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ASBMB TODAY

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METAL ART, MICROBIAL CULTURE

ANNUAL MEETING

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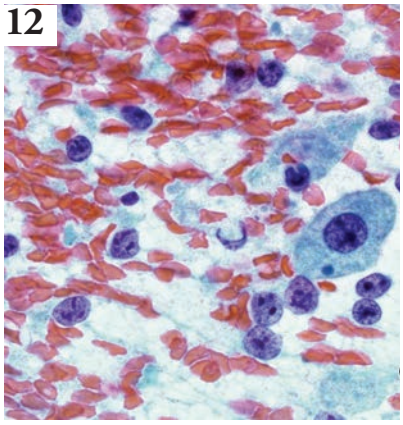

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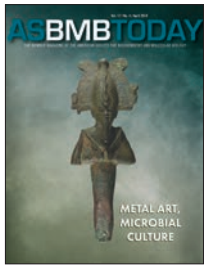

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WHEN SCIENCE MEETS SICKNESS

ASBMB TODAY
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Gathering our community

By Natalie Ahn

Get ready for the 2018 American Society for Biochemistry and Molecular Biology Annual Meeting.

Co-chairs Jin Zhang and Wilfred van der Donk and the ASBMB Meetings Committee have put together a truly exciting program, with trend-setting research at the cutting edge of BMB and myriad opportunities for participants to present their work. To those of you who are planning to come, welcome — I look forward to seeing you at the year's most important event. To those still undecided — please join us.

So why should you attend the ASBMB annual meeting?

In this age of accelerating discovery, none of us can conduct research without interdisciplinary breadth. It's the challenge of 21st-century science to stay abreast of new ideas, even in areas you don't engage with directly. But keeping up can be tough, especially when more than 60,000 papers are published each year in BMB alone.

At ASBMB 2018, you'll grok the molecular mechanisms of life in all its breadth and beauty. Symposia, awards and spotlight presentations will showcase the latest findings on topics that bring together biomolecular structure and folding, chemical and metabolic regulation, CRISPR/Cas9 gene editing, chromatin and epigenetics, regulatory RNA, signaling and biochemical communication, enzyme catalysis, and large-scale systems biology. Advanced technical workshops will offer everything from big picture concepts to nitty-gritty details of the technologies everyone needs to know: cryoEM, optogenetics, molecular biosensors, nanodiscs and organoid cultures. The knowledge you gain at the annual meeting will keep you up to date and sharpen your competitive edge.

On top of this is the value of networking with our broad and brilliant community. Find new colleagues and collaborators at poster sessions, social mixers, and daily "Meet the Speakers" events. Learn about the latest strategies in science education and methods for teaching concepts-driven and hypothesis-based thinking. And learn how to advance your career at any stage, with workshops on strategically building your CV, achieving success in scientific publishing, and presenting your work to any audience.

Staying current also means staying abreast of research funding. Your ASBMB Public Affairs Advisory Committee is investing wide-ranging advocacy efforts to promote federal support for basic research. Hear the latest on the state of federal investment in science research and policy changes affecting the research community at the Advocacy Town Hall.

Where else can you get this much bang for your buck? Don't miss this opportunity to build your knowledge, meet leaders in research and education, and make lifelong friends — all in one place. We'll see you April 21–25 in San Diego.

Natalie Ahn (natalie.ahn@colorado.edu), a professor of chemistry and biochemistry at the University of Colorado, Boulder, is president of the ASBMB.

We want you to be part of #ASBMBHillDay

By Benjamin Corb

Members of the Public Affairs Advisory Committee and 20 student scientists from across the country will descend on Washington this month for the American Society for Biochemistry and Molecular Biology's Capitol Hill Day. Hill Day is one of our most exciting events. We will take thousands of steps in the marble hallways of Capitol Hill, attending more than 100 meetings with elected officials and their staffs all in one fast-paced day. Participants will discuss the need for increased and sustainable funding for the scientific enterprise and for Congress to put forth a legislative agenda to ensure a fertile environment for American science.

This year, we are working hard to provide advocacy outlets for the Hill Day applicants we can't bring to Washington, D.C., and we want to offer you the same opportunities. The ASBMB public affairs office and the committee invite you to participate in a cyber Hill Day. We want you to send messages to your elected officials through telephone calls, emails and social media tools. Together, we will amplify the message we are delivering in person on the Hill.

How is this going to work?

The in-person Hill Day happens April 12. While your colleagues are sprinting from one meeting with lawmakers to the next, you can sit comfortably in your lab, home or office and deliver the same messages. The public affairs staff is developing a materials, everything from telephone scripts to tweetable internet memes for you. Your involvement is key. We need you to spread the importance of science research by re-sharing Hill Day posts and adding your thoughts.

Beyond your own social network, ASBMB staff will provide you with relevant information (phone numbers, email addresses, and Twitter and Instagram handles like #ASBMBHillDay) to ensure that your elected officials hear and see a steady stream of messages throughout the day. Our staff will monitor social media, looking to reinforce your messages through sharing and retweeting. We'll also create a Storify, capturing the day's activities in one place so we can look back and see all the messages we've delivered and the impact we've had.

The young scientists joining us in person for Hill Day come from across the country and were chosen for a variety of reasons. Some live in states or congressional districts represented by politicians who hold key committee assignments and influence funding of such federal agencies as the National Institutes of Health or the National Science Foundation. Others were chosen because they wrote provocative essays expressing their passion and commitment to science advocacy. Some participants come from parts of the country that do not receive much research funding, where federal research dollars have high economic impact and where the research is just as important as in well-funded areas. About 300 scientists applied for the 20 spots for this year's Hill Day, which means we had to make very difficult decisions and turn away hundreds of great scientist-advocates. But, thanks to our social media campaign, even the folks we won't be able to bring to Washington will still have their voices heard!

While we cannot bring everyone to Capitol Hill, we invite you, your colleagues, your friends and family to join us in this effort. The more people get involved and the more messages we deliver, the greater impact our advocacy efforts will have.

If you want to participate or want more details, visit www.asbmb.org/advocacy/HillDay.

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

Member update

By Erik Chaulk

Members named Sloan fellows

Hannah Shafaat, Timothy Wencewicz and Xin Zhang are among the 126 scientists named as 2018 Sloan Research Fellows.

Since 1955, the Alfred P. Sloan Foundation has awarded fellowships annually to early-career scientists who have distinguished themselves among their peers and have demonstrated the potential to contribute significant future research in their field.


SHAFAAT

Hannah Shafaat is an assistant professor in the department of chemistry and biochemistry at the Ohio State University. Her research is concentrated on the study of metalloenzymes.


WENCEWICZ

Timothy Wencewicz is an assistant professor in the department of chemistry at Washington University in St. Louis. His research is focused on antibiotic drug discovery.


ZHANG

Xin Zhang is an assistant professor of chemistry and biochemistry and molecular biology at Penn State. At his lab, he develops novel chemical tools to gain greater understanding of protein misfolding and aggregation.

Sloan fellows each receive $65,000 to support their research over a two-year term.

Hall honored at BioAsia

Michael N. Hall, a professor at the Biozentrum University of Basel, Switzerland, has received the Genome Valley Excellence Award for his research on TOR proteins.


HALL

The award was presented to Hall in February in Hyderabad, India, at BioAsia 2018, a biotechnology conference promoting collaboration and innovation in the life sciences.

Awarded by the government of Telangana, India, since 2004, the Genome Valley Excellence Award recognizes individuals and organizations for their contributions in life sciences research and public health.

Hall was honored for his discovery of nutrient-activated target of rapamycin, or TOR, proteins and their role in controlling cell growth.

World Academy honors Visweswariah

Sandhya Visweswariah is among 55 new fellows elected to the World Academy of Sciences in 2018.


VISWESWARIAH

Visweswariah is a professor and chair of the department of molecular reproduction, development and genetics at the Indian Institute of Science, Bangalore. She also serves as co-chair at the Centre for Biosystems Science and Engineering at the Indian Institute of Science.

Visweswariah's research focuses on signal transduction mediated by cyclic nucleotides. Among her research accomplishments, Visweswariah characterized novel enzymes and proteins involved in cAMP-mediated metabolism in Mycobacteria. She also studies a mammalian receptor guanylyl cyclase, Gucy2c, and characterized genetic mutations responsible for human diarrheal disease.

Founded in 1983, the World Academy of Sciences promotes scientific research, education and policy in developing countries.

Carpenter wins grant

Susan Carpenter, an assistant professor of molecular, cell and developmental biology at the University of California, Santa Cruz, has been awarded a $550,000 grant for her research on chronic obstructive pulmonary disease.


CARPENTER

The grant comes from the California Tobacco-Related Disease Research Program, which is funded by the state's tax on cigarettes. COPD is a lung disease involving chronic bronchitis and emphysema, commonly caused by smoking.

Carpenter's lab studies the molecular mechanisms that control the innate immune responses. She will use this grant to research the molecular signals involved in the response of immune system cells to cigarette smoke and the impact on COPD. This grant will help Carpenter discern the pathogenesis of COPD, which could lead to the development of

therapeutic treatments.

Booker named Eberly chair

Squire J. Booker, a professor of chemistry and of biochemistry and molecular biology at the Pennsylvania State University and an investigator with the Howard Hughes Medical Institute, has been appointed the Eberly Family Distinguished Chair in Science at Penn State.


BOOKER

The Eberly chair is one of the university's highest honors, recognizing the outstanding achievements of a member of the faculty.

Booker received the Penn State Faculty Scholar Medal in 2016 and the Arthur C. Cope Scholar Award from the American Chemical Society in 2011.

Since he joined the faculty at Penn State in 1999, Booker has mentored numerous students. His research explores the molecular details by which enzymes catalyze reactions in the cell, and he has published close to 100 papers throughout his career. He is also a member of the ASBMB Minority Affairs Committee.

In memoriam: Angelo Scanu

University of Chicago professor emeritus Angelo Scanu passed away Jan. 12 after a fall in his home. He was 93.


