients with chemoresistant AML.
DOI: 10.1194/jlr.RA119000251

Disrupting pathogens' protective biofilms

The fungal pathogen Aspergillus fumigatus causes invasive infections in immunocompromised patients and evades host immune responses by encapsulating itself in a biofilm. A cluster of genes in A. fumigatus recently was linked to the production and modification of key components of the fungal biofilms, galactosaminogalactans, or GAGs. Natalie Bamford of the Hospital for Sick Children in Toronto and colleagues expressed a gene from this cluster in yeast, producing the protein Ega3 from the glycoside hydrolase family 114, or GH114. Functional assays revealed that Ega3 disrupts GAG-dependent biofilms, and structural analysis revealed substrate binding sites on the enzyme. These findings, recently published in the **Journal of Biological Chemistry**, provide valuable mechanistic insights into the GH114 family, which contains hundreds of members found in plants and human pathogens.
DOI: 10.1074/jbc.RA119.009910

Analyzing diffuse gliomas for personalized medicine

Diffuse gliomas, including astrocytomas, oligodendrogliomas and glioblastomas, are the most common brain tumors. Based on histology and genomic and transcriptomic data such as DNA and RNA copy number and DNA methylation, gliomas broadly are classified as isocitrate dehydrogenase-mutant or IDH–wild-type. Patients with IDH mutations typically live longer, but the mutations are not yet used as therapeutic biomarkers. Ugljesa Djuric and a team in Toronto recently did a proteomic analysis of diffuse gliomas to improve understanding of the downstream pathways involved in their malignancies. Their findings were published in the journal **Molecular & Cellular Proteomics**.

The authors used mass spectrometry and protein cluster analysis to study more than 5,000 unique proteins in tissue samples from a variety of gliomas. Overall, IDH-mutant gliomas had an increased abundance of proteins involved in mRNA splicing, whereas IDH–wild-type gliomas were enriched in proteins involved in invasiveness and epithelial-to-mesenchymal transition, an important driver of the disease progression. This study sheds light on the changes at the protein level caused by genetic alterations in glioma subtypes, defined by their IDH status, and identifies distinct targetable proteins and pathways, which might aid in developing specific and personalized treatments.
DOI:10.1074/mcp.RA119.001521

Inactivating a moonlighting enzyme

Tryptophanyl-tRNA synthetase, or WRS, plays key roles in protein synthesis within cells, but the enzyme also performs nonclassical extracellular functions such as the regulation of inflammation. To elucidate how moonlighting WRS is regulated in the extracellular milieu, Parker Jobin of the University of British Columbia and colleagues performed secretion and cleavage assays and proteomic studies of WRS from macrophages. They write in the **Journal of Biological Chemistry** that they found that WRS increases the activity of matrix metalloproteinases, some of which were shown to cleave WRS at several sites, curbing the proinflammatory signaling initiated by the moonlighting enzyme.
DOI: 10.1074/jbc.RA119.009584

An isolation strategy for cytokines

Cytokines initiate biological activities by binding to and dimerizing receptors. These ligands have garnered interest for use in immunotherapies, but their short half-lives and pleiotropic binding have raised concerns. To improve the stability of cytokine-receptor interactions, Jamie Spangler, Ignacio Moraga and colleagues at Stanford University devised an evolutionary strategy for the isolation of monovalent antibodies that lock receptors into a dimerized state. They developed a stapler that could stabilize the interleukin-4 receptor dimer and another that could stabilize the bond between interleukin-2 and its receptor subunit. These new methods potentially offer a means to modulate the activity of other ligands for a wide scope of therapeutic applications. This study was published in the **Journal of Biological Chemistry**.
DOI: 10.1074/jbc.RA119.009213

The lipid buildup problem

Our intestinal cells store lipids through carefully regulated pathways. When there are problems,

A deep dive into mesenchymal stem cell differentiation

Human mesenchymal stem cells, or MSCs, are part of our bodies' connective tissue. They can differentiate into bone, muscle, cartilage and fat cells and are thus beneficial for treating conditions like type 1 diabetes and spinal cord injury and for organ transplantation. However, quite a few challenges are associated with using these cells for therapy. For example, tissue-derived MSCs can trigger an unnecessary immune response, leading to uncontrolled cell proliferation, or can undergo unwanted differentiation. To better control such off-target effects of tissue-derived MSCs, these cells can be differentiated from human embryonic stem cells, or hESCs, in the lab in a more controlled manner. But researchers need to know more about the changes that occur during this differentiation.

To address this, an international team of researchers came together for a multidisciplinary study of hESC-to-MSC differentiation. Led by Anja M. Billing of Weill Cornell Medicine – Qatar, the team combined transcriptomics, proteomics and phosphoproteome analysis for an in-depth understanding of the process. Their findings, recently published in the journal **Molecular & Cellular Proteomics**, identified cellular pathways and key factors involved in ESC-to-MSC differentiation.

Using RNA sequencing and performing RNA-to-protein correlation, the authors identified specific subsets of genes coding for transcription factors, kinases and phosphatases as well as noncoding RNAs, all of which are differentially expressed in ESCs and MSCs. Using phosphoproteomic analysis, the authors deduced that the proteins that most were most expressed during differentiation also underwent the most extensive phosphorylation, hinting at the biological function of such proteins in this process. Overall, proteins involved in cell-to-cell adhesion, cytoskeleton organization and extracellular matrix formation were the most prominent players driving this differentiation. This study enriches our understanding of the biology of ESC–MSC differentiation, paving the way for better use of MSCs in stem cell–based therapy.

DOI:10.1074/mcp.RA119.001356

— Isha Dey

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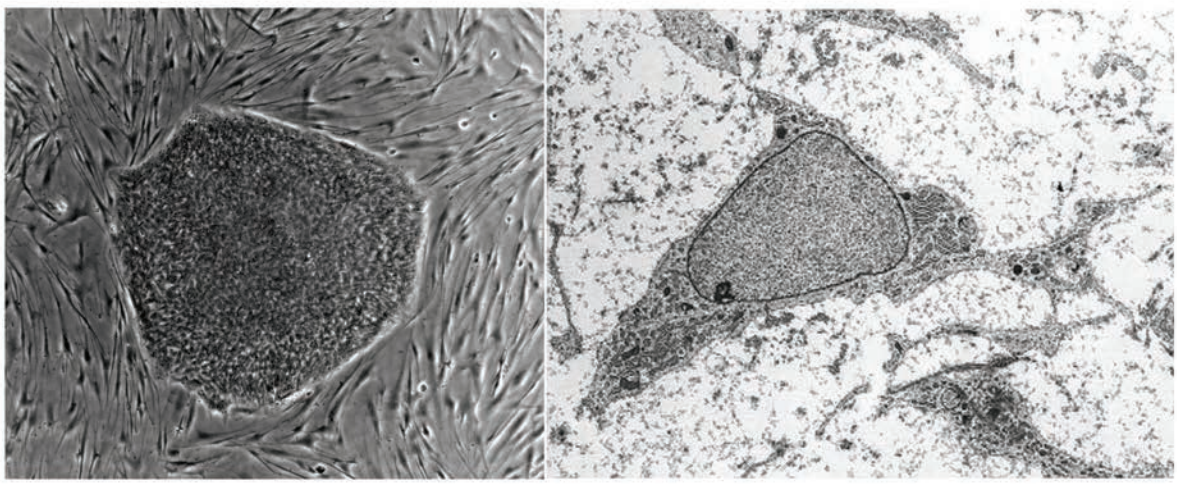

These two images show human embryonic stem cells on mouse fibroblast cell feeder layer (left) and a more highly magnified electron micrograph of a mesenchymal stem cell (right).

Even more reasons to take your DHA

The fatty acids DHA and EPA are popular dietary supplements and are known to slow tumor growth, but how do they do it? Researchers at Iwate Biotechnology Research Center in Japan investigated the effects of docosahexaenoic acid and eicosapentaenoic acid on melanoma cells, uncovering a pathway that fatty acids take to reduce melanin content in tumor cells. If cancer cells no longer can make melanin, the pigment in skin cells, they can undergo apoptosis.

DHA and EPA are considered omega-3 fatty acids because of their structure. Like saturated fatty acids, omega-3 or unsaturated fatty acids have a hydrophilic head and a long hydrophobic tail, like a snake, but an omega-3's tail has double bonds, or "kinks," in certain places. These kinks make it difficult for unsaturated fatty acids to stack on top of one another. Saturated fatty acids, with no kinks, easily can stack and potentially clog arteries.

Hidetoshi Yamada and the research team analyzed melanin content in melanoma cells treated with saturated and unsaturated fatty acids. Unsaturated fatty acids such as DHA and EPA lowered melanin content in the tumor cells. To determine further the role of fatty acids, the researchers looked at melanin synthesis, which involves several steps. They found that EPA reduced the protein levels of an enzyme involved in making melanin in cancer cells, which could contribute to EPA's anti-tumor effects.

DAWN HAYWARD

DHA, a supplement many already take, could play a role in suppressing melanoma growth.

The researchers also found that unsaturated fatty acids prevented synthesized melanin from getting to its destination. Actin, a protein that other molecules can ride on as they move throughout the cell, was reduced in cells treated with EPA. DHA decreased a specific signaling pathway in cancer cells and disrupted their cell cycle.

These findings, which were published in the **Journal of Lipid Research**, strengthen the argument that increased unsaturated fatty acid intake is beneficial against certain cancers.
DOI:10.1194/jlr.M090712

— Dawn Hayward

lipids can accumulate, causing inflammation and oxidative stress. To investigate the enzymes that may play a role in this regulation, researchers at the Université de Montréal used genetically modified intestinal cell lines to find out what happens when an important GTPase (an enzyme involved in breaking down GTP) called Sar1b is knocked out. Sar1b is involved with transporting fat-carrying molecules called chylomicrons and associated with certain intestinal lipid diseases. Their findings were published in the **Journal of Lipid Research**.

Alain Sane and the research team looked at oxidative stress, inflammation and fatty acid oxidation to determine the effects of losing the GTPase protein. They found a reduction in antioxidant protection by measuring levels of glutathione along with a decrease in redox homeostasis regulation. Inflammation markers also were increased in response to GTPase knockout. The researchers then looked at fatty acid synthesis and breakdown. Breakdown was decreased but synthesis increased in cells with GTPase knockout, indicating a disruption in homeostasis. GTPase function is therefore critical to preventing lipid accumulation and inflammation that can occur in chylomicron retention disease.
DOI: 10.1194/jlr.RA119000119

Solving structure of useful enzymes

Xyloglucans, or XyGs, are glycans contained in the cell walls of most land plants. Because of their potential applications in various industrial sectors, enzymes that can alter or degrade these glycans are sought after. The GH74 family of enzymes has demonstrated a specificity for XyG, but there have been conflicting reports of their structures and modes of action. In a paper in the **Journal of Biological Chemistry**, Gregory Arnal of the University of British Columbia and colleagues write that they performed an in-depth biochemical characterization of several proteins, solving the crystal structures of four GH74 enzymes. The study unveiled critical structure-function relationships that help refine our understanding of GH74 catalysis.
DOI: 10.1074/jbc.RA119.009861

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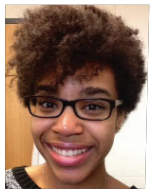
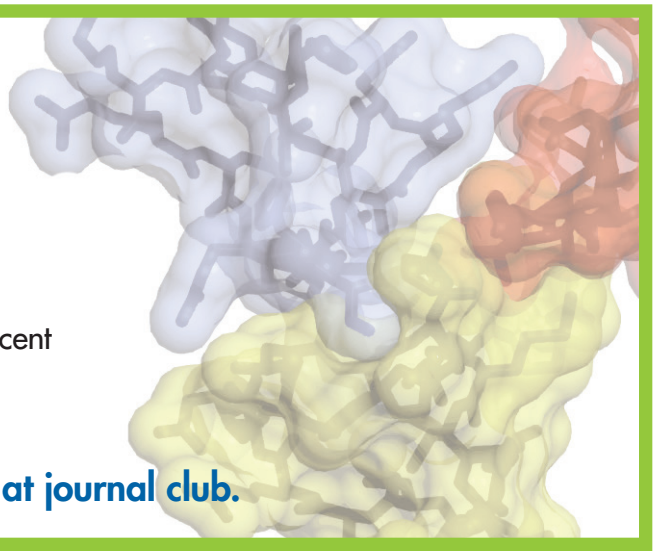
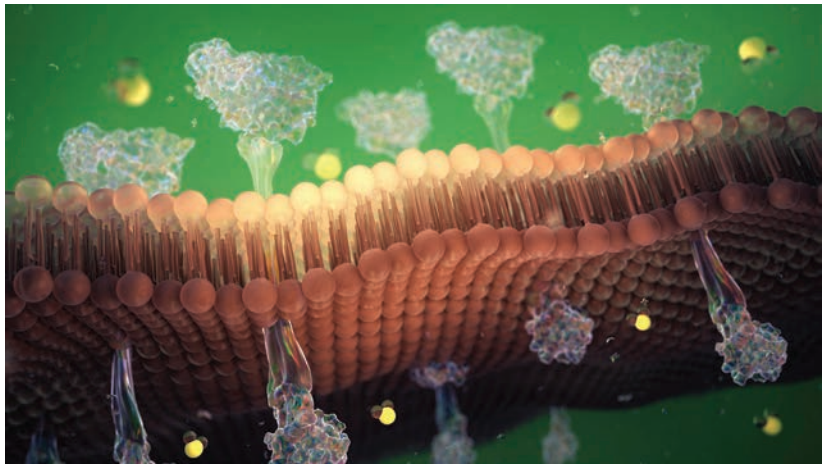




Phospholipids and innate immunity

By Valerie O'Donnell



This representation of a phospholipid bilayer shows integral membrane proteins protruding throughout.

The innate immune system is an ancient evolutionary arm of defense that responds to acute trauma by generating a barrier that prevents pathogen invasion and arrests bleeding. It also patrols healthy epithelial tissues, monitoring and responding to foreign antigens and supporting development of adaptive immunity.

Healthy functioning of the innate immune system relies on communication among diverse cell types, both from the bloodstream and based in stromal tissues such as epithelia and fibroblasts. Here, phospholipid signaling takes center stage in diverse ways, many of which we are only beginning to understand.

Phospholipids, or PLs, provide the membranes that hold our cells together. Researchers increasingly appreciate how these unique and diverse lipids also play essential roles in communicating within the immune system and how this is required for human health and disease. Indeed, PLs and their metabolic products are central players in vascular inflammation, hemostasis, immunity, cancer, infection and cardiovascular disease.

Here is some of what we know about PL biology in mammals so far:

Prostaglandin and eicosanoid precursors: Researchers long have known that PL hydrolysis provides polyunsaturated fatty acid substrates for generation of eicosanoids and prostaglandins by cyclooxygenases and lipoxygenases. This involves large families of phospholipases expressed in a cell-specific manner. Prostaglandins signal by activating well-characterized G protein-coupled receptors, or GPCRs, after they are secreted from immune and stromal cells during inflammation.

Phosphoinositides: The phosphorylation of inositol headgroups of phosphatidylinositol at up to three sites leads to a multitude of PL products that are potently bioactive and highly transient. These lipids form short-lived membrane anchors for kinases that regulate GPCRs, apoptosis and endocytosis.

Platelet activating factor: This structurally unusual and extremely transient phosphatidylcholine PL has a plasmalogen fatty acyl (a specialized bond) at sn1 and an acetyl group at sn2. It signals via the PAF receptor (a GPCR) to stimulate innate immune cell functions in the vasculature.

Phospholipase C and phospholipase D: Families of enzymes called PLCs cleave PLs to form diacylglycerol and release the phosphorylated headgroup. Diacylglycerols are potent activators of the protein kinase C pathway, while the PL headgroup mobilizes calcium. PLD metabolizes phosphatidylcholine to form phosphatidic acid, an intracellular molecule that regulates proteins involved in Ras and Rac1 signaling.

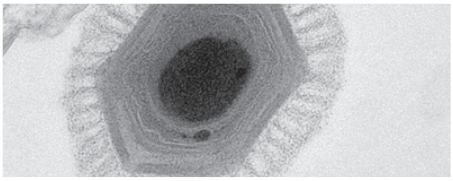
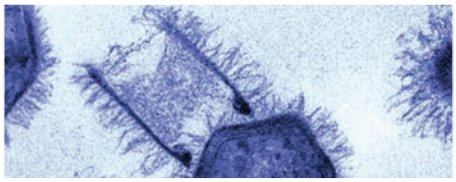
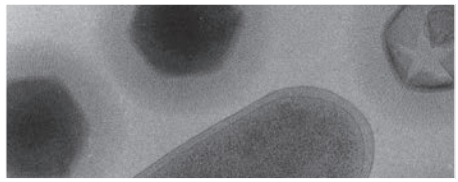
Enzymatically oxidized PL: Researchers long have known that PLs oxidize in atherosclerosis and inflammation via nonenzymatic processes. Now, they are finding that a cell-specific group of related lipids, generated by enzymatic oxidation, is formed in innate immune cells in the bloodstream. These lipids allow the interaction of coagulation factors with cell membranes, an event required for blood clotting. A deficiency of enzymatically oxidized PLs, or eoxPLs, leads to too much

bleeding, and studies suggest eoxPLs are involved in vascular inflammatory diseases such as aneurysms. In some situations, eoxPLs and their nonenzymatically generated analogs may be regulators of ferroptosis, an iron-dependent cell-death process relevant for cancer and organ failure.

Phospholipid innate immune recognition: Both self- and pathogen-derived PLs can act as ligands for a family of MHC class I-like antigen-presenting molecules called CD1. Lipid reactive T cells such as natural killer T cells then recognize the lipid-CD1 complexes. This type of antigen recognition shows significant molecular diversity in terms of PL species implicated, and a role is emerging for CD1-lipid presentation in human allergies, including to dust mites, pollen and bee sting.

Our lab recently published a review covering these aspects of PL signaling in the innate immune system in the Journal of Clinical Investigation.

Valerie O'Donnell
(O-DonnellVB@cardiff.ac.uk) is co-director of the Systems Immunity Research Institute at Cardiff University, U.K.

Giant gen

From Siberian ice cores to Australian lakebeds, massive viruses are changing what we know about evolutionary biology and viral structure

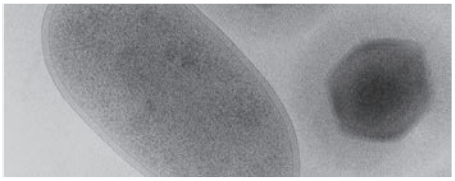
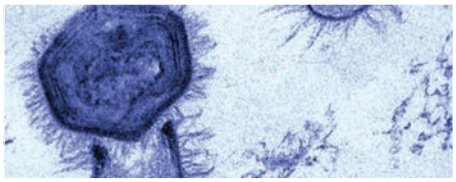
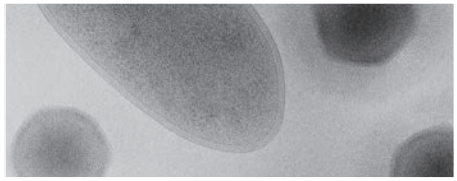
If the words "giant viruses" strike fear — or nihilistic delight — you need not worry. The vast majority of the pseudo-lifeforms want nothing to do with humans, preferring to prey instead on cyanobacteria, phytoplankton, and protists and prokaryotes writ large. The corpulent cocci-catchers are of interest, however, to a close-knit community of virus hunters, geneticists and structural biologists.

One of those structural biologists, Chuan Xiao, who goes by River among colleagues and in correspondence, is an associate professor at the University of Texas at El Paso, where he co-directs the university's cryo-electron microscopy facility. Xiao recently received a $1.75 million grant from the National Institutes of Health to continue characterizing the processes by which a giant virus, cafeteria roenbergensis virus, or CroV, assembles its protein shell.

Xiao's analysis of CroV is made possible by a 14-foot-tall electron microscope housed in an interference-minimizing room — a dedicated piece of equipment that, while not rare, carried a $1.8 million price tag for the department and demands intense computing power to render images of viruses that are more than three times larger than HIV or influenza virions.

"It took me almost two years about — 3 million CPU hours at the supercomputer center — to get the reconstruction (of CroV's membrane) to 14 Angstrom definition," Xiao said. "You almost can see the 14 atoms lined up together — that's how accurately we can put all these pieces together."

While some of these viruses have potential medical applications — the methods CroV uses to assemble its protein shell, or capsid, are similar to those used by influenza viruses — many more play a quiet role in bringing balance to aquatic ecosystems.

e thieves

By John Arnst

Massive missives

When Bradfordcoccus first was isolated from the amoebae that had caused a pneumonia outbreak in Bradford, England, in 1992, it refused to replicate in the lab. This response confounded the researchers at the Université de la Méditerranée in Marseille, France — Bradfordcoccus was the size of a small bacterium, and it responded to Gram staining but not to amplification of 16S ribosomal RNA, a slowly evolving sequence used to reconstruct prokaryotic evolutionary trees.

It took several years for the French microbiologists Didier Raoult and Bernard La Scola to recognize that Bradfordococcus was, in fact, a virus nearly as large as the amoeba Acanthamoeba polyphaga that it was hunting. In a paper published in the journal Science in 2003, La Scola, Raoult and their colleagues renamed the pathogen Acanthamoeba polyphaga mimivirus, and "mimivirus" — short for "mimicking microbe" — stuck.

Some of Raoult's samples made their way to the lab of the late Michael Rossmann, a structural biologist and X-ray crystallography pioneer who led the first team to map the common cold on an atomic level, at Purdue University.

At the time, Xiao was a graduate student in Rossmann's lab working with picornaviruses, a viral family that includes Rhinovirus, Poliovirus and Hepatovirus. He immediately was drawn to the challenge presented by the new, massive quarry.

"Cryo-EM was just beginning to become a powerful tool," Xiao said. "Mostly we were working on smaller viruses (because) we still couldn't get high resolution."

In cryo-EM, researchers flash-freeze molecules and microorganisms in an aqueous environment and then fire electrons at them with a transmission electron microscope, gathering data about a sample from the electrons that pass through it. This gets around the difficulty of crystallizing samples but results in a lower-resolution image.

IVAN PIERRE AGUIRRE/UTEP COMMUNICATIONS

At the University of Texas at El Paso, Chuan Xiao, who also goes by River, makes use of a 10-foot transmission electron microscope to puzzle out how Cafeteria roenbergensis virus assembles its protein shell.

Thomas Klose

Matthias Fischer

When the mimivirus samples arrived, Xiao was one of the only students capable of both operating the electron microscope and writing programs to compensate for the limitations of the computer's encoded memory running up against the sheer size of the micrographs. Xiao, who had almost finished his thesis, quickly wrapped up his work on picornaviruses and stayed on as a postdoctoral fellow in the lab.

In autumn 2005, just months after he received his Ph.D., Xiao's cryo-EM description of mimivirus at the level of 70 angstroms appeared in the Journal of Molecular Biology. For Xiao, the paper marked the beginning of a nearly three-year struggle to reconstruct the virus' membrane, which is dotted with asymmetrical, rodlike fibers.

"It's very hard to work with, because those fibers don't follow any symmetry. They just add noise to your images," he said. "I spent close to two and a half years trying to break through it, because at that time, we didn't have an electron detector."

The recent explosion of cryo-EM facilities has been largely thanks to the development of direct electron detectors, which allow for digital renderings of cryogenic samples.

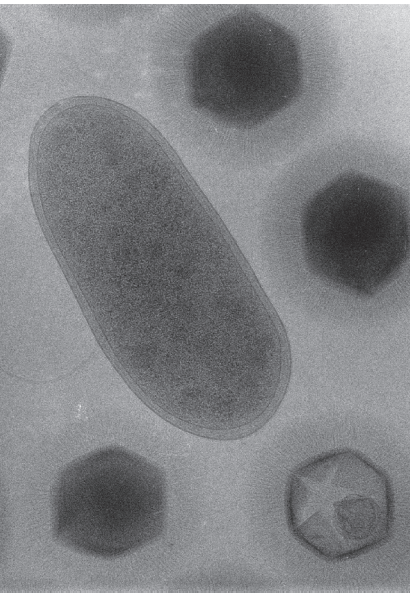
"Now, we have cameras that can essentially detect electrons and count electrons," said Thomas Klose, the technical director at the Purdue Cryo-EM Facility and a frequent collaborator with Xiao. "So we can recover much, much more of the theoretical signal that one would expect in an image. And that makes it easier to see things, and the contrast of your image improves greatly."

But when Xiao was a postdoc, images created by the scattering of electrons off a sample's surface were recorded on film that needed to be developed in a darkroom. His portfolio ran into the thousands.

"I collected almost 3,000 films. So just think about developing 3,000 films in a darkroom," he said. "Every session of cryo-EM, we could only take about 128 films maximum … we did a reconstruction, but never were able to improve resolution."

In 2008, Xiao took a job in the University of Texas at El Paso's emerging structural biology program. Within two years, a grant from the National Science Foundation would fund the towering modern microscope Xiao and his colleagues use today.

CHUAN XIAO/UTEP



Mimivirus, here pictured with E. coli, were initially mistaken for bacteria when they were isolated in 1992.

A lost domain?

While mimivirus was the first identified nucleocytoplasmic large DNA virus, or NCLDV, it wasn't alone for long. Giant viruses began cropping up anywhere wet — off the coast of Chile, in a 30,000-year-old Siberian ice core, inside an amoeba in the contact lens of a woman with keratitis — all of them bulked up with almost enough transcriptional machinery to exist outside of a host.

Because these massive genomic caches had previously been seen only in eukaryotic cells, their presence left microbiologists and geneticists unsure whether the viruses had evolved from smaller viruses that had scooped up genes from hosts or from cellular ancestors trading lives of full-time protein synthesis and ribosomal activity to live off the ATP of others.

According to Matthias Fischer, an environmental microbiologist at the Max Planck Institute for Medical Research in Heidelberg, Germany, who specializes in gigantic viruses and provides samples for structural biologists like Xiao, the latter hypothesis, suggesting a lost fourth domain of life outside of Archaea, Bacteria and Eukarya, was tantalizing for a time.

"There were two opposite hypotheses," Fischer said. "One was that they reduced from a cellular ancestor and became viral, and that's why they're so large, because they retained a lot of the genes they had previously."