SCANU

Scanu was born in Sassari, Italy, in 1924. He received his bachelor's degree from the Scientific Lyceum in Sassari and later earned a medical degree from the Sassari University Medical School, where he also completed his internal medicine internship and residency training.

Scanu served as a research fellow at Barcelona University Medicine School and Lund University Medical School before returning to Italy in 1953 to join the faculty at Naples University.

He won a Fulbright Scholarship to study biochemistry at the Cleveland Clinic and then joined the faculty at the University of Chicago, where he held numerous positions until his retirement in 2010.

Scanu's research focused on the study of the structure and function of plasma lipoproteins. He contributed to the understanding of the structure and biology of the lipoprotein known as Lp(a), which has been associated with cardiovascular disease.

Among his numerous accolades, Scanu received the 1994 Samuel R. Natelson Award from the American Association for Clinical Chemistry and the 1997 George Lyman Duff Memorial Lecture award from the Council on Arteriosclerosis, Thrombosis and Vascular Biology.

He is survived by his daughter, Gabriella; his son, Marco; and his two grandsons.

In memoriam: William Wells

Former Michigan State University professor William W. Wells passed away in May at the age of 89.

Wells was born June 8, 1927, in Traverse City, Michigan. He served in the Navy during World War II before attending the University of Michigan, where he earned his bachelor's degree in zoology and master's degree in biochemistry.

After attending the University of Wisconsin for his doctorate, Wells joined the faculty at the University of Pittsburgh School of Medicine. He stayed for nearly 10 years before leaving to become a professor of biochemistry at Michigan State University, where he remained until his retirement.

Wells' research focused on the metabolism of steroids, phosphoinositides and vitamin C. He authored more than 125 publications and 18 book chapters in his career.

Helen Wayt Wells, his wife of 64 years, passed away in 2015. He is survived by his four children, Thomas, Christopher, Jon and Anne, and his nine grandchildren.

In memoriam: Andrew Robertson

The ASBMB recently learned that Andrew David Robertson passed away Aug. 14, 2014, in Portland, Oregon. He was 55.

Robertson was born Feb. 20, 1959, in Gardena, California. He graduated from the University of California at San Diego with a bachelor's degree in biology. He earned his Ph.D. in biochemistry at the University of Wisconsin-Madison, where he met his future wife, Sue Travis.

They moved to San Francisco, where Robertson completed a postdoctoral fellowship studying RNAse. He later joined the faculty at the University of Iowa as a professor of biochemistry.

Robertson was named director of medical communications at Merck in 2004 and subsequently worked as chief scientific officer at Keystone Symposia, where he co-founded the Keystone Fellows, a diversity-centered program devoted to educating early-career scientists.


Erik Chaulk (echaulk@asbmb.org) is a peer-review coordinator and digital publications web specialist at the ASBMB.

Send us your news

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

Günter Blobel (1936 – 2018)

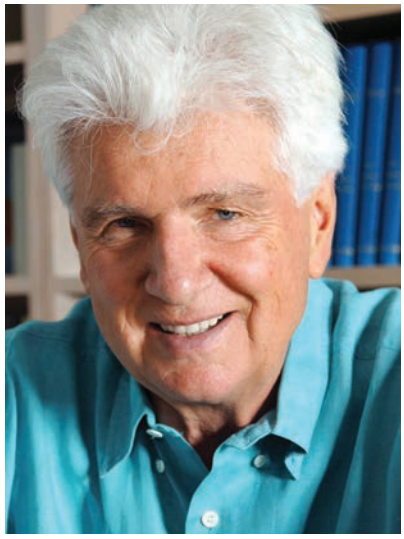
By Tom Rapoport

Günter Blobel, who died in late February at age 81 in New York City, was a giant of cell biology, a pioneer in determining how proteins are distributed to different sites in the cell. His most famous contribution, the signal hypothesis, now an established paradigm, earned him the Nobel Prize in Physiology or Medicine in 1999.

Early moves

Blobel was born May 21, 1936, in the Silesian village of Waltersdorf, back then in Germany and later part of Poland. After the war, the Blobel family settled in Freiberg, in East Germany. Günter graduated from high school in 1954 but was denied entry into university because his family was considered "capitalist" by the new authorities. He then moved to West Germany and studied medicine in Frankfurt, Kiel and Munich. He earned his medical degree at the University of Tübingen in 1960 and worked for two years as a hospital intern in Germany.

In 1962, Blobel decided he wanted to pursue science instead of clinical work. Following his brother's lead, he moved to the U.S., to the University of Wisconsin–Madison, where he joined the laboratory of Van R. Potter. In 1967, Blobel moved to the laboratory of George Palade at the Rockefeller University in New York City. This move could not have been better timed. At the Rockefeller, Palade, Albert Claude and Keith Porter had revolutionized cell biology, discovering all the major structures of the cell. Blobel arrived in time for the next stage of this revolution, the molecular and functional analysis of these structures.



COURTESY OF ROCKEFELLER UNIVERSITY

Günter Blobel

The science

Blobel's most influential papers were published together with his postdoctoral fellow Berhard Dobberstein in 1975 in the Journal of Cell Biology. These papers established that N-terminal signal sequences direct nascent secretory proteins across the endoplasmic reticulum membrane, an idea previously proposed by Blobel and David D. Sabatini in 1971, with first experimental evidence provided by César Milstein and colleagues in 1972. The Blobel and Dobberstein papers rigorously showed that a secretory protein is co-translationally translocated across the membrane and that the signal sequence subsequently was cleaved off.

The labs of Blobel and Dobberstein, the latter now independent and back in Germany, then discovered the signal recognition particle and its membrane receptor, which together target the ribosome/nascent chain complex to the endoplasmic reticulum membrane. Blobel extended his signal hypothesis to a general ZIP code system in the cell, where different amino acid sequences serve to target proteins from the cytosol to distinct organelles such as mitochondria, chloroplasts, peroxisomes and the nucleus. His lab provided some of the crucial experimental evidence for the new concept. He postulated that proteins move through membranes via protein-conducting channels, an idea that initially was controversial but later confirmed by various experiments.

Nuclear transport ultimately became Blobel's major interest. His laboratory contributed numerous discoveries, including insight into nuclear transport receptors, the role of the Ran GTPase and structural analysis of many components of the nuclear pore.

An amazing lab

I met Günter Blobel at a meeting in 1976 in East Germany, the country where I grew up. This was the first time I heard about the signal hypothesis, as scientific journals from the West took a whole year to arrive in our library. His talk was a revelation. I realized that the puzzling behavior of my in vitro-synthesized proinsulin was due to the absence of membranes, which resulted in the lack of signal sequence cleavage and disulfide bridge formation. This was the beginning of my own interest in protein translocation.

In subsequent years, Günter invited me for visits at the Rockefeller, and on one occasion, I even spent two months in his lab. I would give lab seminars, which always ended

COURTESY OF CHRISTIAN FLEMMING/LINDAU NOBEL LAUREATE MEETINGS

Günter Blobel talks to young scientists at the 57th Lindau Nobel Laureate Meeting in 2007.

up in a disaster, because all my slides were East German style and got stuck in the projector. Günter's lab was simply amazing, an assembly of extraordinarily talented people. I was impressed that each person had his or her own project and was competing successfully with larger labs working on the same problem. I believe that it was one of Günter's secrets of success that everybody in the lab was responsible for his or her own project. But it was Günter's passion that drove everything. His enthusiasm for science was obvious in discussions and seminars. I remember that, during a plenary talk, he got so carried away by his excitement that he repeatedly ran away from the microphone.

I am eternally grateful to Günter for his help in difficult times, when he allowed me to use my honoraria to order chemicals that I then would bring back to East Germany. Although I cannot consider myself a real "Blobelite," I benefitted from his generous support.

A man of culture

For his numerous trainees, he was the most loyal and supportive mentor. On one occasion, he invited them all to Dresden for visits to the opera and the Frauenkirche. This church, and much of Dresden, had been destroyed completely toward the end of World War II in a bombing attack by the Allies. After the unification of Germany, it was decided to rebuild the Frauenkirche, and Günter was one of the major forces behind the reconstruction. He not only donated the money of his Nobel Prize for this endeavor but was also the major fundraiser in the U.S. He was very passionate about the maintenance and restoration of cultural heritage in Germany, and he was not shy about fighting for it with the local authorities.

Günter was a charming and educated person with a great love for the arts and music. This, in large part, was stimulated by his wife, Laura Maioglio. I fondly remember joining the Blobels for a visit to the New York City Ballet, where Laura showed her Italian temperament, jumping out of her seat in joy when it was announced that Mikhail Baryshnikov would replace a sick dancer.

Günter Blobel was one of the most influential cell biologists of our time. He leaves numerous discoveries, now the content of textbooks, and a large number of friends and grateful trainees. He will be deeply missed.

Tom Rapoport (Tom_Rapoport@hms.harvard.edu) is a professor of cell biology at Harvard Medical School and a Howard Hughes Medical Institute investigator.

Using phospholipids to combat influenza A

By Dennis R. Voelker

The latest seasonal influenza A outbreak has delivered unpleasant surprises worldwide, strained emergency rooms and hospitals, and produced unanticipated levels of mortality among vulnerable populations.

Given the limited protection offered by vaccines, researchers are investigating other ways to address influenza A, including chemical inhibitors and, in the case of our lab, phospholipids that regulate innate immune processes and suppress infection by certain viruses.

The culprit in this year's outbreak, an H3N2 influenza strain, initially appeared well targeted by the current vaccine, which also includes immunogens for pandemic H1N1 and influenza B. However, while being propagated in eggs to produce the current vaccine, the H3N2 strain acquired a new mutation. The resulting viral immunogens constituting the vaccine were mismatched to the originally targeted H3N2 strain.