Comparative genomics, however, appears to have provided an answer in the form of a small number of genes, including those used to make viral capsids and the DNA polymerase essential for viral replication, that are conserved across all known giant viruses.

"It's sometimes tricky to infer a common ancestry based on less than a percent of your genome," Fischer said. "But these genes are so-called core genes, and they are present in

so many different viruses, because they're very important."

The remaining 99% of giant virus genomes, which sometimes can include virophages, could be accounted for by the mechanisms the viruses use to cycle through genes, something Fischer likens to a "genomic accordion."

"There's a hypothesis called the genomic accordion, where these giant viruses can duplicate genes very rapidly to select for the best adapted version after mutations happen, and then they get rid of all the other copies they don't need. And then it collapses again," he said.

"In the long term, you find these extremes. You find a norovirus, for example, which has apparently had tremendous genome expansion, and it's 2.5 megabases,

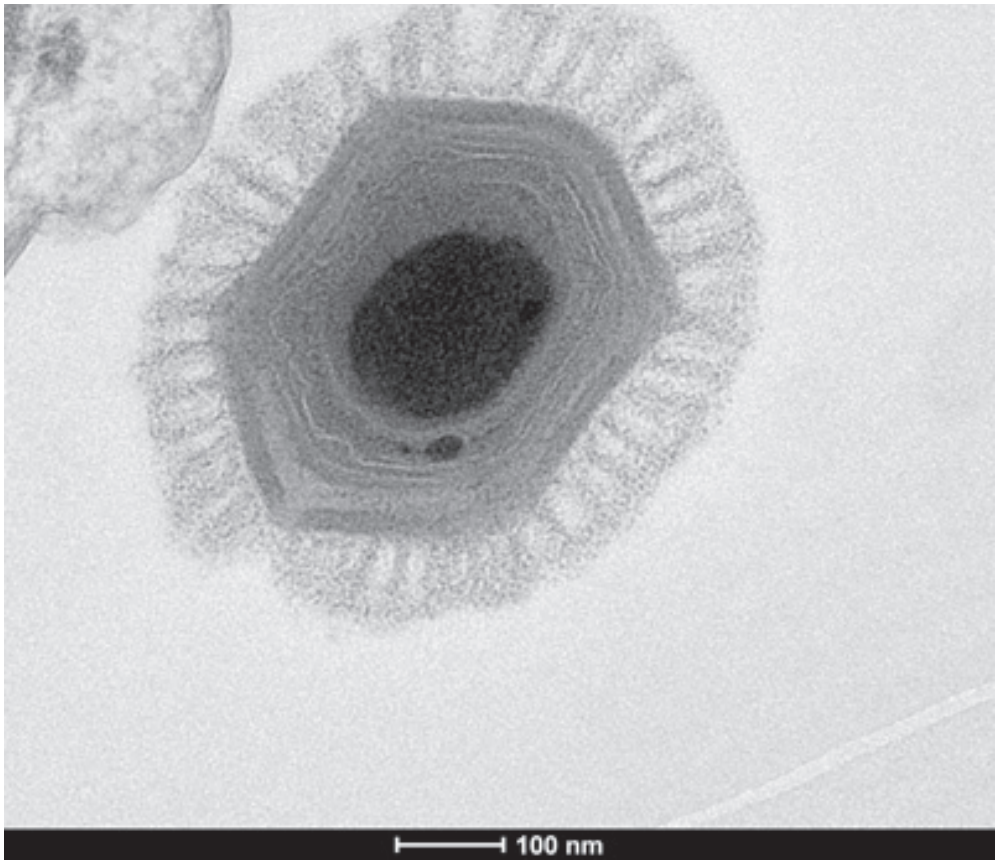
Viruses of viruses

Even viruses have predators. Over eons of acquiring and shedding genes, a number of giant viruses picked up smaller viruses known as virophages, whose DNA has infiltrated their own and springs to pseudo-life when the host virus begins its own transcriptional hijacking of bacteria.

"Complexity comes at a cost, right?" said Matthias Fischer, a microbiologist at the University of Heidelberg. "These giant viruses have acquired so many genes, and they can do so many things that other viruses rely on the host cell for, that now they're paying the price for that by attracting this other type of parasite.

"One was isolated from a patient with keratitis — there was an amoeba causing an eye infection, the amoeba was infected with a giant virus, and that giant virus was infected with a virus."

CHANTAL ABERGEL/CNRS



Megavirus chilensis, colloquially referred to as "megavirus," was discovered off the coast of Chile in 2010. It was the largest identified nucleocytoplasmic large DNA virus until pandoraviruses — so named because the scientific team that discovered them, led by French virologist Chantal Abergel, were primarily women — were found in 2013.

> "It doesn't matter whether you go out in the open ocean, whether you go to the bottom of the ocean, whether you go to freshwater ponds, soil samples — they'll pretty much always have viruses as the most abundant biological entities."
> – Matthias Fischer

all with genes that we don't really recognize because they are mostly only found in that lineage of viruses. So, for example, by gene duplication and diversification, you don't recognize the genes anymore or where they came from. And this is specific for each subgroup of giant viruses."

Genomic arsenals

Why these viruses need such massive genomes, however, remains unclear.

"Maybe that enables them to quickly switch hosts and adapt to many different intracellular environments if they're already bringing a large set of genes," Fischer said. "Combine that with the genomic flexibility — that they can lose genes and take off genes from the hosts — that makes them very versatile and adaptable organisms, right?"

Whether those viruses are able to utilize their genome fully is another question — one Steven Wilhelm, an environmental microbiologist at the University of Tennessee, Knoxville, recently set out to answer. In research published in Frontiers in Microbiology, he and his colleagues performed a transcriptomic analysis of the infection of the bloom-causing algae Aureococcus anophagefferens with its giant predator virus, AaV.

"One obvious question is, Do the viruses actually use these genes? Are they just tagging along like spare baggage? Or are the viruses actually transcribing them?" Wilhelm said. "We detected all but, I believe, three of the genes in the entire virus genome, which was kind of surprising to me. I thought there would be genes that weren't being used, but that wasn't the case."

And AaVs constantly are refreshing their genetic arsenal to keep up with mutations, born out of natural selection, that allow surviving Aureococcus anophogefferens to subvert them. Wilhelm likens this genomic arms race to the Red Queen in Lewis Carroll's "Through the Looking-Glass."

"She stopped at one point and quipped, 'Sometimes it takes all the running you can do just to stay in the same place.' And we think about these virus host relationships like that," Wilhelm said. "The viruses are trying to evolve constantly to affect all the hosts, and hosts are being pushed away from the viruses by selection and evolving. And the two of them keep moving forward to just stay in one place."

Viral bloom

By numbers alone, viruses rule the oceans. They also outnumber every other microorganism in lakes, rivers and rivulets.

"In every environment, you find somewhere around 10 million virus particles per milliliter (of water)," Fischer said. "It doesn't matter whether you go out in the open ocean, whether you go to the bottom of the ocean, whether you go to freshwater ponds, soil samples — they pretty much always have viruses as the most abundant biological entities."

"The big ecological question is, What is the effect of these viruses, right? Now, do they all kill the hosts and are bad for them?" Fischer said. "No, that doesn't seem to be the case. Instead, it looks like they're fueling the ecosystem by providing nutrients."

Giant marine viruses such as Wilhelm's quarry AaV accomplish this by breaking up blooms of phytoplankton, whose bodies then rain down to the seafloor to sequester carbon. By doing so, AaVs return valuable phosphorus, iron and nitrogen that had been hoarded by a handful of highly competitive bacteria in the food web.

"Without viruses, all this would stagnate, basically. And you would get a few winning microbes that just do the same thing," Fischer said. "And also, the diversity would be much lower, because viruses affect the most abundant hosts."

Last year, two Tupanviruses, named after Tupã, the indigenous South American Guarani god of thunder, that had been isolated from water samples off the coast of Brazil and at the bottom of an alkaline lake bed in the same country, were described by a team of Brazilian and French scientists in a paper in Nature Communications. The viruses, mem-

bers of the viral family Mimiviridae, possess the long tails, or fibers, that confounded Xiao in his days at Purdue as well as extraordinarily complex translational apparatuses.

While dozens of giant viruses are discovered each year, far fewer are characterized and added to the tree of terrestrial ancestry. Last year, researchers at the U.S. Department of Energy's Joint Genome Institute brought mini-metagenomics tools to bear on soil samples from Harvard Forest, a 4,000-acre ecological research area in Petersham, Massachusetts, discovering 16 novel giant viruses.

Wilhelm chalks the boom up to technological growth.

"That, in part, is due to the democratization of tools for high-throughput molecular biology and bioinformatics and our ability to understand how to use these tools better," he said.

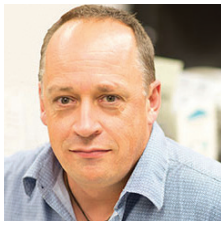
Unfortunately, the time it takes for each newly identified giant virus to be characterized — its membrane, its genome, its relatives ancient and extant — is not insignificant, especially for a field with fewer than a dozen senior researchers.

La Scola, the virus hunter in Marseille who was the first author on the 2003 paper that identified Mimivirus as a virus and the senior author on the paper identifying Tupanvirus, has a backlog that could take him more than two decades to work through, collaboration and technology notwithstanding.

"In my freezer, I have 24, 25 completely new giant viruses, but I have no time to publish about them," La Scola said. "Each time you find a virus, to describe it is probably one year of work, between microscopy and all the genome analysis."

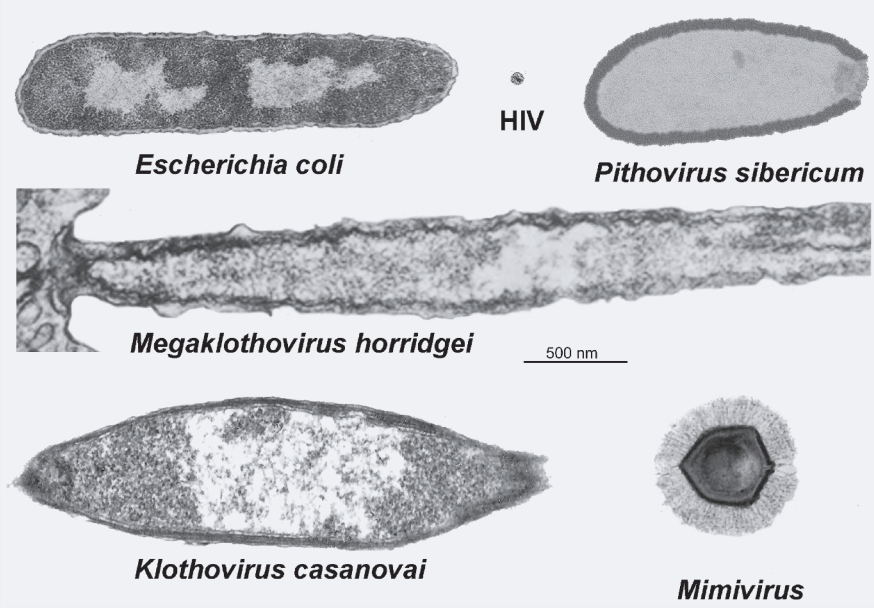
Continuing resolution

At UTEP, Xiao continues to examine the mechanisms CroV uses to assemble its capsid. Though he has ample access to cryo-EM



Steven Wilhelm

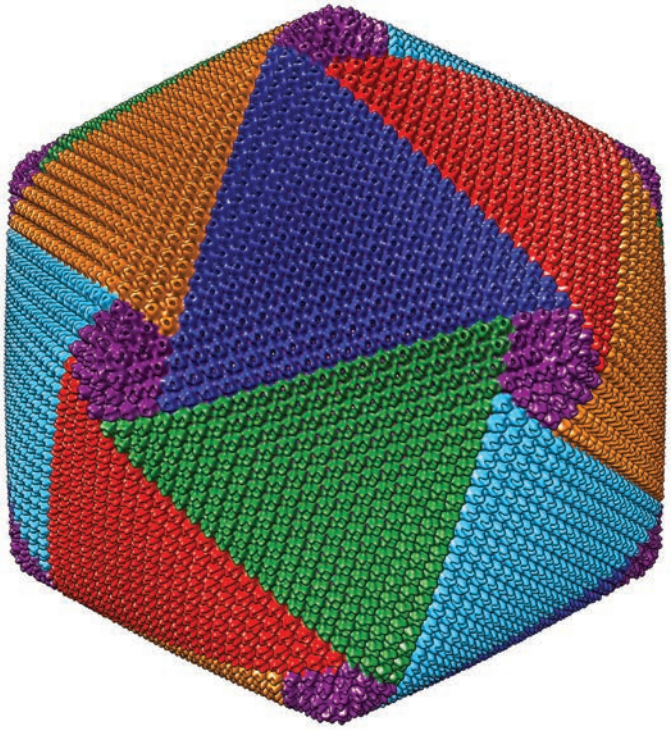
Bernard La Scola



CREDIT: ROXANE-MARIE BARTHÉLÉMY/AIX MARSEILLE UNIVERSITY

Giant viruses have recently been found in marine arrow worms. In 2018, scientists at Truman State University in Missouri discovered a giant virus, which they named Meelsvirus, in the epidermal cells of the arrow worm Adhesisagitta hispida.