Mutation frequencies are relatively high in influenza strains because they are negative-strand RNA viruses, dependent upon the fidelity of RNA polymerases for replication of the genome. The RNA polymerases are much more error-prone than DNA polymerases, thus ensuring new mutations will occur every year. As a result, the current vaccine is estimated to be about 10 percent effective. Or, stated another way, 90 percent of vaccinated individuals will not be protected from infection. The ineffective vaccine also results in the general loss of herd immunity (the likelihood that a person next to you on a bus, train or plane is immune), increasing the probability of viral transmission from infected to uninfected individuals. Consequently, a large number of people are being infected with influenza this year compared to many previous years.

The present situation exemplifies some recurrent problems with the generation of annual influenza vaccines. It is not widely known that even in a year with a good match of vaccine to circulating virus, only about 55 percent of the immunized population is protected from infection. In years with a bad match between virus and vaccine, the efficacy is 10 percent to 20 percent. Over the past 13 years, the efficacy of influenza vaccines has averaged about 41 percent. Such statistics are likely to continue until a universal vaccine is found.

One approach to dealing with the influenza vaccine's shortcomings is to develop chemical inhibitors of virus infection, propagation and dissemination. Neuraminidase inhibitors, or NAIs, are one such class of compound that act by retarding the spread of virus from infected to uninfected cells. However, bypass of NAI action is known to arise spontaneously in many influenza A strains, even in the absence of selective pressure. Moreover, NAI treatment initiated early in influenza infection only reduces the course of disease by one or two days.

Our laboratory has been focused upon another class of molecules, the minor anionic lipids of pulmonary surfactant, exemplified by phosphatidylglycerols, or PGs, and phosphatidylinositols, or PIs. These lipids are secreted uniquely from the apical surface of the alveolar epithelium into the thin layer of fluid that separates the cell membrane from the air space. Surprisingly, these lipids exhibit potent regulation of innate immune processes. Among their activities, the lipids suppress infection of the epithelium by two classes of respiratory viruses: respiratory syncytial viruses and influenza A viruses such as H3N2 and H1N1. PG and PI inhibit the most crucial step of viral infection, the attachment of virus to cell surface receptor. This site of action by the lipids is most important because virus mutations that prevent interaction with lipids are likely also to prevent recognition of cell surface receptors, thereby making mutational bypass of lipid inhibition unlikely.

In addition to PG and PI, we have created libraries of lipids with similar headgroup structures that also exhibit anti-viral and immunoregulatory properties. Some of these analogs of PG and PI are likely to have improved pharmacological properties that could make them effective as short-term preventives or as therapeutics for established influenza infections. We believe that PG and PI along with their structural analogs should be considered as complementary approaches to vaccines for reducing influenza infections and their progression.

Dennis R. Voelker (voelkerd@njhealth.org) is the director of research of the pulmonary division in the department of medicine at National Jewish Health and a professor of biochemistry and molecular genetics at the University of Colorado, Denver.

Upcoming ASBMB events and deadlines

MAY

2: ASBMB award nominations deadline
11: Science Outreach: Models, Methods and Measures application deadline
20: World Autoimmune/Autoinflammatory Arthritis Day

JUNE

Alzheimer's & brain awareness month
1: Marion B. Sewer Distinguished Scholarship for Undergraduates deadline
14–16: IMAGE grant-writing workshop
21: Frontiers in RAS Pathobiology and Drug Discovery oral abstract deadline

JULY

10: Frontiers in RAS Pathobiology and Drug Discovery early registration deadline
19: Transcriptional Regulation by Chromatin and RNA Polymerase II oral abstract deadline
20: Frontiers in RAS Pathobiology and Drug Discovery poster deadline
28: World Hepatitis Day

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How an interest in bipolar disorder drugs led to a better understanding of leukemia

By Sasha Mushegian

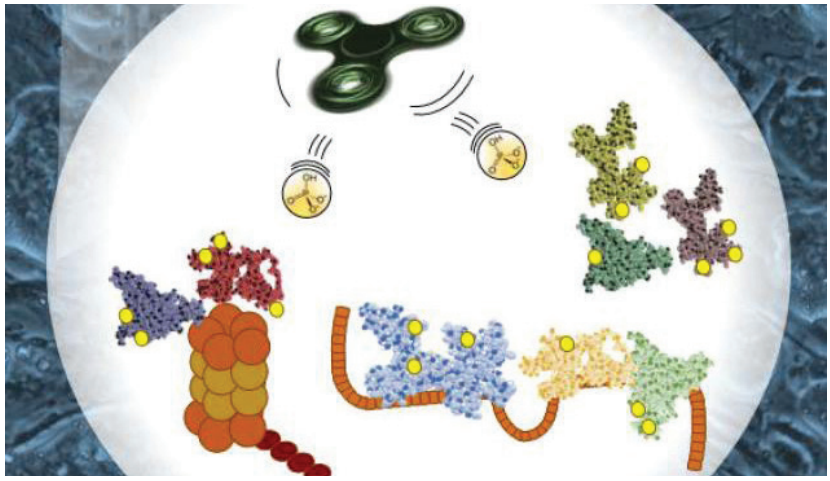
A research project that began 20 years ago with an interest in how lithium treats mood disorders has yielded insights into the progression of blood cancers such as leukemia. The research, which centers on a protein called GSK-3, was published in the **Journal of Biological Chemistry**.

Lithium is considered a highly effective treatment for bipolar disorder and other mood disorders, but it still works in only a fraction of patients and has a number of side effects. Furthermore, its mechanism of action is poorly understood, hampering efforts to improve on it.

In 1996, Peter Klein of the University of Pennsylvania discovered that one of lithium's biological activities was inhibiting GSK-3, an enzyme that modifies other proteins by attaching phosphate molecules, a process called phosphorylation. Lithium's effect on GSK-3 affected the development of animal cells, but it is still unknown what connection, if any, this has to psychiatric disease.

Since then, Klein — now a professor of medicine at Penn — has been investigating many aspects of GSK-3 activity. "In this paper, we were trying to find out what proteins in the cell are affected by GSK-3 inhibition," Klein said. "We compared cells with GSK-3 to cells completely lacking GSK-3 to ask how other proteins changed."

Mansi Shinde, a former graduate student in Klein's research group, led the new study. "Mood disorders are so multifaceted in terms of the pathways and pathologies involved; it's really difficult to pin down a specific pathway," Shinde said. "We said: 'Let's look at what GSK-3 does, and that would maybe lead us toward what lithium does.'"



COURTESY OF MANSI SHINDE AND SIMONE SIDOLI

A new project reveals that the enzyme GSK-3, a target of the mood disorder drug lithium, has a role in controlling alternative splicing in cells. This observation may yield insights into leukemia.

The research team used mass spectrometry to compare phosphorylation of proteins from mouse embryonic stem cells with fully functioning GSK-3 to cells in which the gene-encoding GSK-3 had been deleted. The resulting massive data set is called a phosphoproteome — a comprehensive catalog of proteins that are phosphorylated by GSK-3. Analyzing the data yielded some surprising findings.

Conventional wisdom had suggested that GSK-3 phosphorylates proteins that contain a specific amino acid sequence, but the new phosphoproteome showed that the majority of proteins whose phosphorylation depended on GSK-3 did not contain this sequence. Notably, the phosphorylated proteins included a group called splicing factors, which splice together different sections of messenger RNA, changing the proteins they encode. Absence of GSK-3 changed the splicing patterns of more than 200 messenger RNAs.

The finding that GSK-3 could affect RNA splicing pointed to an unexpected connection: leukemia. Several factors newly discovered to be phosphorylated by GSK-3 also are known to be mutated in acute myeloid leukemia, a condition in which aberrant splicing causes uncontrolled white blood cell proliferation. This observation could also explain why one of the side effects of taking lithium is increased white blood cell count.

"The effect on the splicing factors and other mutations associated with leukemia was completely surprising to me," Klein said. The group now is pursuing investigations into how GSK-3 affects the growth of healthy and leukemic blood cells.

Shinde and Klein are not sure whether GSK-3's effect on RNA splicing explains its role in mood disorders. The effect of GSK-3 on

CONTINUED ON PAGE 11

A molecular garbage disposal complex has a role in packing the genome

By Sasha Mushegian

Researchers from the Korea Institute of Science and Technology have found that the proteasome, an essential protein complex that breaks down proteins in cells, has an unexpected second function: directly regulating the packing of DNA in the nucleus. Their work was published in the **Journal of Biological Chemistry**.

The proteasome breaks down proteins that the cell has tagged for degradation in a process called proteolysis. Dysfunction in the proteasome has been observed in diseases of many physiological systems, from the immune, nervous and cardiovascular systems to the whole organism's aging processes. Increasingly, research suggests that, like a Swiss army knife with hidden tools, the proteasome is able to perform additional functions that don't involve proteolysis.

DNA is organized in the nucleus in complexes with protein in a form called chromatin. Broadly speaking, loosely packed chromatin, or euchromatin, allows DNA to be transcribed and genes to be expressed, whereas tightly packed heterochromatin prevents gene expression.

In experiments using yeast cells, Hogyu David Seo, a graduate student in Daeyoup Lee's lab, found that the proteasome could induce heterochromatin to form in some parts of the genome but stop it from spreading to other regions. Surprisingly, the mutations in the proteasome that revealed the proteasome's effects on chromatin had no effect on proteolysis, meaning that the proteasome affects heterochromatin through an activity other than proteolysis. How it does this is not yet known.

The proteasome "can exert force on proteins and translocate, tilt, bend them," Seo said. "So I believe the proteasome physically modulates proteins that act as a shield for heterochromatin. That's how I think it might work."

COURSTESY OF JOURNAL OF BIOLOGICAL CHEMISTRY

This artistic rendering by the authors was on the cover of the October 13 issue of JBC.

Heterochromatin formation and spread is of interest in the field of epigenetics, because changes in the chromatin state of cells in one generation potentially can be passed on to the next generation.