Inspired by this discovery, researchers at Aix Marseille University scrutinized electron micrographs taken in 1967 and 2003 of dissections of the arrow worms Spadella cephaloptera and Paraspadella gotoi, reasoning that structures previously described as bristles and bacteria bore were, in fact, giant viruses. They named the viruses (above) Megaklothovirus horridgei and Klothovirus casanovai after both the Greek spindle-spinning goddess of fate Klotho and the names of the professors who had micrographed each, George Adrian Horridge and Jean-Paul Casanova. While twice as long as a typical Escherichia coli bacterium and significantly longer than an average Pithovirus sibericum, M. horridgei's total volume falls short of the largest observed pithoviruses.



CHUAN XIAO/UTEP

In 2017, Chuan Xiao and colleagues found that Cafeteria roenbergensis virus assembles its protein shell by spiraling together capsomers, colored here by their orientation, on a five-fold axis.

facilities, he worries about running up against his computer's memory restrictions while reconstructing the virus' capsid.

"I don't know how long it would take us to finish the reconstruction, because we immediately hit a memory issue," he said. "One terabyte of memory, which is the biggest they can put on the current supercomputer, isn't enough. If we just look at the protein shell, if we count all of the hydrogens, it's about 120 million atoms. A couple of years ago, when I tried to load and visualize 120 million atoms, my computer crashed."

About two years ago, Xiao and his colleagues discovered that CroV assembles its protein shell in a spiral pattern made up of five interlocking vertices. They hope eventually to develop therapeutic viruslike nanoparticles by refining their resolution of CroV's capsids.

"That's what my new project is really focused on," Xiao said. "We need to push the resolution higher."

At Purdue, Klose and Richard J. Kuhn are carrying the torch from the lab of Xiao's former PI, Michael Rossman, and continuing to bring the cryo-EM facility's modern, fully digital electron microscopes to bear on pathogenic viruses, including Zika, West Nile and hepatitis C.

But their work puzzling out understudied viruses still is informed by and dependent on the discoveries of their colleagues.

"It's kind of challenging for a lot of these projects to establish the right foundation, because we do structural biology so we don't do any of the proteomics or genomics part, and we rely on our collaborators," Klose said. "But if they've moved on to the next giant virus, it can be sometimes very difficult for us to get the information that we need."

Basic research can be a hard sell when it comes to pulling in grants from the National Institutes of Health and National Science Foundation, something Klose predicts may become more difficult without Rossmann. While interrogating the capsids of giant viruses sometimes provides insight into structures with relevance to pathogenic viruses — as with CroV and influenza viruses, or with African swine fever and faustovirus, an NCLDV that Klose and Rossmann reconstructed a few years ago — those connections can't be predicted.

"In the last few years, we have made a lot of progress in understanding what actually holds these (giant viruses) together and how they assemble," Klose said. "But we also still have a long way to go to fully understand what's going on and understand what these viruses do in the environment, which was always a question that Michael had.

"There are so many of them. They're so diverse, they're so big. They've been ignored for so many years. But what do they actually do?"

John Arnst
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MEET THE JLR JR. ASSOCIATE EDITORS

As a way to offer early career researchers an opportunity to learn the ropes of the peer-review process, the Journal of Lipid Research launched its junior associate editor program in 2019. Throughout the year, each of the four new junior associate editors will curate a virtual collection that focuses on their research area and highlights standout researchers who are pushing each field forward.

Raymond Blind
Vanderbilt University School of Medicine

Research area:
Nuclear lipid signaling and structure

Mentor:
George Carman

Gissette Reyes-Soffer
Columbia University Irving Medical Center

Research area:
Regulation and metabolism of Lipoprotein(a)

Mentor:
Henry Ginsberg

Brandon Davies
University of Iowa Carver College of Medicine

Research area:
Lipid metabolism in endothelial cells

Mentor:
Stephen Young

Rotonya Carr
University of Pennsylvania Perelman School of Medicine

Research area:
Metabolism and lipid droplets in liver disease

Mentor:
Nick Davidson

Read more about the JLR Jr. AEs in the December issue of ASBMB Today.

MEET Sean Davidson

The JLR associate editor rethinks cholesterol

By Laurel Oldach

Sean Davidson is a confirmed Midwesterner.

"My entire career has been pretty much on the I-70 corridor," said Davidson, a professor at the University of Cincinnati. "I've been across the highway but not more than an hour north or south of it."

Davidson grew up and went to college in Indiana. After doctoral studies at Drexel University in Philadelphia and a postdoc at the University of Illinois Urbana–Champaign, he started as an assistant professor at the University of Cincinnati in 1998. Today, he leads the university's division of experimental pathology, has won numerous excellence in teaching awards, and runs a research lab with physician-scientist Amy Shah.

The lab focuses on high-density lipoprotein particles, which to many people are synonymous with "good cholesterol." But Davidson cringes at that term. To him, HDL is much more than a vessel for cholesterol transport; it's a complex mixture of dozens of proteins and hundreds of lipids.

"If we can understand the different subparticles within the family of HDL," he said, "we can impact biology that affects a lot of different disease states."

ASBMB Today writer Laurel Oldach talked to Davidson, an associate editor of the Journal of Lipid Research, about his research into the composition of HDL particles and their roles in disease. The interview has been edited for length and clarity.

What draws you to studying high-density lipoproteins?

HDL has been a controversial area in the past couple of years. Epidemiological evidence suggests that HDL cholesterol levels in blood are a negative risk factor for cardiovascular disease. People thought for a long time that it promotes cholesterol efflux and removes cholesterol from the coronary arteries around the heart, helping to prevent cardiovascular disease. But there's been a lot of evidence recently that drugs that can raise HDL cholesterol really high — which makes your doctors very happy — don't translate to the protection you'd expect from the epidemiology. From that perspective, HDL is not popular

Sean Davidson expresses his appreciation for high-density lipoprotein with a vanity plate on his 1966 Mustang convertible.

to work on right now because the drugs that target HDL haven't been that successful.

But I tend to look at HDL from a different viewpoint — as a platform that circulates in the plasma that allows different proteins to get together, dictating distinct functions. I don't think HDL evolved to protect us from heart disease; I think it evolved as almost an extracellular version of a plasma membrane. A plasma membrane has a barrier function, but it also acts as a medium that allows proteins to find each other more easily than if they were diffusing randomly. HDL serves this function outside the cell — kind of a singles' bar for circulating proteins.

Some of the proteins it assembles are involved in cardiovascular disease. That's for sure. But many are involved in the immune response; some are involved in blood clotting and protease inhibition; some are even involved in metal and vitamin transport. It's such a fascinating and complex platform for a lot of biology that we don't fully understand.

Is HDL one thing? Or is it a lot of different things that behave similarly?

I don't think there's one type of HDL. I think there are probably upward of 50 different particles in a family that happen to spin out at the same density in an ultracentrifuge. If you put protein and lipid together, no matter what, they're probably going to have about the density of HDL. In terms of its composition, there are about 100 different

> "There's been a lot of evidence recently that drugs that can raise HDL cholesterol really high — which makes your doctors very happy — don't translate to the protection you'd expect from the epidemiology."

COURTESY OF SEAN DAVIDSON

Sean Davidson (in red) outstrips opponents in the 2018 Ohio state road racing championships.

proteins that can be associated with HDL and hundreds of different lipid species.

I think the initial studies may have done us a disservice by thinking about HDL only in terms of its cholesterol composition rather than thinking of it as a constellation of different particles. We got onto cholesterol back in the old days because it was easy to measure, and it has just carried over.

Since different HDL particles have similar physical characteristics, it's hard to tease them apart and figure out what they do individually. That's what my lab is specializing in doing. We're trying to find ways to separate HDL subspecies and figure out what they do and how that functionality may differ from other particles.

Technically, how do you approach analyzing HDL particles? It sounds like they all look similar in some ways.

HDL is a good example of the observer effect problem in science. It's kind of like counting butterflies in a box. You have to open the box to count them, but opening the box causes you to lose some before you can get an accurate count. Similarly, you have to isolate HDL before you can study it, and how you isolate it can affect its composition and function.

We have taken the approach of using very gentle biochemical methods to get at these particles without putting them under harsh ionic strength conditions or high G-forces. We do a lot of chromatography to complement analytical approaches, and we have been working to come up with antibodies that can label very specific subspecies of HDL. The goal is to use those clinically to link certain subspecies to specific functions and eventually to different disease states.

> "I joke that apoA-I is like a piece of spaghetti that you take out of the pot and throw on the wall. However it lands, that's the shape it is."

Are there special challenges to raising an antibody against a lipoprotein?

ApoA-I, the major protein on HDL, exists in at least three different conformation states. It can be lipid-free; it can be bound in nascent, immature HDL particles; and it can be found in larger, spherical HDL particles. The immunoreactivity is different in each of those states.

And it's so dynamic. I joke that apoA-I is like a piece of spaghetti that you take out of the pot and throw on the wall. However it lands, that's the shape it is. That's the major challenge.

Are all these different types of HDL particles pretty highly regulated? Is the variety of compositions uniform, or is HDL more of a random jumble?

In the studies that we've done, different people have clearly different subspecies patterns. I don't think they're randomly distributed. There's definitely a method to the distribution; it's just we don't fully understand it.

I really hope that we can understand this heterogeneity and we can design drugs or therapies that skew the HDL particle populations toward the particles that are most beneficial for certain disease states.

(With current therapies) we raise HDL cholesterol in the general sense. Companies have invested billions of dollars in a class of drugs that target cholesterol ester transfer protein, which exchanges cholesterol and triglycerides between HDL and other lipoproteins. If you shut that off, the HDL accumulates lots of cholesterol. And your doctor wants to see your HDL cholesterol levels as high as possible. So, from that standpoint, these drugs work great: They can raise HDL cholesterol levels upward of 100%.

But these are very large, abnormal HDL particles that we think either are dysfunctional themselves or have metabolically eliminated other HDL particles that are important. And unfortunately, these drugs haven't been terribly successful in preventing cardiac outcomes. So indiscriminately raising HDL cholesterol across the board is probably not the way to go. We think it will be better to target certain subspecies that may be more connected with disease.

Besides heart disease, what other disease states might HDL be involved in?

Because a lot of these particles have different immune molecules, they could have a role in many disease states. For example, we've got a project now studying how different HDL subspecies might guard against sepsis in a mouse model.

The problem with sepsis is not necessarily the underlying infection. The clinical aspect that's so damaging is the immune response that follows. The immune system hyper-responds, and that causes cytokine release and, eventually, organ damage. HDL is linked to anti-inflammatory effects, so we think that HDL is a natural target for calming the body's immune response in the face of sepsis.

Stepping back a bit, how did you get into science? What made you decide on research?

I've always been pretty analytical, a geek, if you will. I was one of those annoying kids that took things apart and wanted to figure out why things worked. Both my parents were pharmacists, so I knew a bit about science from them. In high school, I thought about being an architect. But as soon as I got to college and took my first chemistry class, I said, "This is pretty cool stuff!" and just locked into it.

When you do a series of experiments, you learn something that nobody else knows and nobody in the history of mankind has ever known. That's an amazing feeling.

I also enjoy training students in the laboratory and helping them on their careers. That's been really fulfilling, along with the science.

I hear you're a cyclist in your spare time. Is that a hobby where you get to take stuff apart and put it back together again a lot?

Yes, unfortunately. The three important things in my life are my family, science, and cycling — not necessarily in that order. I've been racing a bicycle since I was in high school, so pretty much all my spare time I'm riding my bike. I'll usually go for a three- to five-hour ride on Saturday and the same on Sunday. I do a lot of road racing, and I was fortunate enough to win the Ohio state championship this year for road time trial among men in my age group.

It's hard to remain competitive in cycling and still keep my lab running, but I think I've struck a good balance. Physical exercise and doing something you love like that are important to maintain a balance, because otherwise you'd go crazy.

And it's important for creativity. Sometimes, I'll be out for a long ride and I'll zone out, and I'll come back and hang up my bike in the garage and have designed a whole experiment in my head without thinking about it.

"When you do a series of experiments, you learn something that nobody else knows and nobody in the history of mankind has ever known. That's an amazing feeling."

How did you become associated with the JLR?

It's always been one of my favorite journals. I have a file folder filled with papers from different people, but the JLR ones always seem to be the most ragged. The important papers that I go back to are usually in JLR.

I can't remember when my first JLR paper was — it must have been not long after I started my career. (JLR Associate Editor) Alan Attie invited me to join the editorial board soon after I became an assistant professor, and after three or four cycles, they invited me to be an associate editor.

Do you have any advice for young scientists?

My advice is to stick with it. I see a lot of kids who see how tough grant writing is and postdocs that last a lot longer than three to four years, and a lot of them chose to do something else. I hate to see that.

This is a tough business. You put your best work into a paper or a grant, and you send it out to people whose job it is to criticize it. That can be hard. But the rewards outweigh the setbacks, eventually. My advice is to get as broad an experience as possible in different laboratories, get with advisors who will help you come up with a project that will be yours, and just keep working at it.

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

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EB Experimental Biology

2020 Award Winners

Among the unquestionable highlights of every American Society for Biochemistry and Molecular Biology annual meeting are lectures by the society's award winners. These awards are given to outstanding professionals who have been recognized by their peers for contributions to their fields, education and diversity.

On the following pages, we introduce the dozen distinguished scientists who will be honored at the 2020 annual meeting, April 4 – 7 in San Diego. Our contributing and staff writers talked to them about their professional journeys and the research they plan to discuss in their lectures.

As you read these profiles, think about the outstanding scientists you know. We hope you'll be inspired to nominate one of them (or yourself) for an award. Nominations for the 2021 awards will be accepted March 2 – May 11, 2020. Nominating instructions will be posted at asbmb.org/awards.

2020 RUTH KIRSCHSTEIN DIVERSITY IN SCIENCE AWARD

Allison focuses on thyroid hormone receptors and equity

By Nathalie Gerassimov

When Lizabeth Ann Allison was the biology department chair at William & Mary, she recruited Shantá Hinton as the college's first minority tenure-track-eligible scientist. Almost a decade later and now a tenured professor, Hinton remembers Allison's words to her then: "You are scientifically strong, emotionally strong, and I know that you are capable of handling this."

Allison, now a chancellor professor of biology at W&M, will receive the American Society for Biochemistry and Molecular Biology's 2020 Ruth Kirschstein Diversity in Science Award. Hinton nominated her for the honor, writing, "She has truly been a trailblazer in serving and changing the dynamics of our institution, and encouraging underrepresented minorities to continue to pursue scientific careers, by supporting our passion for science."

Allison's support for diversity stems partially from her own experience in the 1980s when few women were high ranking academic scientists. Without female role models, it was her male predoctoral research mentors who "saw a potential in me that I didn't know I had," she said.

She explored many interests as an undergraduate at the University of Alaska, but when those mentors told her she needed to earn a Ph.D. and become a faculty member, science won out over creative writing and theater.

She was the first woman to chair the biology department at W&M; during her tenure, the percentage of underrepresented minority students graduating in biology and neuroscience more than doubled.

Allison has a keen eye for untapped potential. "In my lab, there are some students that would have succeeded in any lab," she said, "and then there are those students that need just a little bit of extra encouragement to show their true potential; those are the students that most benefit from my mentorship."

Lizabeth Ann Allison

Getting there: Thyroid hormone receptor intracellular trafficking

The butterfly-shaped thyroid gland, located at the base of the neck above the collarbones, uses iodine derived from food together with the amino acid tyrosine to make the hormones thyroxine and triiodothyronine. These two hormones circulate in the blood and are taken up by cells where they bind to thyroid hormone receptors, or TRs, which then can act as transcription factors.

TRs mainly are found in the nucleus but also can be shuttled to the cytosol, and the Allison lab studies the post-translational regulation of the nucleocytoplasmic shuttling of TRs. In a recent paper the group showed that acetylation promotes cytosolic TR localization and affects the ligand-dependent transcriptional activity.

Asked about her interest in this trafficking, Allison said that understanding TR function "gets to be such a complicated story, which is, of course, why I find it all really exciting and fascinating."

Molecular and cellular biologists sometimes can get lost in all the details. "Although we want to know the nitty gritty of the molecular mechanism," she said, "we also have to keep a big picture in mind."

Allison's lab at William & Mary continues to study how disruptions of TR transport and interactions can lead to endocrine disorders.

Allison will give a lecture tentatively titled "Getting there: thyroid hormone receptor intracellular trafficking" at the ASBMB annual meeting.

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

HERBERT TABOR RESEARCH AWARD

Campbell builds partnerships to study muscle biology

By Nathalie Gerassimov

Kevin Campbell always knew he wanted "a job with no tie," he said. His daily commute in a hot train to and from Wall Street for a summer college job reinforced that preference.

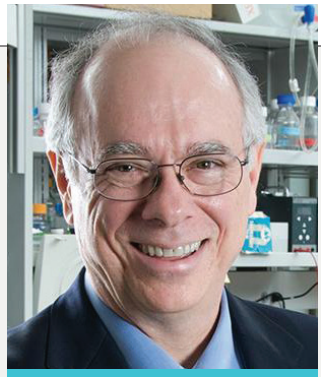
More than four decades later and now a Howard Hughes Medical Institute investigator at the University of Iowa, Campbell might be tieless when he receives the American Society for Biochemistry and Molecular Biology's 2020 Herbert Tabor Research Award. In a joint nomination letter, Gerald W. Hart and Lance Wells of the University of Georgia called Campbell's lab "the world leader in the study of the molecular mechanisms of muscular dystrophy."

Campbell's group has published more than 450 papers, many on groundbreaking discoveries such as the identification and characterization of dystroglycan as an extracellular matrix receptor involved in anchoring the muscle membrane and cytoskeleton to the basement membrane. He also is dedicated to maintaining the highest standards in training and mentorship for students and postdoctoral fellows in his lab.

After starting his lab in the 1980s, Campbell realized he needed dystrophin mutant tissues to test a hypothesis. He met a physician who routinely operated on patients with Duchenne muscular dystrophy, a genetic disorder involving a dystrophin deficiency. During the operations, tissues were removed and discarded. Campbell started to collect these discarded tissues for experiments that confirmed his hypothesis.

This began a decades-long collaboration with physicians around the world. It was also the conceptual beginning of the Wellstone Muscular Dystrophy Cooperative Research Center, dedicated to diagnosis and development of therapeutic approaches. Campbell is its director.

When high schoolers ask about joining his lab, Campbell encourages them first to try odd jobs and learn to interact with all kinds of people; his high school job at a cemetery and his Wall Street job in college taught him a lot about working with people.



Kevin Campbell

Elucidating mechanisms underlying dystrophies

Kevin Campbell's lab focused on muscle excitation contraction coupling until a failed hypothesis (that dystrophin associated with Ca^{2+} channel) opened a new research direction. His team purified and later cloned and characterized dystroglycan. They elucidated the molecular pathway involved in dystroglycan maturation and how mutations in dystroglycan processing enzymes therein cause muscular diseases.

The lab studied the functions of two molecules involved in dystroglycan maturation and implicated in muscular dystrophies: LARGE and POMK. They showed that LARGE is a bifunctional glycosyltransferase that synthesizes a matriglycan, a polysaccharide containing a novel O-glycan. They found a mechanism where one disaccharide suffices for high-affinity binding of the extracellular matrix independent of the underlying protein.

POMK previously was thought to be a pseudokinase because its structure lacks several amino acids thought to be essential for a kinase. Campbell's group in collaboration with Jack Dixon's lab found that the ER-resident POMK adopts a kinase fold due to formation of disulfide bonds, a finding that has reinvigorated the pseudokinase research field.

Jamey D. Marth wrote in support of the award nomination that such discoveries make Campbell "the most innovative and accomplished biomedical researcher in the field of muscular dystrophy."

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

ASBMB–MERCK AWARD

Winding path leads to plant enzyme breakthrough

By Elizabeth Stivison

After finishing high school in Singapore, where she grew up, Manajit Hayer–Hartl trained as a teacher because, she said, "Most educated women in those days in Singapore ended up being teachers."

She lasted about a year before realizing that she didn't want to read the science her 14-year-old students read; she wanted new, exciting science. So she applied to a chemistry Ph.D. course in Scotland. It wasn't what her parents had in mind, but "my parents couldn't really stop me since I wasn't relying on (them) for funding," she said.

"I can laugh about it now, but 40 years ago you really had to fight against the system."

Her fight paid off with a distinguished career and, most recently, the American Society for Biochemistry and Molecular Biology's 2020 ASBMB–Merck Award for research in biochemistry and molecular biology.

After her Ph.D. and postdoc, Hayer–Hartl met her future husband, Ulrich Hartl, at a meeting in Greece. He wanted to move to the U.S., and "I'm a nice wife so I went along," she said. She worked in his protein folding lab in New York, which led to some new experiences.

"I'd never run a gel in my life," she said. Others in the lab were unfamiliar with her chemistry skills. It was a great melding of knowledge. When the couple moved to the Max Planck Institute of Biochemistry, Hayer–Hartl worked independently in her husband's lab.

With the goal of studying how the photosynthesis enzyme RuBisCo is synthesized in plant cells, in 2006 Hayer–Hartl became the leader of her own research group at Max Planck. She was the first person to synthesize plant RuBisCo in Escherichia coli and firmly established herself as the leading expert on RuBisCo biogenesis. This work not only earned her the respect of colleagues across fields from plant biology to biochemistry but brings her daily joy.

"Every day I learn something new," she said. "This is where I find the greatest satisfaction."

Manajit Hayer–Hartl

Synthesizing plant RuBisCo in E. coli for the first time

RuBisCo is the most abundant protein on Earth; all biomass depends on its function, because plants need it to incorporate carbon dioxide into glucose. But RuBisCo is inefficient. About 25% of the time, it incorporates oxygen instead of CO_2, effectively wasting the enzyme's function, and this has a direct effect on crop yield.

Researchers have the skills to do mutagenesis and screen proteins for optimal function, but they could not do this with RuBisCo, because no one was able to synthesize the enzyme from plants in the lab; its assembly of eight large subunits and eight small subunits was too complicated.

Manajit Hayer–Hartl and her lab team solved this problem when they found the factors that help plant RuBisCo fold and assemble. In addition to the chaperone system that includes Cpn60/Cpn20, there are four other required factors: Raf1 and 2, RbcX, and Bsd2. Each of these proteins acts at different stages: Some help with folding, some help stabilize the folded form and some assemble the whole hexadecameric complex.

When Hayer–Hartl's lab expressed these factors in E. coli along with the components of RuBisCo, for the first time scientists were able to synthesize plant RuBisCo outside of chloroplasts, a huge step for optimizing its function.

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

AVANTI AWARD IN LIPIDS

Schaffer is motivated to pass on good mentoring

By Laurel Oldach

Jean Schaffer wasn't expecting any more major news this summer as she wrapped up a move from Missouri to Massachusetts.

"I got the email from (ASBMB President) Jerry Hart the day I was closing on my house and getting on a plane to come to Boston," Schaffer said. "It was so unexpected."

That email advised Schaffer, who was moving to assume the role of senior investigator and associate research director at the Joslin Diabetes Center at Harvard Medical School, that she had won the American Society for Biochemistry and Molecular Biology's 2020 Avanti Award in Lipids.

When she decided to move her lab, Schaffer's main concern was for her trainees. "The most challenging part is to make sure that everybody from my group who can't come can land on their feet and move ahead, and that this won't be a big bump in the road for them," she said.

Her commitment to mentoring comes from her own experiences. "I was incredibly fortunate to have worked with outstanding mentors who really helped shape my career," she said. "So I'm highly motivated to pay that forward."

After graduating from Harvard Medical School, Schaffer pursued further clinical training in cardiology followed by a postdoc at the Massachusetts Institute of Technology with cell biologist Harvey Lodish. She joined the faculty at Washington University in St. Louis in 1995. There, she built a lab studying lipid-induced metabolic stress and cell death and was promoted to full professor and director of the university's Diabetes Research Center. Now she's launching a new chapter in Boston.

"Colleagues who I've known for many years in the metabolism and diabetes fields are here in the Boston metro area," Schaffer said. "It's wonderful to be closer to collaborators and to really drink up some of this exciting environment."

Schaffer's other service to the field includes helping to organize the Deuel and Kern conferences on lipids for some years and service as an associate editor for the Journal of Lipid Research and on two other editorial boards.

Jean Schaffer

Understanding — and preventing — lipotoxicity

Inspired by cardiovascular comorbidities in diabetic patients, Jean Schaffer studies lipotoxicity, the means by which metabolic stress can harm cells. Her award talk tentatively is titled "Death by lipids: The role of noncoding RNAs in metabolic stress."

Using a genetic screen for variants that protect cells from death after excess lipid intake, Schaffer's lab discovered a role in lipid-induced death for a class of noncoding RNAs known as small nucleolar RNAs. The snoRNAs in question are encoded in the introns of a protein-coding gene, so confirming the discovery involved some tricky genetic dissection and rescue experiments; the unexpected result has become a core element of Schaffer's scientific reputation.

Projects involving other genes revealed in that screen are approaching a stage when they'll be ready to present. It's too soon to know whether they'll be ready by the ASBMB annual meeting in April, Schaffer said, "but you can rest assured that I will talk about how we've leveraged genetics to uncover the molecular transducers of metabolic stress."

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

WILLIAM C. ROSE AWARD

Schiffer takes a multidisciplinary approach

By Mohor B. Sengupta

Celia Schiffer prefers to approach problems from a multidisciplinary viewpoint. She studied physics as an undergraduate at the University of Chicago and then expanded to biophysics — combining biology, chemistry and physics — for her Ph.D. at the University of California, San Francisco.

"Even when I did my Ph.D., … I worked at the interphase between doing experimental crystallography and computational molecular dynamics," she said, "and that continues to this day when I apply biophysics, structural biology and chemistry to elucidating the molecular mechanisms of drug resistance in quickly evolving diseases."

For her multidisciplinary work on drug resistance, Schiffer will receive the American Society for Biochemistry and Molecular Biology 2020 William C. Rose Award recognizing contributions to biochemical and molecular biological research and commitment to the training of younger scientists.

Schiffer started the Institute for Drug Resistance in the University of Massachusetts Medical School, which she currently heads. Her lab is known for a culture that enables researchers from diverse backgrounds to pursue their work amicably within the group.