The proteasome "may have some effect on epigenetic programming inheritance because it affects the spreading of heterochromatin," Seo said. "I'm not really sure how it might work, because there are so many ways that it could act, but I'm sure that it may exert some effects on epigenetic programming."

For now, the team is focused on understanding how the proteasome regulates heterochromatin in organisms besides yeast, including mice and human cells.

"The proteasome engages with virtually every protein in our body with respect to the protein-degradation function," Lee said. "We believe that our work is just a glimpse of what this protein can do ... Dissecting the proteasome functions will definitely help to develop therapeutic strategies to various diseases, such as neurological diseases and cancer."

DOI: 10.1074/jbc.M117.790824

Sasha Mushegian (amushegian@asbmb.org) is scientific communicator for the Journal of Biological Chemistry.

CONTINUED FROM PAGE 10

disorders. The effect of GSK-3 on messenger RNA in neuronal cells, with or without lithium, would need to be examined to determine this. The study underlines how investigations into the basic biological function of a drug target can lead in unexpected directions. The GSK-3 phosphoproteome is "a really large data set," Shinde said. "It's a resource for the field."

"The relevance to leukemia could be direct and something worthy of immediate study," Klein said. "The role in psychiatric disorders is a major interest of the work, but the impact would be down the road, not immediate."

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Sasha Mushegian (amushegian@asbmb.org) is scientific communicator for the Journal of Biological Chemistry.

Proteome profiling dissects variations in tumors

By Saddiq Zahari

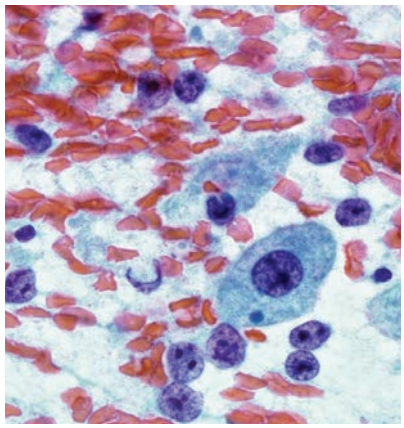
It is well established that tumors, even those of the same type, exhibit differences in genetics and morphology. This heterogeneity not only exists for tumors from different patients but also across regions within the same tumor. The latter, termed intratumoral heterogeneity, is of particular interest because it directly affects diagnosis and prognosis.

Martin Beck and others at the European Molecular Biology Laboratory study intratumoral heterogeneity. "This has important implications for tumor development because certain cells might be more aggressive than others," Beck said.

Most studies have looked at intratumoral heterogeneity at the genomic level. It remains largely unknown to what extent the local proteome of tumors intrinsically varies. In a new study in **Molecular & Cellular Proteomics**, Beck and a group of researchers at the EMBL attempt to answer this question. "We were interested to find out if the proteins contained within individual cells of the tumor are the same or different," Beck said. Since heterogeneity in the tumor microenvironment, such as the presence of a neighboring blood vessel, may drive genetic changes, he reasoned that it might also be reflected on the level of proteins.

The researchers looked at hepatocellular carcinoma, or HCC, the most common type of liver cancer. They used HCC samples biopsied from patients and then formalin-fixed and paraffin-embedded on microscope slides. Such samples, commonly referred to as FFPE, preserve the integrity of the tissue architecture of the original tumor, allowing the researchers to study the spatial differences in protein expression.

FFPE samples, however, present technical challenges for proteomic analysis, particularly because only a limited amount of proteins can be extracted. To overcome this problem, the researchers developed a novel method that efficiently extracts proteins from FFPE samples. To profile the spatial expression of proteins, they combined this method with a technique called laser-capture microdissection to carve out microscopic regions within the tumor. The extracted proteins then were run on a mass spectrometer for identification.



COURTESY OF JIAN-HUA QIAO/NIH FLICKR

This microscopic photo shows tumor cells from a fine needle aspiration cytology smear of a liver mass. Tumor cells exhibit nuclear enlargement, opened chromatin and multiple nucleoli.

The researchers first looked at the differences of protein expression between the tumor tissue and the normal tissue immediately adjacent to it. They detected consistent changes of multiple proteins known to be associated with HCC. More importantly, they also identified a few proteins that previously were not known to be HCC-related, opening possibilities for candidate biomarker development. Among these were members of the NADH dehydrogenase complex I. This finding was striking because the researchers showed that the changes were not reflected at the gene expression level, underscoring the importance of proteome profiling.

The researchers went deeper and dissected different regions within the tumor bulk. Here they found significant variations in expression of multiple proteins between areas from the center and the periphery of the tumor. "We could show that even between seemingly identical cells, with the same morphology and the same genome, there are surprisingly pronounced differences on the level of the proteins," Beck said.

These spatial differences of protein expression include proteins that have previously been identified as HCC biomarkers. "In our analysis, we saw that even proteins that have been proposed as such biomarkers are not evenly distributed across the tumor," Beck said.

This finding is of immediate clinical importance. Only a small fraction of a tumor can be obtained in a diagnostic or pretreatment biopsy, and thus the region of withdrawal could have a direct impact on the acquired expression profile. "It is possible that the tissue sample taken during biopsy does not reflect the actual state of the entire tumor," Beck said.

Beck believes the method developed in this study not only allows for studying intratumoral heterogeneity but also can improve cancer proteomics research in general. "Proteomic intratumoral heterogeneity should be taken into account for future cancer research," he said, "for example in the design of biomarker discovery experiments."

DOI: 10.1074/mcp.RA117.000189

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Unique solid-liquid lipid organization could regulate what gets under your skin

By Eduardo R. Martínez-Montes

Like any great fortress, the body's first line of defense is a physical barrier. Our skin is our largest organ, and it controls much of what gets in and out of the body. Given this critical role, understanding the structure and function of this outer membrane is of great interest to biomedical researchers. A study published in the **Journal of Lipid Research** reports novel skin architecture where lipids exist in both solid and liquid phases, which could give rise to the skin's unique permeability.

The stratum corneum, or SC, the outer layer of mammalian skin, dictates the rate of water loss through the skin as well as absorption of outside substances. This membrane's limited permeability is thought to be due largely to a crystalline organization of its lipids. Lead author Michel Lafleur became interested in the structural character of lipids in the skin during his postdoctoral work. In a previous project, he used deuterium nuclear magnetic resonance, or 2H NMR, which allows for structural characterization of lipid phase behavior. Conversations with Neil Kitson, a dermatologist, sparked the idea for his current study. "During group meetings and discussions around coffees, he discussed the importance of skin lipids whereas I presented the information we can get about lipid phase behavior from 2H NMR," Lafleur wrote. "(W)e thought it would be interesting to try to get information about the structure and the phase behavior of SC lipids."

Lafleur and Adrian Paz Ramos at the Université de Montréal and their collaborators at the Leiden Academic Centre for Drug Research in the Netherlands used advanced spectroscopic techniques to study lipid mixtures designed to mimic SC architecture. With 2H NMR, they got a detailed characterization of the phase behavior of a series of lipid mixtures. The technique detects signals from a rare hydrogen isotope (deuterium) that is only present if deliberately incorporated during lipid synthesis. This allowed them to study the structure and dynamics of deuterium-labeled SC components in varied lipid environments.

The researchers wanted to understand the role of an oleate-containing sphingolipid necessary in SC architecture, N-melissoyl-oleoyloxy hexacosanoyl-D-erythro-sphingosine, commonly called ceramide EOS. They found that the oleate chain of ceramide EOS formed disordered pockets within the crystalline lipid structure. Not only were these long chains of lipids disordered, but for the first time the researchers found them to be in the liquid phase. These results suggest that hydrocarbon nanodrops existed in their SC lipid model. They found that these nanodrops maintained their liquid phase down to -30°C. This was surprising, given that this lipid's chemical analogs typically have a melting point between 0°C and 20°C. The authors believe these findings substantially modify the structural description of the SC and propose a novel role of ceramide EOS as a strong modulator of SC solid-liquid balance.

This research is a big step forward in understanding the unique structural dynamics of human skin and could lead to improvement of a number of therapeutic techniques, including transdermal drug delivery, artificial skin and skin disease treatments, Lafleur suggested. This model is yet to be verified in animals; however, he believes that, should it hold true, these nanodrops could be manipulated to facilitate drug delivery across the skin barrier.

It is proposed that the nanodrops formed by the oleate chains of Cer EOS are involved in skin permeability increase by some transdermal penetration enhancers; these could partition preferentially into the nanodrops, and the percolation of these structures could lead to a facilitated diffusion path.

DOI: 10.1194/jlr.M080432

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From the journals

By Sasha Mushegian & Laurel Oldach

We offer a selection of recent papers on a variety of topics from the **Journal of Biological Chemistry**, the **Journal of Lipid Research** and **Molecular & Cellular Proteomics**.

A new weapon in bacterial warfare

Bacterial type VI secretion systems, or T6SSs, through which some bacteria can inject toxins into others, are recognized to be important for interbacterial competition, including in the context of the plant microbiome that protects plants from pathogens. The identities of the toxic effectors delivered through these systems are often unknown. Jenny Tang, Nathan Bullen and colleagues at McMaster University write in the **Journal of Biological Chemistry** that they discovered that the T6SS effector of the plant-protective bacterium Pseudomonas protegens is an NAD(P)+-degrading enzyme. Searching other bacterial genomes suggested that NADases are found in many other bacterial species with type VI and type VII secretion systems, hinting that these enzymes may be widespread weapons in bacterial competition, with consequences for plant and human health.