"My lab has gained the reputation for being a friendly, supportive place to learn and do science," Schiffer said.

She believes being respectful to fellow researchers is the key to a successful lab where science can be pursued without stresses that often selectively affect international students and those from underrepresented minority backgrounds.

Schiffer finds that some students suffer from imposter syndrome — believing they are not as good as their peers — despite what their professors or peers actually think. Exposure to broader scientific platforms, such as attending conferences, helps these students realize their potential, she said.

"I try to encourage my students so that they are able to see how their project fits into the bigger picture."

Celia Schiffer

Beating drug resistance

Much of Celia Schiffer's work is on elucidating how mutations in drug targets affect resistance to the drug. Schiffer is interested in the specificity of molecular recognition.

"Drug resistance occurs as a result of evolution," she said, "when drug pressure changes the balance of molecular recognition events, selectively weakening inhibitor binding by mutation while maintaining the biological function of the therapeutic target." These changes involve alteration of both the structure and the dynamics of the target.

In her award lecture at the 2020 ASBMB annual meeting, Schiffer will talk about strategies to avoid drug resistance in the drug-design process.

One such strategy arose from her team's recognition that many resistance mutations occur where the inhibitor protrudes beyond the volume necessary for substrate recognition.

By targeting an inhibitor to the substrate envelope, the probability of resistance can be decreased, as a mutation impacting the inhibitor binding will compromise substrate turnover.

"We discovered and validated this strategy through inhibitor design and testing in several systems," Schiffer said. These systems include viral proteases in HIV and hepatitis C. The concept is broadly applicable to other quickly evolving diseases such as cancer.

Mohor B. Sengupta (mohorsengupta@gmail.com) has recently transitioned into a science writing position from being a postdoctoral researcher at the National Institutes of Health. Read her blogs at mohorsengupta.com and sciencepolicyforall.wordpress.com.

DELANO AWARD FOR COMPUTATIONAL BIOSCIENCES

Zhang takes the lead in protein modeling

By Courtney Chandler

The old adage "Function depends on structure" has been taught in protein biology courses for decades. Yet as some of the most complex and versatile biomolecules, proteins can be challenging to structurally define. Bioinformatics algorithms that predict 3D protein structure based on amino acid sequence are crucial for deducing the biological function of proteins that have not been structurally characterized by other methods.

Yang Zhang, a professor of biological chemistry and computational medicine and bioinformatics at the University of Michigan, has developed a repertoire of computational methods for predicting protein structure. For his work, Zhang is being awarded the American Society for Biochemistry and Molecular Biology's 2020 DeLano Award for Computational Biosciences.

After earning a Ph.D. in physics, Zhang began applying his background to translational science, partially because biomolecules were more tangible than the theoretical concepts of particle physics.

"As a scientist and human being, I want to understand how and why a protein that's coded from DNA can fold into a stable 3D structure," he said. "That is the secret of life."

His methods, including prediction algorithms I-TASSER and QUARK, have been listed consistently as top-tier based on fieldwide assessments. William Smith, a professor emeritus at the University of Michigan, described Zhang as "a worldwide leader in structural bioinformatics and protein structure modeling" in his letter nominating Zhang for the award.

For Zhang, the thrill of basic discovery goes hand-in-hand with translational impact. Both can be aided significantly by structural prediction and modeling algorithms.

"If we can computationally model protein shape, it will have a big impact on drug design and discovery, and on human health in general," he said. "But … it is also important for us to understand protein systems and the life science systems they are involved in outside of disease."

Zhang also has begun to harness the increased power that comes with machine learning, which enables computational systems to improve their function based on experience without explicit programming.

"Now you can tell a computer to learn the principles of a system even if you don't understand them, and the computer will generate a model," he said. "This will represent a big change for the field."

Yang Zhang

Enhancing protein structure prediction algorithms

Computation-based protein structural modeling provides a fast and inexpensive way to investigate protein-related scientific queries across many disciplines. However, partially due to the complicated nature of proteins and their folding patterns, the researchers behind computational programs have struggled to make protein structure prediction methods more accurate.

Using machine learning, Yang Zhang recently has leveraged big data from whole-genome sequencing studies to improve upon his existing computational models. This approach enables him to derive co-evolutionary relationships among proteins, which helps improve prediction of protein structure.

Zhang's award lecture, "Toward the solution of the protein structure prediction problem," will focus on the progress the field has made in improving protein prediction models and what the future will look like.

Courtney Chandler (courtneyec19@gmail.com) is a postdoctoral researcher at Johns Hopkins University and a careers columnist for the ASBMB. Follow her on Twitter @CourtneyEChan.

WALTER SHAW YOUNG INVESTIGATOR AWARD IN LIPIDS

Labeling lipids and playing piano

By John Arnst

For Jeremy Baskin, learning a new arrangement on the piano isn't so different from tagging and tracking phospholipids.

"When you play the piano, and you want to learn a hard passage, you have to do it slowly. And you have to do it over and over again to get the muscle memory correct," said Baskin, a professor at Cornell University's Weill Institute for Cell and Molecular Biology and department of chemistry and chemical biology. "That's a good preparation for laboratory research, where you often have to repeat experiments and change variables in order to get it to work just right."

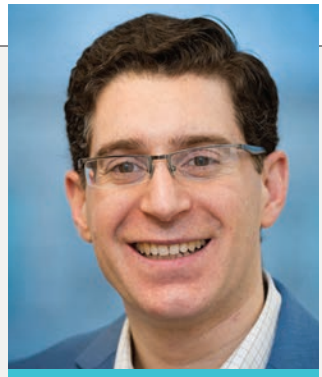
For about a decade of getting his work right, Baskin has been selected to receive the American Society for Biochemistry and Molecular Biology's 2020 Walter Shaw Young Investigator Award in Lipids.

He grew up in Montreal in a family with an artistic bent — both his parents are classical musicians, and his younger sister is now an actress. When he pursued chemistry as an undergraduate at the Massachusetts Institute of Technology, he found relaxation and camaraderie among fellow musicians.

"It being MIT, it wasn't populated with a bunch of future professional musicians," he said. "There was a lot of energy and focus on science and engineering majors that were doing music on the side."

In 2004, Baskin joined Carolyn Bertozzi's lab at the University of California, Berkeley, where he began developing chemical tools for imaging cell-surface glycans. In 2009, he took a postdoctoral fellowship in the lab of Pietro De Camilli at Yale University, where he narrowed his focus on membrane biology and lipid metabolism.

Baskin's lab primarily focuses on two types of phospholipids that represent extremes in terms of size: phosphatidic acids, which have tiny headgroups, and phosphoinositides, which have massive headgroups. The lab recently has been focusing on phospholipase D, a precursor to several cancer-associated phosphatidic acids that often is upregulated in cancer.



Jeremy Baskin

Studying in a rich playground

Jeremy Baskin's lab at Cornell University constantly is working on new tools to interrogate phospholipase D, an enzyme upregulated in a wide swath of cancers.

"There's a push in other academic laboratories to develop selective inhibitors of phospholipase D for the purpose of downregulating the proliferation of cells, which is a hallmark of cancer," Baskin said. "In the phosphatidic acid area, we've really focused much of our energy on the development of tools."

In his award lecture at the 2020 ASBMB annual meeting, Baskin will speak about recently developed lipid imaging methods.

"These enzymes are, I think, a really rich playground for a chemical biologist to operate in, because they have a relaxed specificity that it allows us to come in with synthetic probes and trick the enzyme into accepting our synthetic probes instead of their natural substrates. And that is the key that allows us to develop our imaging tools," Baskin said.

"We're currently using them to uncover how the phospholipase D enzymes and the phosphatidic acid lipids that they produce regulate fundamental cell signaling and disease-associated signaling."

John Arnst
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ASBMB AWARD FOR EXEMPLARY CONTRIBUTIONS TO EDUCATION

Black's career balances teaching and research

By Mohor B. Sengupta

When Paul Black was a postdoc at the University of California, Irvine, two undergrads helped him with projects on long-chain fatty acid transport that succeeded due to their combined efforts. The research was published in the Journal of Biological Chemistry, and that one-on-one interaction with students became the foundation of Black's teaching philosophy.

In honor of a career shaped by that philosophy, Black will receive the American Society for Biochemistry and Molecular Biology's 2020 ASBMB Award for Exemplary Contributions to Education.

Black was teaching biochemistry at the University of Tennessee in 1992 when the dean of medical education assigned him to develop a molecular cell biology program for medical students.

"This was in a time when there were more discipline-based classes being taught in the medical curriculum," Black said. His course used a multidisciplinary approach, something new in those days, and the medical students and the biochemistry department honored him with the Golden Apple Award for excellence in teaching.

At the University of Nebraska–Lincoln, Black developed a new approach to biochemistry education using experiential learning and critical thinking skills. "His mission at UNL has been to develop a biochemistry program of inclusive excellence," Donald Becker wrote in his letter nominating Black for the award.

Paul Black

Lipid metabolism and its practical applications

Paul Black's lab has done seminal studies addressing fatty acid uptake into the cell. His team purified and characterized the bacterial fatty acid transport protein FadL and, working with a Harvard group, crystallized the protein and verified it was a fatty acid-responsive channel. They discovered fatty acid transport protein 1, FAT1p, which plays a role in getting fatty acids into yeast. Recent work with the Wistar Institute shows increased expression of FATP2 (an ortholog of FAT1p) in certain cancers, where it appears to regulate arachidonic acid uptake.

Beginning with a $2.4 million Department of Energy grant, Black's team has addressed triglyceride synthesis in green algae for bioproducts and biofuels. By understanding the carbon–nitrogen balance during growth, they showed this system was also effective in removing nitrate from groundwater.

The aim is to mitigate a broad spectrum of health issues caused by high nitrate levels in groundwater prior to use for municipal drinking water.

Black bucks tradition with a specialized approach to designing biochemistry courses informed by basic research. He introduced a second-year course on scientific writing and analysis of scientific discourse and continues to receive positive feedback from students.

Black is passionate about inclusion in academia. "It is essential that we have inclusive excellence," he said, "and it is extremely important that in the STEM disciplines there is a balance between men, women, minorities and individuals from communities marginalized by the scientific community."

As chair of the UNL biochemistry department, he is close to his goal of a department with comparable numbers of male and female faculty. He is proud that his lab is enriched by students from many demographic and racial backgrounds.

Mohor B. Sengupta (mohorsengupta@gmail.com) has recently transitioned into a science writing position from being a postdoctoral researcher at the National Institutes of Health. Read her blogs at mohorsengupta.com and sciencepolicyforall.wordpress.com.

BERT AND NATALIE VALLEE AWARD IN BIOMEDICAL SCIENCE

A quest to understand plasma membranes and develop lipidomics

By Tori Zirul

What began as a high school passion for science developed into a fascination with stereochemistry when Edward Dennis took an organic chemistry class at Yale. Stereochemistry became a common thread in his career, beginning with his Ph.D. research with Frank Westheimer at Harvard, where he applied pseudorotation to explain phosphate ester hydrolysis, and continuing with lipid enzymes as a postdoc with Eugene Kennedy.

Now a professor at the University of California, San Diego, Dennis will receive the American Society for Biochemistry and Molecular Biology's 2020 Bert and Natalie Vallee Award for his accomplishments in biomedical research.

As a new assistant professor at UCSD in the 1970s, Dennis was studying enzymes acting on phospholipid membranes when he obtained a vial of snake venom from India. Cobra venom contains a small stable enzyme, phospholipase A_2, or PLA_2, that is easy to work with in the laboratory. The Dennis group took advantage of this, analyzing PLA_2 from structure to function. What they learned from this research and the lab's later work on human PLA_2s advanced the understanding of enzymes acting on membranes and inflammation's role in numerous illnesses. It also led to the development of stereo-specific inhibitors as potential drugs for conditions such as inflammation and neurological diseases.

Dennis also has been a pioneer in the lipidomics movement. In 2002, as the principal investigator of a $73 million, multisite 10-year grant from the National Institutes of Health, he conceived of and led the LIPID MAPS initiative, which developed and applied techniques for characterization and classification of tens of thousands of lipid molecular species.

In recommending Dennis for the Vallee award, Jean-Pierre Changeux noted "his many basic discoveries on lipids and phospholipases and … the opening and promotion of an entirely new field of research, lipidomics, together with the creation of an international consortium of scientists at the world scale."

Edward Dennis

Paths to pain and inflammation

In his lecture at the ASBMB annual meeting, Edward Dennis will talk about how membranes interact allosterically with enzymes to regulate cell signaling and metabolic pathways leading to inflammation.

Dennis has used substrate lipidomics coupled with molecular dynamics to reveal enzyme specificity linked to hydrophobic binding sites for membrane phospholipid substrates. He discovered unexpected headgroup and acyl chain specificity for each of the major human phospholipase A_2 enzymes that explains the observed specificity at a new structural level.

Dennis' lab discovered that a unique hydrophobic binding site — and not each enzyme's catalytic residues or polar headgroup binding site — dominates each enzyme's specificity. Each PLA_2 shows unique specificity for its required fatty acid ranging from pro-inflammatory arachidonic acid to membrane remodeling linolenic acid, antibacterial saturated fatty acids and oxidized fatty acids in low-density lipoproteins.