DOI: 10.1074/jbc.RA117.000178

Why FGFR inhibitor therapy may fail

Fibroblast growth factor receptors, called FGFRs for short, activate many cell-growth pathways and are overactive in some types of cancer. Although FGFR inhibitors seem like a promising possible drug class, they have failed in clinical trials because they sometimes, puzzlingly, cannot stop the growth of cancers with high FGFR activity. A study published in **Molecular & Cellular Proteomics** has revealed a new regulator of at least one FGFR, and that finding may help explain why treatment frequently fails. Researchers supervised by Jørgen Wesche at the Norwegian Radium Hospital in Oslo found a new FGFR1 regulator, the protein tyrosine phosphatase receptor PTPRG. PTPRG is required to shut down FGFR signaling. When PTPRG is absent, osteosarcoma cells more effectively resist treatment with an FGFR1 inhibitor. The authors suggest that the effective-

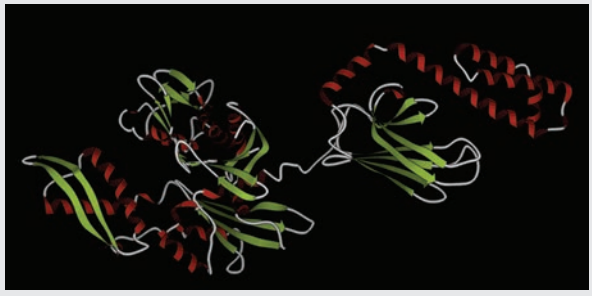
A chaperone-client relationship in cancer cells

Many aggressive tumors have an overabundance of the chaperone Hsp70, which is thought to stabilize proteins that promote tumor growth. Until recently, not much was known about the identities of Hsp70's clients, hindering efforts to develop cancer drugs targeting Hsp70.

New research from labs at the University of California, San Francisco, and the University of Michigan identifies some of these clients. The results were published in the **Journal of Biological Chemistry.**

According to Jason Gestwicki, the professor at UCSF who oversaw the study, "It has been known for many years that Hsp70 is one of the major proteins required (for rapid cell division in tumors). Yet chemical inhibitors of Hsp70 have not advanced to clinical trials. One of the stumbling blocks is that it is difficult to tell if Hsp70 has been inhibited in a cell."

The new study, led by then-graduate student Laura Cesa, demonstrates that Hsp70 stabilizes two proteins that inhibit apoptosis, or programmed cell death, in breast cancer cell lines. Importantly, one of these (X-linked inhibitor of apoptosis protein, known as XIAP) is uniquely stabilized by Hsp70, not the better-studied chaperone Hsp90.



COURTESY OF MENG0987/WIKIMEDIA COMMONS

In this illustration of Hsp70, the alpha helices are shown in red, and beta strands are shown in green.

"Now that we know that XIAP levels decrease in the presence of Hsp70 inhibitors, we can use XIAP levels as a way to estimate how much Hsp70 has been inhibited," Gestwicki said. "This knowledge will allow us to more rapidly create improved Hsp70 inhibitors as potential anti-cancer agents."

DOI: 10.1074/jbc.RA117.000634

—Sasha Mushegian

Fat balance matters for mouse health

Polyunsaturated fats are the "good fats" according to diet magazines and clean-living advocates. But some unsaturated fats are better than others. In a recent study in the **Journal of Lipid Research**, a team led by Rayane Ghandour at the Universite Cote d'Azur in France, in collaboration with nutritionists from Germany, compared the effects of diets supplemented with two types of unsaturated fatty acid on formation of brown adipose tissue in mice. Brown fat heats the body and can dissipate excess energy; converting white fat tissue, which is metabolically inert, into brown fat is a hypothetical target for weight-loss treatment. Ghandour tested the effect of supplementing a mouse's diet with either omega-3 essential fatty acids, which are abundant in fish, or omega-6 fatty acids, which are high in some vegetable oils and soy. High omega-6 intake is known to correlate with inflammation, impaired brown fat formation, and obesity. Although both groups of mice ate the same amount of calories and weighed the same, they responded differently to a treatment that stimulated brown fat tissue production. The mice with omega-3-supplemented feed showed mildly greater weight loss and better ability to convert white adipocytes to brown adipocytes when stimulated than those with omega-6 supplementation. Just one lipid mediator of inflammation, the prostaglandin PGF2-alpha, was significantly different between mice on the two diets. PGF2-alpha is made by an enzyme from omega-6 fatty acids. The researchers tested the enzyme's activity in cultured cells with omega-6 or both types of fatty acid and found that omega-3 could out-compete omega-6 fatty acids for enzyme activity. This research provides a mechanism for why diets high in omega-6 fatty acids may cause inflammation.

COURTESY OF WELLCOME IMAGES/WIKIMEDIA COMMONS

DOI: 10.1194/jlr.M081091

—Laurel Oldach

ness of many FGFR inhibitors may depend on whether PTPRG is present in a cancer. If they are correct, clinicians may be better able to predict whether an individual patient would benefit from the drugs.

DOI: 10.1074/mcp.RA117.000538

Making heads or tails of sperm

Acephalic spermatozoa syndrome is a rare genetic condition wherein sperm are produced as decapitated flagella or tailless heads because of defects in the head-tail coupling apparatus. Yonglian Shang and colleagues at the Chinese Academy of Sciences examined the effects of disease-associated mutations in SUN5, a testis-specific nuclear envelope protein, on sperm function. In a paper in the **Journal of Biological Chemistry**, they write that they found these mutations resulted in SUN5 proteins that were unable to interact with a specific heat shock protein. They hypothesize that the newly discovered interactor is a chaperone that helps SUN5 fold and localize correctly in the "neck" of developing sperm.

DOI: 10.1074/jbc.RA117.000861

When swapping sugar for ketones doesn't work out

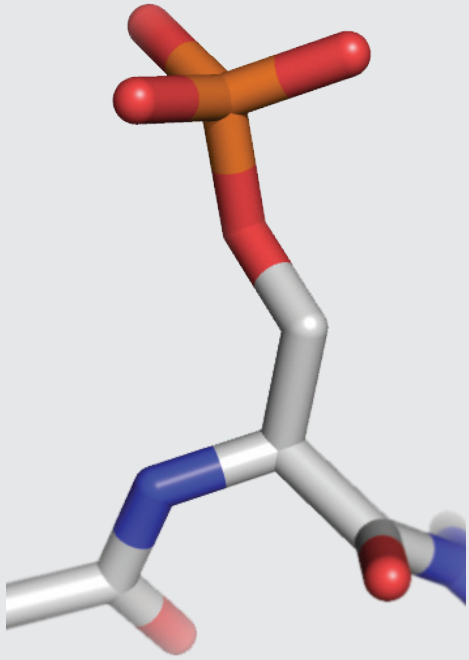
At present, there are 15 studies on clinicaltrials.gov recruiting or preparing to recruit cancer patients to test the ketogenic diet as a therapy. This diet, high in fat and very low in carbohydrates, is said to induce a fasting state without the actual fast. It dramatically lowers the amount of glucose in circulation and increases fatty ketone bodies. The change in energy source is proposed to cut off the sugar supply to metabolically active cancer cells. But preclinical results are surprisingly mixed. A paper in the **Journal of Lipid Research** explained some of the variability observed in models of ketogenic therapy for cancer. The researchers, led by Jie Zhang and Ping-Ping Jia of Huai'an Hospital in Jiangsu, China, found that some types of cancer are unlikely to respond well to the diet because their cells are well prepared to use ketone bodies as an energy source instead of glucose. The researchers identified four key ketolytic enzymes and found that when the isoforms BDH1 and OXCT1 were expressed at high levels in a cancer cell line, feeding mice with a tumor of those cells a ketogenic diet would in fact speed tumor growth. Conversely, mice whose tumors had lower expression of the enzymes saw slower tumor

Better prepping of phosphoproteins

Phosphorylation is a simple, reversible modification that can change protein function completely. Because of phosphorylation's role in the regulation of nearly every cellular process, it is of great interest to researchers. However, phosphoproteins make up a very small subset of the proteome, making enrichment of phosphorylated proteins mandatory for phosphoproteomics. Immobilized metal-affinity chromatography can be used to enrich phosphoproteins in a sample prior to mass spectrometry due to the high affinity of positively charged metal ions in the column to negatively charged phosphate groups. However, phosphorylated proteins are not the only molecules that can bind to the column. In a recent article in **Molecular & Cellular Proteomics**, researchers in Simone Lemeer's group at Utrecht University in the Netherlands identified ions from nucleic acid contaminants that bound to an immobilized iron ion column, making MS analysis more difficult. The same compounds were identified in several published works, confirming that nucleic acid contamination is a widespread problem. The team developed a robust protein sample cleanup using a combination of protein precipitation and nuclease treatment to remove contaminants. As a result, the researchers, led by Clement Potel, identified more than 50 percent more phosphorylation sites in humans and 10-fold in bacteria. This work opens the way for the study of phosphorylation dynamics in microorganisms, which may help further our understanding of signaling in pathogens.

DOI: 10.1074/mcp.TIR117.000518

—Laurel Oldach



COURTESY OF THOMAS SPLETTSTOESSER/WIKIMEDIA COMMONS

This diagram represents a phosphorylated serine residue.

growth. This research has important implications for when it is appropriate to recommend a ketogenic diet to cancer patients.

DOI: 10.1194/jlr.M082040

A redox 'off' switch for a celiac-related protein

Transglutaminase 2, or TG2, is an enzyme involved in the pathogenesis of celiac disease; patients produce autoantibodies against TG2 in complex with dietary gluten. TG2 is post-translationally regulated by a redox switch consisting of a disulfide bond that must be broken by thioredoxin in order to activate the enzyme. In a paper in the **Journal of Biological Chemistry**, Michael Yi and colleagues at Stanford University identify isomerase ERp57 as the factor that inactivates TG2, thus demonstrating the first example of a reversible disulfide bond switch modulated by two different proteins. The discovery could lead to treatments for celiac disease that target TG2, rather than requiring patients to stay on a lifelong gluten-free diet.