PLA_2 releases a specific fatty acid after the enzyme associates allosterically with membranes and extracts the phospholipid substrate, which can be blocked by stereospecific inhibitors. After decades of work, Dennis and his team now can correlate PLA_2 specificity and inhibition potency with molecular structure and physiological function, using a novel lipidomics platform.

Tori Zirul (tezirul@gmail.com) studied molecular virology at Montclair State University and is passionate about communication, advocacy and education of the sciences.

ALICE AND C.C. WANG AWARD IN MOLECULAR PARASITOLOGY

Johnson innovates in the study of a neglected parasite

By Courtney Chandler

The parasite Trichomonas vaginalis causes the world's most common nonviral sexually transmitted infection. In 2014, the Centers for Disease Control and Prevention named trichomoniasis one of the U.S.'s "Neglected Parasitic Infections." Yet Patricia Johnson has done anything but neglect this parasite — she's made a career of it.

For her work, Johnson, a distinguished professor at the University of California, Los Angeles, will receive the American Society for Biochemistry and Molecular Biology's 2020 Alice and C.C. Wang Award recognizing seminal contributions to the field of molecular parasitology.

Johnson began working on Trichomonas 30 years ago. Research on this parasite was minimal at the time, she said, describing the field as a blank slate. She used her training in molecular biology to lay the groundwork for what we know about Trichomonas today. She was the first researcher to clone and analyze a gene in T. vaginalis, and she led a team of researchers to sequence and annotate the first T. vaginalis genome.

"I realized that many systems could be studied in parasites," Johnson said. "I'm fascinated by how many properties parasites have evolved to interact with the host and survive in such hostile environments."

For the past decade, Johnson has focused on these interactions. Her work has shed light on a novel mechanism of immune-cell killing of T. vaginalis and has defined critical factors that influence infection outcome, including parasitic surface molecules that are involved with adherence and lysis of host cells.

In her letter nominating Johnson for the award, Sabeeha Merchant, distinguished professor at the University of California, Berkeley, lauded Johnson's "distinguished career, defined by innovation, creativity, and discovery" and called her a "leader and innovator" in the field.

Johnson said she finds comfort in her research as a refuge from real-life worries, which is part of what keeps her motivated, along with the challenge of answering scientific questions.

"I like solving the puzzle," she said, "looking at new information and trying to make sense of it."

Patricia Johnson

Killing a parasite with trogocytosis

Trichomonas vaginalis infects an estimated 3.7 million people annually in the U.S. Men typically have no symptoms, but in women the parasite causes pain, itching and, if they are pregnant, a risk of premature delivery.

Patricia Johnson's recent research focuses on the aspects of the host–parasite interaction that affect infection outcome. Her lab has found that neutrophils, white blood cells involved in the early immune response to infection, use a mechanism called trogocytosis to kill T. vaginalis. Trogocytosis is essentially immune cells nibbling away at the parasite until a critical level of damage is reached, leading to the parasite's death. This work is the first to describe trogocytosis as a mechanism of neutrophil killing.

Johnson also has characterized extracellular vesicles called exosomes that are secreted by T. vaginalis during infection. These vesicles then are internalized by host cells and can modify the host cell response to infection, essentially reprogramming these cells and the host response in a way that is beneficial to the parasite. Johnson's research will continue to expand the field's understanding of parasite–host interactions.

Courtney Chandler (courtneyec19@gmail.com) is a postdoctoral researcher at Johns Hopkins University and a careers columnist for the ASBMB. Follow her on Twitter @CourtneyEChan.

EARL AND THRESSA STADTMAN YOUNG SCHOLAR AWARD

Pagliarini chanced into groundbreaking mitochondrial research

By Gelareh Abulwerdi

Dave Pagliarini's research career had a bumpy start. By his third year of graduate school, he had followed his advisers to three labs across the Midwest and West Coast. He finished his Ph.D. in biomolecular sciences at the University of California, San Diego. Pagliarini learned a lot from each adviser, he said, and "those challenges became my accelerators."

Those accelerators have propelled him through almost a decade of productive mitochondria research, for which Pagliarini will receive the American Society for Biochemistry and Molecular Biology's 2020 Earl and Thressa Stadtman Young Scholar Award.

Pagliarini got into mitochondria research by chance when, as a grad student, he identified a new mitochondrial phosphatase that plays a critical role in biosynthesis of the essential cardiolipin required for optimal mitochondrial bioenergetics. This discovery led him to look for other mitochondrial proteins with unknown functions that could play a role in mitochondrial diseases.

Mitochondrial diseases affect one in every 4,000 individuals; uncharacterized mitochondrial proteins contribute to diseases such as mitochondrial encephalomyopathy, a neurodegenerative disorder for which there are no curative treatments.

During his postdoc in Vamsi Mootha's laboratory at Harvard, Pagliarini established a compendium of more than 1,000 mitochondrial proteins by combining in-depth computational biology and biochemistry. He called it MitoCarta and published his findings in the journal Cell. Although this approach at first provided only a descriptive dataset, what set Pagliarini apart from others in his field was "his ability … to gain understanding of underlying cellular, biochemical, and physiological processes and mechanisms," Christopher Newgard wrote in a letter supporting the award nomination.

Pagliarini is now the lead investigator and Arthur C. Nielsen chair of metabolism at the Morgridge Institute for Research. His lab works to discover additional orphan mitochondrial proteins and characterize them from molecular to organ level.

Dave Pagliarini

MitoCarta: the key to unlock mitochondrial diseases

As a postdoc, Dave Pagliarini led the development of MitoCarta, a compendium providing an extensive map of mitochondrial proteins. Since then, his lab has become known for using systematic lipidomics, proteomics and metabolomics screens to study the effects of the loss of individual mitochondrial proteins and then digging into those proteins' biochemical activities. One example is the team's analysis of the biosynthetic pathway that generates coenzyme Q.

Coenzyme Q, or CoQ, a lipid member of the mitochondrial electron transport chain remarkable for its redox activity, was discovered in the late 1950s just down the street from Pagliarini's laboratory in Madison, Wisconsin. Although this unusual lipid is involved in myriad mitochondrial diseases, its biosynthesis and transport are not completely understood, which makes understanding the associated diseases difficult.

Mapping the CoQ synthesis pathway led Pagliarini's lab to discover the functions of multiple orphan proteins. One is CoQ9, a lipid chaperone that binds to CoQ intermediates and is essential for its biosynthesis. Another is CoQ8A, an atypical kinase/ATPase essential for the assembly of the CoQ biosynthetic complex. Each of these proteins has been shown to play a role in mitochondrial diseases.

Gelareh Abulwerdi (gelareab@umaryland.edu) is a Ph.D. candidate at the University of Maryland, Baltimore. Follow her on Twitter @gelareh_science.

MILDRED COHN AWARD IN BIOLOGICAL CHEMISTRY

Fierke works as a catalyst for change

By Kerri Beth Slaughter

When she was a professor at the University of Michigan, Carol Fierke helped draft a proposal to increase diversity in the chemistry department. With funding from the National Science Foundation Michigan ADVANCE program, Fierke and her colleagues developed strategies to make the department more welcoming for women and minorities.

Building her knowledge of social science literature was crucial to modifying the culture, Fierke said. She worked with a universitywide committee to develop a workshop to teach faculty about the literature and to train search committees on best practices. The Michigan chemistry department faculty went from a low of 8% to now almost 30% women.

"We completely changed the face of the department," she said.

Now provost and executive vice president of Texas A&M University, Fierke is a distinguished enzymologist who continues her work on behalf of underrepresented groups. Scientists like Mildred Cohn, the first woman to hold the presidency of the American Society for Biochemistry and Molecular Biology, opened doors for women in the sciences and inspired her to follow their example, Fierke said, so it is fitting that she will receive the ASBMB's 2020 Mildred Cohn Award in Biological Chemistry.

Fierke's experience as an advocate for diversity influences the way she mentors her students, particularly women and underrepresented minorities, who often struggle with building confidence.

"I tell my students you don't have to be confident, just act confidently — eventually you become confident because people see you that way," she said.

She encourages her students to learn skills beyond the bench and do some soul searching to find careers in which they can thrive.

"I know that when I was a doctoral student, I thought there was one career pathway, but that's not true," she said. "There are lots of pathways to get to a final goal."

Fierke's advocacy continues at Texas A&M, where she aims to increase faculty diversity, enhance interdisciplinary research and increase student success.

Carol Fierke

Analyzing protein deacetylase mechanisms

Biological catalysts have unique active sites that determine the specificity and efficiency of substrate binding. Carol Fierke's research has focused on understanding how metal ions in the enzyme active site can regulate catalytic mechanisms. Her award lecture during the ASBMB 2020 annual meeting will highlight her work on a group of enzymes known as protein deacetylases.

Deacetylase enzymes are involved in removing specific post-translational modifications from proteins. Fierke uses her expertise in catalysis and metal homeostasis to answer questions about which metal ions are physiologically important for the function of the enzymes. Additionally, she has made strides in understanding how metal ion switching may regulate biological function. Her lab is developing a toolbox of methods to identify the pathways and substrates utilized by these deacetylases.

The Food and Drug Administration has approved several histone deacetylase inhibitors as anticancer compounds, but the inhibitors often have serious side effects. Findings by Fierke and others may contribute to the development of new histone deacetylase inhibitors with reduced side effects and enhanced efficacy as therapeutic agents.

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

Weaving social innovation and scientific methods for a bright future

By Pingdewinde Sam

When I was growing up in a small district of Ouagadougou, the capital city of Burkina Faso, my parents made sacrifices that showed me the importance of education, sharing knowledge and giving back to my community.

My native country is small, just a little larger than Colorado, and underdeveloped. Although the United Nations Development Programme ranked us second to last in the world for education in 2009, I believe it is a country with a better future. For the past eight years, through a foundation I call Teêbo, I have been working from the U.S. to help make that future.

My parents never made it past primary school. Through their faith, they showed what it means to love and give with very limited resources. We were poor, yet they joyfully practiced true hospitality. Sometimes more than 14 people lived in our house; we didn't have enough, but my parents welcomed others who needed help, offering a place to stay or a meal. Continually exposed to this spirit of giving, I wanted to help improve other people's lives.

My childhood in one of the poorest countries in the world shaped my mind. My parents made sacrifices to send me and my three siblings to school. I was sent home many times during primary school for not paying the full $70 tuition. Public schools were full, and my grades were not excellent enough for a national scholarship, but my parents never gave up. They encouraged me to do well in school, and I realized then that knowledge is so powerful no one should be deprived of it.

Over the years, seeds were planted in my heart to create learning opportunities for those who couldn't afford school and, above all, to mentor and help those in need.

The land of opportunity

Through a green card lottery, I immigrated to the United States at the age of 19. My older brother Barkwendé Bonaventur, who dreamed of coming to the U.S., registered himself in the U.S. Diversity Immigrant Visa Program and forcibly took my weekly allowance of 500 CFA francs (the equivalent of $1) to register me as well. The registration was free, but my precious dollar paid 60 cents for one hour at a local internet café to complete the online application and 40 cents to scan in my profile picture. The average Burkinabé lives on less than $1 per day.

I was angry when my brother took my money. He applied two years in a row before me but never was selected, and to this day, he still applies. I wasn't interested, but he believed I had a chance. It turned out to be a wonderful opportunity that changed my life and created financial sustainability for my family and many people in my community.

Without any of my immediate family, I moved to San Francisco. I was a young immigrant from a developing country who spoke no English. Fortunately, my wonderful and supportive uncle Beniwendé George Kabré lived there and was an exceptional mentor to me.

Because I was studious and worked hard, my chemistry teacher in junior college, Ronald Drucker, advised me to apply to the National Institutes of Health Bridges to the Baccalaureate Research Training Program in 2011. I seized the opportunity and was accepted. Since then, I have been guided and trained by incredible mentors at the City College of San Francisco; San Francisco State University; the University of California, San Francisco; and Johns Hopkins University. I am now a fifth-year Ph.D. candidate in cellular and molecular physiology at the Johns Hopkins University School of Medicine. But I never forgot where I came from.

Making a difference

On Christmas Day 2005, my dad taught me a lesson about the impact of a small action of generosity. It was a difficult year for my family. My father didn't make much profit from his jewelry shop, and my mother was medically disabled. My parents always gave us new clothes and shoes on Christmas, so I went to my dad expecting these gifts. He said that he didn't make enough money to get us new clothes. I went to my room crying.

My dad called me back a few

Farmers in the Goennega village show samples of their corn harvest at an August 2015 meeting to measure the impact of Teêbo's End Starving Season agricultural program.

TEÊBO

ABOUT THE SERIES

Scientific research can be an all-consuming passion, inspired by a desire to build knowledge and make the world a better place. Some scientists find time to go outside their labs and give time to help their communities in other ways. We are sharing their stories in this 2020 essay series, Service Beyond Science. To contribute an essay, go to asbmb.org/asbmbtoday and click the Submit button. Questions? Send an email to asbmbtoday@asbmb.org.

TEÊBO

A sixth-grade student, age 12, in the Vipaolgo Village shows off school supplies she received in October 2017 through the Teêbo Exam Prep Program. The supplies were donated by the Science Education Partnership and Assessment Laboratory at San Francisco State University.