DOI: 10.1074/jbc.RA117.001382

A Western blot sans antibodies

Although antibodies are widely used reagents for semiquantitative measurement of proteins, many are prone to false positives and lot-to-lot variability. A paper in **Molecular & Cellular Proteomics** offers an alternative that may be more reliable. A research team at the Max Planck Institute of Molecular Cell Biology and Genetics developed a geLC-tandem mass spectrometry workflow adapted to calculate absolute molar quantities of several target proteins in a single run. Lead author Mukesh Kumar and colleagues designed chimera proteins that combined signature peptides from a large number of target proteins and expressed them in E. coli in the media with heavy isotope-labeled amino acids. Gel bands of a chimera protein, target proteins and reference protein (e.g., albumin) were co-digested and analyzed by liquid chromatography and tandem mass spectrometry. Characteristic MS peaks from the labeled chimera peptides could be compared to the same peaks from unlabeled target proteins. Since

the chimeric proteins include peptides from a reference protein of known concentration, they can be used to determine a precise quantity of target proteins in the sample. The technique offers a powerful antibody-free tool for analysis of untagged proteins at very low concentrations, which could improve reproducibility in future biochemistry studies.

DOI: 10.1074/mcp.O117.067082

A localization signal for insulin

Signal peptides are short protein sequences, characterized by particular structural features that direct translocation of secretory proteins into the endoplasmic reticulum for folding and maturation. Most mammalian secretory proteins are translocated co-translationally, but some, including the insulin precursor preproinsulin, are not transported into the ER until translation is complete. In a study in the **Journal of Biological Chemistry**, Huan Guo and colleagues at Tianjin Medical University found that the signal peptides of post-translationally translocated secretory proteins contain a positive charge that enables translocation and that a diabetes-associated mutation in preproinsulin affects this charge and thus prepro-insulin transport. Mutations in this region may contribute, therefore, to hereditary forms of diabetes.

DOI: 10.1074/jbc.RA117.000922

More or less, same enzyme effect

High levels of the lipid ceramide are believed to be a stress trigger for autophagy. When the lysosomal enzyme acid sphingomyelinase, or ASM, which makes ceramide by breaking down a more complex lipid, is overexpressed, the self-digestion process is increased. So you'd expect that inhibiting ASM should reduce autophagy. Scientists at Indiana University found, however, that this was not the case. In a recent study in the **Journal of Lipid Research**, the team, led by Matthew Justice, found that when ASM was inhibited, the lysosomal nutrient sensing complex turned off, and signaling by a pro-autophagy transcription factor began. This may have been because inhibiting ASM did not lower levels of its product, ceramide, as would be expected; instead, ceramide production rose. The researchers did observe a decrease in the level of a related lipid, sphingosine. They speculated that this may be because of interactions between ASM and an enzyme that produces sphingosine. However, the mechanisms by which ASM affects lysosomal nutrient sensing and sphingosine level remain to be determined. This research sheds light on how cells decide whether to keep growing or turn on the brakes.

DOI:10.1194/jlr.M080242

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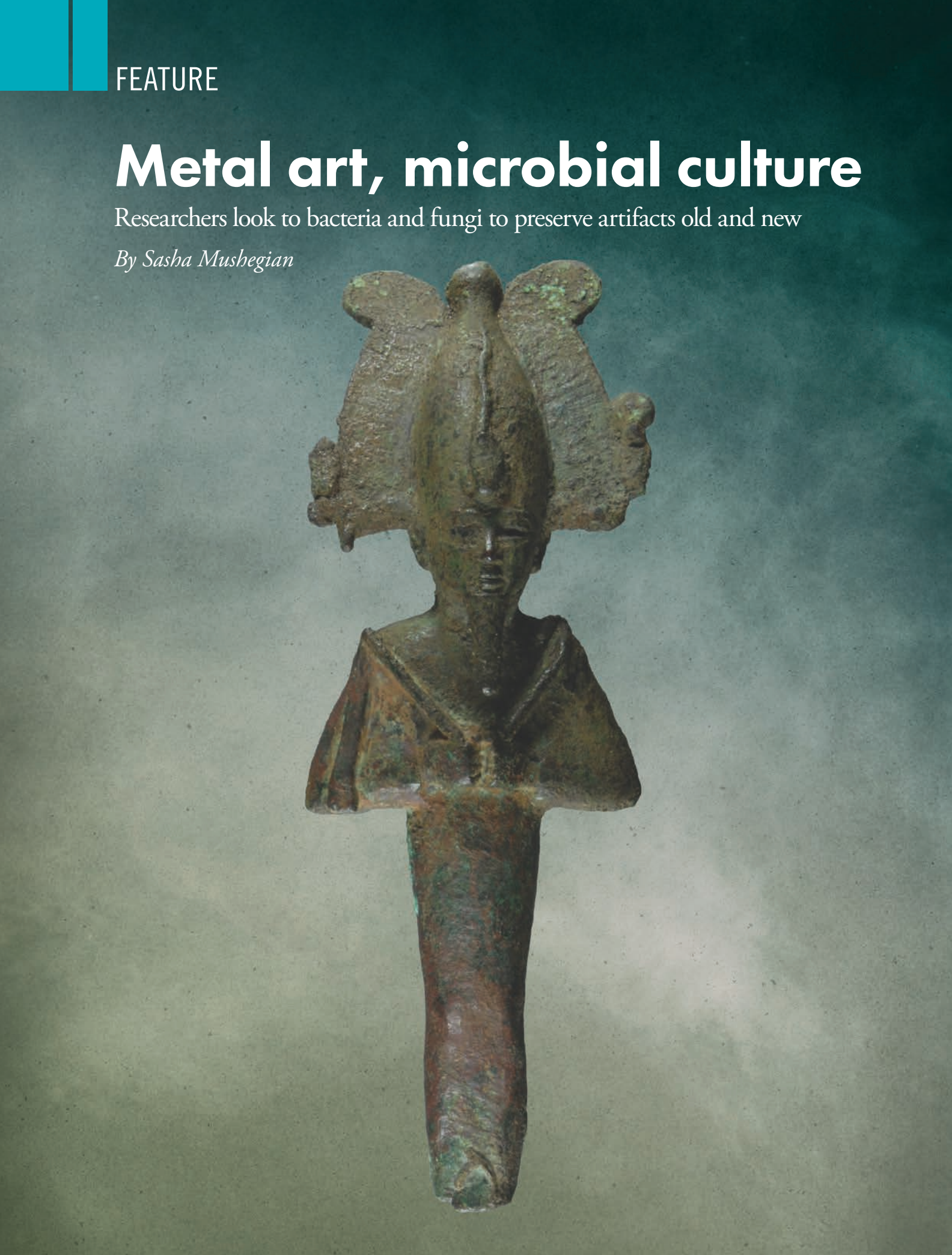
FEATURE

Metal art, microbial culture

Researchers look to bacteria and fungi to preserve artifacts old and new

By Sasha Mushegian



Bacteria and fungi are in many ways the enemies of art and culture — mold destroys books and is threatening the Lascaux cave paintings, biofilms form unattractive scum on roofs and sculptures, and many microbes cause wear and tear on metal and stone. But just as biomedical research on the microbiome is uncovering the many benefits bacteria can provide to human health, some in the field of conservation and restoration science hope that certain bacteria could be used to reverse the deterioration of cultural heritage objects.

Pilar Junier, a professor at the University of Neuchâtel in Switzerland, has spent a lot of time thinking about what bacteria can do. "Every reaction in biology has two sides, like a coin," she said. "One side is deleterious, but the other can be beneficial, if you change the context."

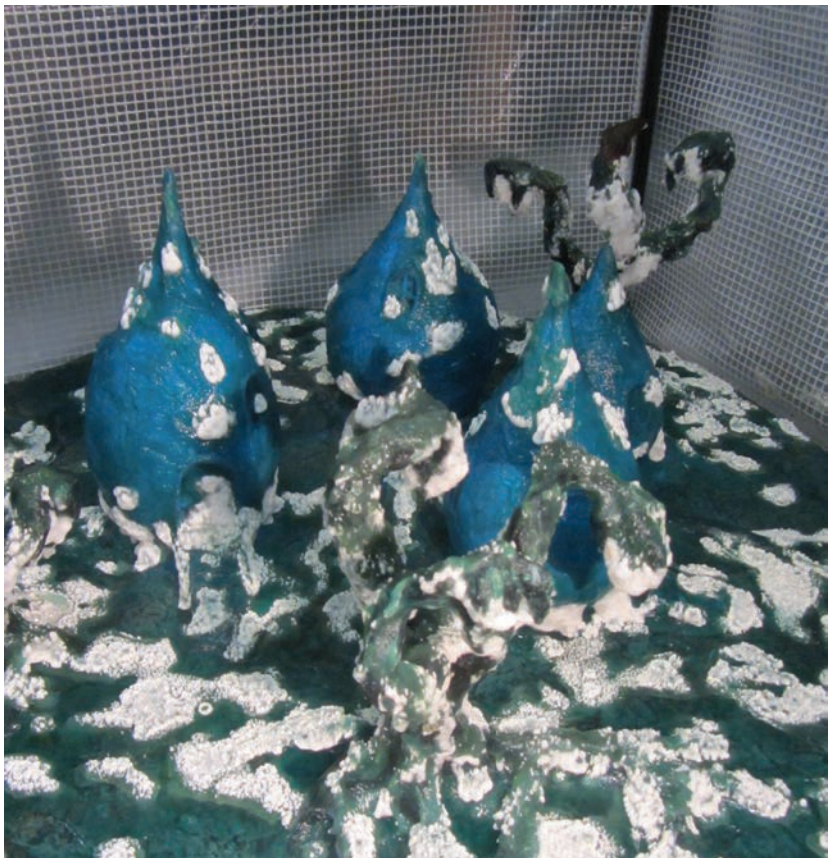
Junier is an environmental microbiologist who has studied microbial activities in lakes and sediments as well as in applied contexts like bioremediation of uranium. She began to collaborate in 2013 with Edith Joseph, a materials chemist with a background in art conservation, who thought that the chemical transformations needed to preserve some objects might be carried more effectively out by living organisms.

Microbes "are the best chemists in the world," Junier said. "Why don't we use them?"

Microbes to the rescue

Edith Joseph started her research in 2006, using microorganisms for the preservation of heritage materials in Italy, and arrived in Switzerland in 2010 to work on this subject at the Swiss National Museum. Today she works at the University of Neuchâtel, collaborating with Junier, as well as in the conservation-restoration department of the nearby Haute Ecole Arc.

Joseph's first project used fungi to preserve copper-containing objects.



COURTESY OF EDITH JOSEPH, UNIVERSITY OF NEUCHÂTEL

Sculptures undergoing microbial bio-passivation treatment before being displayed in the sculpture park Légende d'Automne in Lausanne, Switzerland. These sculptures are part of an accessible art project and are intended to be touched by the blind and visually impaired.

She was interested in corrosion both of large outdoor objects — monuments, sculptures and architectural features subjected to pollution or salty sea air — and of fragile archaeological artifacts. When the copper in these objects comes into contact with corrosive agents such as chloride ions, irreversible decay sometimes called "bronze disease" occurs. Outdoor monuments thus afflicted can leach copper into the environment; small items can flake, crack and fall apart. If items cannot be stabilized by placing them in an environment with controlled humidity and temperature, they often are treated with resins or waxes or with industrial corrosion inhibitors like benzotriazole.

However, if the copper hydroxychlorides on the object's surface are transformed into a nonreactive

COURTESY OF EMMANUELLE DOMON BEURET, LATÉNIUM ARCHAEOLOGICAL MUSEUM

Opposite page: A statue of Osiris from the collections of the Musée d'Ethnographie Neuchâtel, Switzerland, treated with a bio-passivation method to stabilize its corrosive layer.

COURTESY OF DITH JOSEPH, HAUTE ECOLE ARC CONSERVATION-RESTAURATION

Above: Students from the Haute Ecole Arc Conservation-Restauration use the Biopatina bio-passivation method on a contemporary sculpture in the Park Gallet, la Chaux-de-Fonds, Switzerland.
Below: The sculpture after treatment.

"passive" patina, the object could be protected. One such patina is copper oxalate. "Copper oxalate forms a kind of protective layer," Joseph said. "It's passivating the surface (to avoid) any exchange of ions with the copper and water, so you have no over-corrosion."

As it happens, oxalate is produced widely in the fungal kingdom as a defense against insects; oxalic acid-producing fungi sometimes are used as insecticides in organic agriculture. Furthermore, fungi growing in copper-polluted areas produce oxalate to chelate copper ions and protect themselves from copper toxicity.

After several years of research on a copper-resistant strain of the insecticidal fungus Beauvaria bassiana — isolated from a vineyard in which copper had been used for years as a fungicide — Joseph and her colleagues developed a ready-to-use kit called Biopatina for conservator–restorers. The kit consists of the fungus and a growth medium; the two are mixed together, spread on the surface of the copper object, and allowed to incubate for several days or weeks while the fungus produces copper oxalate. Then the fungus is washed off. Joseph has led workshops on the use of Biopatina in Switzerland and France, focusing on outdoor sculptures, and has sent samples of it to conservator-restorers in Europe and Canada.

Myriam Krieg, a conservator–restorer at the Aventicum Site et Musée romains d' Avenches, in the Swiss Midlands canton of Vaud, works mostly on Roman artifacts, although some objects from the Celtic Iron Age also have been found recently in the area. Krieg participated in Biopatina workshops in 2015 and 2016, where a team of conservators practiced using the technique on contemporary sculptures.

"Optically, I think the treatment produces a natural, less shiny surface, in contrast to what we see with other products we use," she said. "I like also

the fact that we induce the formation of copper minerals, and we are not dealing with synthetic (resins or coatings) that are really strangers to the object."

Krieg hopes to soon begin using the Biopatina kit on copper alloy artifacts such as coins or fibulae (Roman or Iron Age brooches) in her work.

Mining microbial resources

Whereas the copper-chelating fungi were isolated from vineyards, Joseph's team looked close to home in the sediments of Lake Neuchâtel for bacteria that could be used in projects involving iron. Under current conservation practice, to remove chloride ions, highly corroded iron objects must be soaked in alkaline sulfide baths in a time-consuming process.

The iron conservation project is at a much earlier stage than the work with copper. The team is carrying out tests first on iron ions in solution, then on solid iron compounds synthesized in the lab, and then on iron offcuts from foundries, experimentally corroded at the French Corrosion Institute in Brest. Recently, they moved on to experiments with Roman nails and other small objects that museum staff has determined can be sacrificed, and they eventually will turn to more valuable artifacts and the iron architectural features of an outdoor music pavilion in Neuchâtel.

The team still is trying to identify iron-reducing bacteria that could convert rust into iron phosphate or iron carbonate and are sufficiently easy to work with. Iron-reducing reactions occur under only anaerobic conditions, which would be difficult to set up in an art-conservation lab; the team therefore plans to identify bacterial species that can grow in the presence of oxygen but then can be applied in a thick gel with minimal oxygen penetration. One bacterial candidate turned out to be a potential fish pathogen, making it problematic to grow in large batch cultures that could be released accidentally into the environment. Another bacterium could perform the needed reactions but only in culture media with high salt concentrations, which would exacerbate the very problem the bacteria are intended to solve.

Although genetic engineering potentially could solve some of these problems, strict regulation of genetically modified organisms in Europe and negative public perceptions of GMOs mean the team is not pursuing that route. Instead, they continue to look for microbes with the right combination of traits in natural environments.

"(We) try to see, 'What are the conditions that we need? What are the potential contaminants in the system that could poison the metabolism?' to try to identify the very organisms that can tolerate those conditions," Junier said. "We always say: 'What do you want to convert? Is it a redox reaction? Is it simply absorption? Is it passivation? What do you want to do chemically speaking?' And then based on that, you say, 'Which are the microbial metabolisms that fit these reactions?'"

These investigations into the capabilities of natural isolates can serendipitously lead to new avenues of research in environmental chemistry and microbiology. For example, iron reduction in bacteria has been studied mainly in the model organisms Shewanella and Geobacter. But the iron reducers the team isolated from lake sediments were from the genus Aeromonas, which is not known to have the cytochrome proteins used in iron reduction reactions in the model species. Aeromonas species are common in aquatic sediments, but it's unknown whether they contribute to metal cycling in aquatic ecosystems.

Very little is known about iron reduction in Aeromonas, Junier said. "So we are trying to pinpoint the mechanism and try to see how much Aeromonas participates in the iron

Edith Joseph is a researcher at the University of Neuchatel and the Haute Ecole Arc who is developing methods for using microbes to preserve art.

Pilar Junier is a microbiologist at the University of Neuchatel who collaborates with Edith Joseph on microbial conservation projects.

Myriam Krieg is a conservator-restorer at the Site et Musee Romains d' Avenches in Switzerland.

COURTESY OF JAVIER KOHEN/WIKIMEDIA COMMONS

The 17th century wooden warship the Vasa sank on its maiden voyage and was salvaged in 1961. It is on display at Stockholm's Vasa Museum.

Robert J. Koestler is the director of the Museum Conservation Institute at the Smithsonian Institution.

cycle in sediments."

Two sides to every coin

Once the right bacteria are identified, successfully deploying them in the real world presents its own challenges. Biotechnological applications always have issues of scale and cost-effectiveness as well as being subject to unpredictable variables when they move out of the lab. There are also issues unique to art and culture.

Robert J. Koestler, the director of the Museum Conservation Institute at the Smithsonian Institution, is familiar with the challenges.

"Several groups in Europe in the 1990s tried to harness bacteria to produce calcium carbonate to repair deteriorated marble or limestone historic buildings," Koestler said. "Initial results seemed promising, but the process is no longer in vogue. This may be because the calcium carbonate formed by the bacteria did not adhere well to the marble or limestone … or because the process itself was spotty — you cannot get microbes to grow evenly across a surface."

There is a further ethical consideration, Koestler said, because chemically altering objects, whether by conventional chemical treatments or using microbes, necessarily destroys information about them. If the original corrosion layer is removed, information about the circumstances under which it corroded and weathered is lost. This makes some types of historical analyses impossible and can make it more difficult to spot fakes by obscuring artificial corrosion introduced by counterfeiters.

"If you can avoid introducing foreign substances, I would not do it," said Krieg, the conservator–restorer at Avenches. "The best thing is to have the least impact." If a treatment is unavoidable, taking a sample before

intervention can make it possible to further analyze the original material, she said. "Often it's a compromise: If you do nothing, you might lose the whole object."

The compromises between conflicting conservation needs, and between the conflicting needs and abilities of microbes and humans, are evident in the example of the earliest-stage project in progress in Joseph's lab: marine archaeological wood conservation. Magdalena Albelda Berenguer, a Ph.D. student in the lab, is working on solving a widespread problem that plagues wood rescued from shipwrecks.

Sunken wooden ships are typically well-preserved in the anoxic conditions in the deep sea. But while they are resting on the sea floor, a series of reactions occur: Iron ions from corroding iron parts of the ship react with sulfur produced by sulfate-reducing marine microorganisms; the resulting iron sulfides permeate the waterlogged wood. When this wood is taken out of the water and exposed to oxygen, acids and sulfate salts form, breaking down the wood.

The problem has plagued the 17th century Swedish warship Vasa, which was recovered fully intact from a harbor near Stockholm in the 1960s and is on display at a popular museum there. Conservators must maintain the ship continuously, attempting to remove iron or raise the pH with applications of ammonia, and research is ongoing to find a long-term solution for the weakening wood.

Albelda hopes to identify bacteria that can remove iron sulfides from future marine wood finds to pre-empt the problem. But wood, as an organic substance, can be consumed by bacteria, introducing the risk of seriously damaging it.

"The most difficult part to start with is to see which microorganism (to use), and to always think how that could be applied later on," Albelda said.

Many bacterial candidates are unsuitable because they cannot risk being used on valuable objects that can't be damaged.