JAMES OSEI-OWUSU

The Teêbo Exam Prep Program provided these sixth graders at Primary School A in Goumsin village with new required French reading books in October 2018 to help them prepare for the national exam to enter seventh grade.

minutes later and gave me two envelopes with less than $10 in each. He told me to take them to two neighboring families from my childhood church. I was confused — he didn't make enough money to buy clothes for us, but he had some to share? The first family was a widow with seven children. When I handed her the small gift, the emotions in the house changed; the family was overjoyed and super excited. The second family responded in the same way, and this transformed my bitterness to joy. From that lesson in sharing, I learned that a small act of generosity could make a big difference.

I had my first real job in 2008 after I moved to San Francisco. My people in Burkina Faso struggle with basic needs such as education, food, clean water and sanitation. To help address these needs, I started to save and frequently wired money for my family to support those who struggled to survive. In 2011, I went home for the first time since moving to the U.S. What I saw saddened me, and I felt called to offer hope to Burkinabés who lack basic needs.

We named our organization Teêbo, which is the word for hope in Mooré, the national language in Burkina Faso. The organization focuses on eliminating poverty and hunger, increasing the literacy rate, combating water-related diseases by drilling wells, and improving health in Burkina Faso. In 2012, it was incorporated as a 501(c) 3 U.S.-based nonprofit organization.

More crops, more education

Teêbo is run by volunteers here and in Burkina Faso. Our U.S.-based board of directors helps us secure financial resources. In Burkina, a local team runs day-to-day activities, while in each village we choose four or five ambassadors to represent us and be our eyes and ears.

With Teêbo, we have built programs to engage, equip and empower Burkinabés in rural areas. Our End Starving Season program aims to increase crop yields that sustain thousands of lives. We equip hardworking farmers with animal-powered plows and bags of fertilizer, and we teach them new farming techniques.

In Burkina Faso, students must pass a national exam to enter the seventh grade, but many fail and drop out of school. Only 29% of adults are literate, and just 2% of all Burkinabés have a secondary education. My team has developed an Exam Prep Program for sixth-grade students in villages. The six-month program provides private tutoring, school supplies, meals and mentors. At the end of the pilot program in 2014, the first school more than tripled their success rate, from 30% to 98%. Since then, we continue to register incredible success rates, sending both girls and boys to school.

Most schools in Burkina lack basic teaching supplies. In 2016, I co-founded EDEN School with my wife, Wendpagnanda Christiane.

We aim to advance knowledge using the 5E model (engage, elaborate, explain, evaluate and examine) that I learned at the Science Education Partnership and Assessment Laboratory at San Francisco State University. Our curriculum and teaching strategies encourage teamwork with pre- and post-lecture assessments. We plan to implement STEM education through collaborations with scientists and teachers in the field and here at Hopkins.

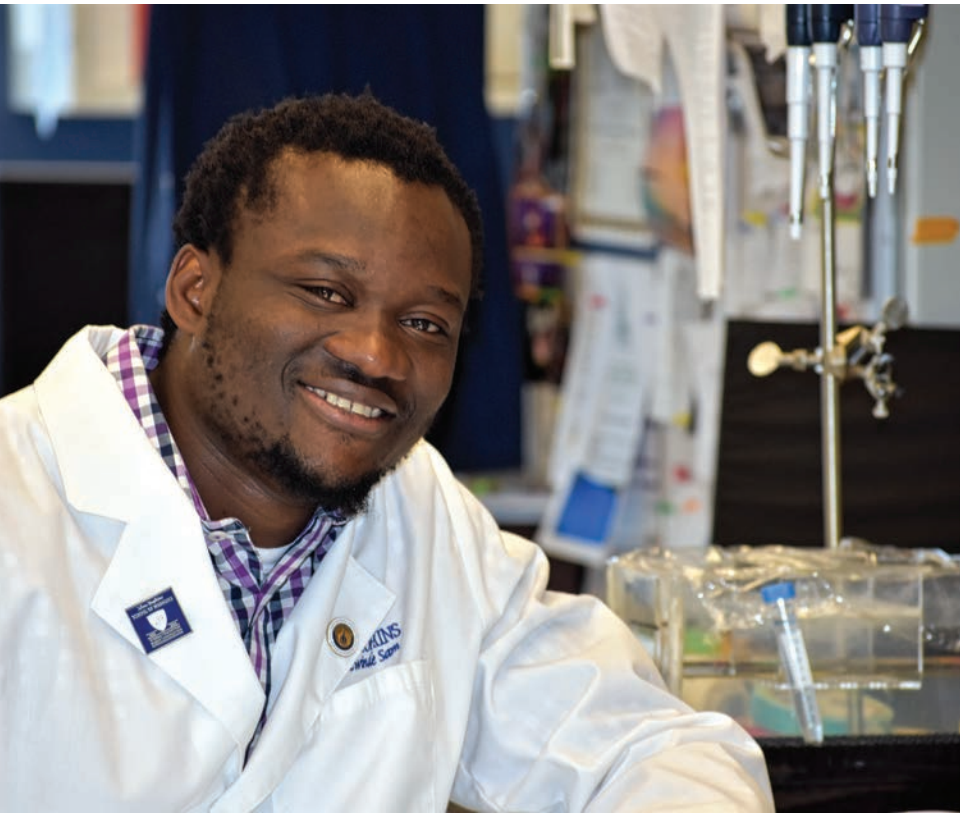
Weaving science and service

In my research lab, my mind often leads me to ask how my experiments can have a positive social impact. My service work is woven with my scientific research. My indelible long-term goal always has been to improve human health through improving quality of life and saving lives. This is constant whether I am wearing the hat of a social entrepreneur or a scientist.

I regularly apply the scientific method as founder and executive director of Teêbo. Our strategies to help the Burkinabés are intertwined with the scientific process of making discoveries. It starts with background research, collecting data in a new village. From that preliminary data, my team and I meet and launch a pilot program, which we then closely monitor to assess its effectiveness. Through measuring and analyzing the impact of the implemented programs, we can report back to partners and donors; this is the publication stage for us.

I have been able to use my research skills to help grow Teêbo and EDEN School. I look forward to a future when I'll contribute actively to enriching lives not just in my naturalized and birth countries but other countries as well, making our world a better place through my experiences in biomedical research and social innovations.

Pingdewinde Sam (psam1@jhmi.edu) is a Ph.D. candidate in the department of cellular and molecular physiology at the Johns Hopkins University School of Medicine and the founder of Teêbo.org. Follow him on Twitter @samestry.



Pingdewinde Sam, a Ph.D. candidate in the department of cellular and molecular physiology at the Johns Hopkins University School of Medicine, founded Teêbo, a nonprofit organization, to help people in need in his native Burkina Faso.

NEW!

ASBMB Today call for submissions

ASBMB Today is publishing a new essay series in 2020

SERVICE BEYOND SCIENCE

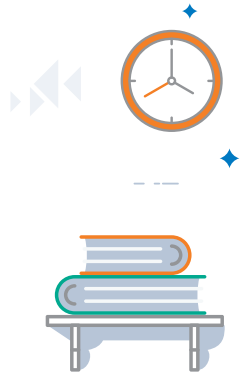
A career in the life sciences is demanding, but some researchers find time to give back to their communities — often in surprising ways. Do you do volunteer work that is unrelated to your life in the lab? Tell us about what you do and why.

Email asbmbtoday@asbmb.org for more information, or submit at asbmb.org/asbmbtoday.

Want to see an example? Pingdewinde Sam's essay, "Weaving social innovation and scientific methods for a bright future," is on page 50 of this issue.

Upcoming ASBMB events and deadlines

NOVEMBER	1	Proposals for 2021 symposia due
	3	Student Chapters northeast regional meeting
	14	Deadline for abstracts for 2020 annual meeting
	16	Student Chapters Outreach Grant deadline
	18–24	**U.S. Antibiotic Awareness Week**
	20	Student Chapters renewal deadline
	27	Deadline for 2020 annual meeting travel award applications
DECEMBER	2–8	**National Influenza Vaccination Week**
	5	ASBMB–Deuel Conference on Lipids early registration deadline
JANUARY	1–31	**National Mentoring Month**
	30	Deadline for last-chance abstracts for 2020 annual meeting
	30	Deadline for scientific outreach abstracts for 2020 annual meeting
	31	Deadline for Student Chapters Honor Society applications



ASBMB

T-SHIRT CONTEST

All ASBMB members are eligible to submit a T-shirt design related to biochemistry and molecular biology.

The winning T-shirt will be sold at the 2020 ASBMB Annual Meeting in San Diego.

Submit your shirt design by Jan. 27. There will be one winner from ASBMB Student Chapters and one winner from all other member types.

For more details visit **asbmb.org/meeting2020/tshirt/**

ASBMB
American Society for Biochemistry and Molecular Biology

IMPORTANT DATES

Dec. 5: Early registration deadline

Feb. 4: Abstract-submission deadline

Feb. 19: Registration deadline

2020 ASBMB–DEUEL CONFERENCE HAVEL LECTURE

Dynamics of membrane trafficking, sorting and compartmentalization within eukaryotic cells

Jennifer Lippincott-Schwartz, HHMI Janelia Research Campus

asbmb.org/deuelconference/

CLASSIFIEDS

University of Calgary
Canada Research Chair (CRC) Tier II in the area of Chemical Lipidomics

The Departments of Biological Sciences and Chemistry in the Faculty of Science at the University of Calgary invite applications for a Canada Research Chair (CRC) Tier II in the area of Chemical Lipidomics. The successful candidate will be appointed at the rank of Assistant Professor (tenure-track) or in exceptional cases as an Associate Professor (with tenure) and will be nominated for an NSERC Tier II Canada Research Chair. The candidate's program is expected to combine recent advances in analytical technology and big biological data analysis via biochemical techniques, including high-resolution mass spectrometry to radically expand the practical scope of Lipidomics analyses of the complex molecular phenotypes that contribute to health or disease. The anticipated start date for the position is September 1, 2020.

http://www.asbmb.org/Careers/Jobs/81758/

Kennesaw State University
Dean of the College of Science and Mathematics

Kennesaw State University invites applications and nominations for the position of Dean of the College of Science and Mathematics.

The Dean of the College of Science and Mathematics acts as its chief academic and administrative officer, charged with fostering growth and development of students, faculty and staff to advance the College. The next Dean will have a body of high impact, peer-reviewed scholarship supported by extramural sources such as federal agencies, national/international foundations, and/or recognized corporate entities. The selected candidate will have a strong track record of fruitful collaborative initiatives comprising varied constituents. The search committee is seeking an individual who will be a powerful advocate for the quantitative and natural science departments of the College, both within and beyond the university.

https://www.asbmb.org/Careers/Jobs/81754/

University of California, Santa Cruz
Physical and Biological Sciences: Biomedical Sciences – Assistant Professors

The Division of Physical and Biological Sciences at the University of California, Santa Cruz invites applications for tenure-track Assistant Professors in global and community health who conduct basic and/or translational research that addresses human health and disease, and have interests in promoting diversity, equity, and inclusion. Four positions will be filled in 2020.

Successful candidates will be invited to join one of the following departments: Molecular Cell & Developmental Biology; Chemistry & Biochemistry; and Microbiology & Environmental Toxicology. Areas of particular interest are: 1) Stem Cell Biology, including the biology of stem cells in development and cancer; 2) Cell and Molecular Biology of Parasitic and Infectious Diseases, with emphasis on diseases that impact large disadvantaged populations or on development of chemical methodologies that lead to better treatments; 3) Structural Biology, with emphasis on cryo-electron microscopy; and 4) Microbiology, with emphasis on the microbiome and the mechanisms by which it influences host physiology and the immune system, or how the microbiome is influenced by environmental, chemical, and genetic factors. In addition to these specific areas, we will consider all candidates with interests in human health and disease who can make exceptional contributions to leadership in diversity, equity and inclusion and whose research interests fit within the broader subject areas encompassed by the participating departments.

https://www.asbmb.org/Careers/Jobs/81755/

Montana State University
Postdoctoral Fellows

Postdoctoral positions are available in three areas concerning redox and metallobiochemistry:

(1) An interdisciplinary study has been funded to describe the symbiotic relationships between the gut microbiome and the animal host that allow both to metabolize different forms of iron. This project is a collaboration between faculty in the biochemistry and microbiology departments, and offers opportunities in sophisticated informatics, computational, gnotobiotic mouse-model, and molecular biochemical studies.

(2) An interdisciplinary collaboration is in place involving the National Renewable Energy Lab (NREL) and U. Portsmouth, UK. It has been formed to study the bioconversion of natural and man-made (plastic) polymers. Collaborative partners span the disciplines of biocatalysis, structural biology, genetic and enzymatic engineering, in vitro evolution, and informatics.

(3) A DOE-funded study of Fe metabolism pertinent to the origins of life on earth and astrobiology is at its inception. This project is a collaboration with the Boyd group at MSU.

https://www.asbmb.org/Careers/Jobs/81751/

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

ASBMB'20

ANNUAL MEETING
SAN DIEGO | APRIL 4-7, 2020

Community Binds Us

Take your place among a diverse network at the 2020 ASBMB Annual Meeting. Attend high-caliber lectures, participate in hands-on workshops and team up with the best minds in your field to strengthen your life's most important work. Discover your common bond.

Regular abstract deadline: Nov. 14

Submit your abstract today! asbmb.org/meeting2020

EB Experimental Biology