But Albelda echoes her colleagues when she talks about the potential for harnessing bacteria for conserving cultural heritage. Conservation and microbiology, she said, "are very separated worlds, but they have a lot of things in common, because a lot of the deterioration in the objects is made by microorganisms."

"In the end, everything is nature," Edith Joseph said. "But it's nice to see that nature can help us to preserve something for the next generation, and we are not alone in front of this problem."

Occupational hazards of art preservation

Edith Joseph pursued microbial methods of treating heritage objects in part because she shares a concern about the occupational and environmental health hazards of standard conservation techniques, which often involve toxic solvents and chemical mixtures.

The U.S. Environmental Protection Agency considers benzotriazole, an industrial corrosion inhibitor often used by conservators to treat bronze artworks, to be a "contaminant of emerging concern" for environmental and human health. On the other hand, if outdoor copper objects are not treated against corrosion, the copper itself is a pollutant if it leaches into the environment.

"At the beginning, the idea was mostly about operator risk, for (conservators) to use safe treatments," Joseph said. "But now, I always point out if there's too much copper in the water, then it's also not good for the environment."

Conservation professionals who were concerned about occupational and environmental safety and sustainability created a new academic conference, called Green Conservation of Cultural Heritage, which now has been held twice in Italy. Joseph has presented at this conference, pitching her team's treatments as safer alternatives for workers and the environment.

Myriam Krieg, the conservator–restorer in Avenches, is not acutely concerned about safety issues in her line of work, because operators use personal protective equipment and facilities designed for chemical safety, but she welcomes the development of biologically based alternatives.

"If we have to, we can deal with (toxic chemicals)," Krieg said. "But if we have the choice, if we have an alternative, we will opt for a less toxic treatment."

Sasha Mushegian (amushegian@asbmb.org) is scientific communicator for the Journal of Biological Chemistry.

Magdalena Albelda Berenguer is a Ph.D. student in Edith Joseph's laboratory, working on microbial preservation of marine archaeological wood.

RUTH KIRSCHSTEIN DIVERSITY IN SCIENCE AWARD

Tsin, a mentor to many, advances diversity

By Nathalie Gerassimov

Andrew Tsin, chair of the department of biomedical sciences and associate dean of research at the University of Texas Rio Grande Valley School of Medicine, has won the 2018 Ruth Kirschstein Diversity in Science Award. The American Society for Biochemistry and Molecular Biology's Minority Affairs Committee selects the winner of this award to recognize an outstanding scientist who has contributed significantly to increasing the participation of minorities in science.

Tsin, an expert in retinal neurobiology, has done notable work on the biochemistry of the visual cycle throughout his career. His prolific contributions to science have resulted in more than 300 journal articles, book chapters and meeting presentations. His research has been recognized with numerous awards, such as the 2015 Gold Fellow Award by the Association for Research in Vision and Ophthalmology.

Tsin also is known as a scientific mentor who has contributed to the advancement of diversity in science. Robert Renthal, professor of biochemistry at the University of Texas at San Antonio, wrote in his nomination letter that Tsin "has an unusual ability to inspire students who are members of groups that are underrepresented in the sciences to successfully pursue careers in science" and that Tsin has

> "worked tirelessly, one-on-one, with research trainees in his lab, sustained over a period of more than 30 years." Tsin has mentored 132 graduate and undergraduate students, including 112 members of groups underrepresented in the sciences. Of these, 20 have earned a Ph.D. in the sciences and 12 have earned an M.D. or D.D.S. Tsin's mentoring also resulted in numerous journal publications with student first authors, Renthal wrote.

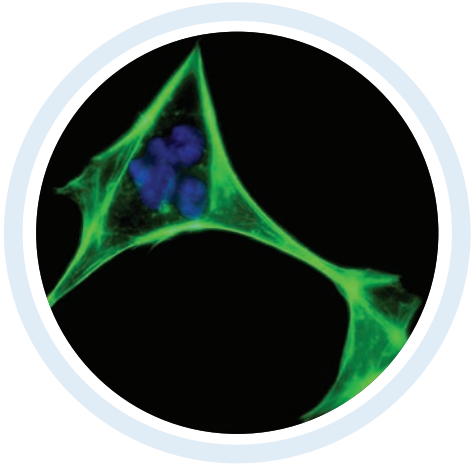
Tsin's legacy of effectively increasing diversity in science goes beyond the walls of his lab. While at UTSA, where he spent most of his career before moving to UTRGV in 2016, he founded and directed the Center for Research and Training in the Sciences, securing more than $52 million in grants to support research and training programs for underrepresented minorities. Additionally, he served on the board of directors of the Society for the Advancement of Chicanos and Native Americans in Science from 2007 to 2009. Tsin's contributions to the advancement of minorities in science earned him the Presidential Award for Excellence in Science, Mathematics and Engineering Mentoring in 2011 and a Lifetime Achievement Award from the American Association for the Advancement of Science in 2014.

Sonia C. Flores of the University of Colorado Anschutz Medical Campus, chair of the ASBMB Minority Affairs Committee, said, "Dr. Tsin has all the necessary attributes that Dr. Ruth Kirschstein championed during her career: compassion, empathy, service, and dedication to diversity in science while maintaining a rigorous and exceptional research career."

Tsin will receive his award during the 2018 ASBMB Annual Meeting in San Diego, where he will deliver an award lecture on the biochemistry of ocular diseases. The presentation will take place at 8:30 a.m., April 24, in Room 6B in the San Diego Convention Center.

"I have worked with Dr. Ruth Kirschstein for many years on NIH minority programs. I am very honored to receive this ASBMB award named after my esteemed colleague. To continue Dr. Kirschstein's outstanding accomplishments in diversity initiatives, I will remain professionally and personally committed to increase diversity in science."

— ANDREW TSIN



Nathalie Gerassimov (nathalie.gerassimov@gmail.com) is a Ph.D. student at Johns Hopkins School of Medicine.

DELANO AWARD FOR COMPUTATIONAL BIOSCIENCES

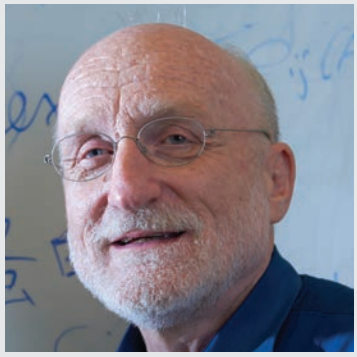
Sander lauded for his efforts to bring science to all

By Isha Dey

Chris Sander, director of the cBio Center at the Dana–Farber Cancer Institute and a professor of cell biology at Harvard Medical School, is the 2018 recipient of the American Society for Biochemistry and Molecular Biology's DeLano Award for Computational Biosciences.

Sander is recognized internationally in the field of computational and systems biology. He is credited with integrating computational sciences into biological research to make scientific resources easily accessible to the public. One example is the cBioPortal for Cancer Genomics, developed with colleagues Ethan Cerami and Nikolaus Schulz in his group during his time at the Memorial Sloan–Kettering Cancer Center. It is now an international open-source project containing cancer genomics data sets from published studies and data generated by The Cancer Genome Atlas and other sources.

As Joan Massagué, director of the Sloan–Kettering Institute and a leading scientist in cancer metastasis, pointed out in his nomination, Sander and his group have developed many online resources that unify scientists from different fields. Examples include the Dictionary of Secondary Structure of Proteins, co-developed with Wolfgang Kabsch at a Max Planck Institute and in widespread use for 35 years; the miRanda microRNA target prediction algorithm, with colleague Debora Marks; and the BioPAX and Pathway Commons resources for sharing biological pathway data, with former postdoctoral fellows Emek Demir and Gary Bader. In 2010, Sander and Marks developed Evfold, a method adapted from statistical physics that predicts protein 3-D structure folds from genetic sequences by analysis of evolutionary covariation patterns. Sander's work "has contributed to key advancements in computational biology, structural biology, cancer genomics and cancer systems biology," Massagué wrote.



"I subscribe to Warren DeLano's mission statement: 'Lack of access to effective software continues to be a major hindrance to scientific progress and therapeutic discovery. For the benefit of all society, we need to pursue new and complementary approaches to the creation and dissemination of scientific software.' I am grateful we can make scientific software available to the world."

— CHRIS SANDER

Sander was trained in physics and mathematics at the University of Berlin, the University of California, Berkeley, and the Niels Bohr Institute in Denmark, and he earned his Ph.D. in theoretical physics from the State University of New York at Stony Brook. He founded the biocomputing program at the European Molecular Biology Laboratory and, with Michael Ashburner, co-founded the research section of the European Bioinformatics Institute. After working as scientific founder at a biotech startup, Millennium Information, he established the Department of Computational Biology at Memorial Sloan–Kettering.

Sander has co-authored more than 400 publications. He has a patent,"Models for combinatorial perturbations of living biological systems," and has served on scientific advisory boards for organizations worldwide and helped shape many research programs. The International Society for Computational Biology awarded him its 2010 Accomplishment by a Senior Scientist Award.

The DeLano award recognizes the use of computational tools in biological research and providing public access to those tools. Sander is the ideal candidate, Massagué wrote in his nomination letter. Following the legacy of Warren DeLano, who advocated open-source practices in the sciences, Sander not only "built highly productive bridges between the computational and biological sciences through interdisciplinary and translational collaborations" but also "always ensured that resources developed by his team, as well as experimental data, are freely available to the public," Massagué wrote.

Sander will receive his award during the 2018 ASBMB Annual Meeting in San Diego. His lecture, "Solutions to the computational protein folding problem," will take place at 9 a.m. April 23 in Room 6B at the San Diego Convention Center.

Isha Dey (isha.dey@my.rfums.org) is a graduate student at Rosalind Franklin University of Medicine and Science, North Chicago, USA

BERT AND NATALIE VALLEE AWARD IN BIOMEDICAL SCIENCE

Groundbreaking telomere research yields award for de Lange

By Amber Lucas

Titia de Lange, professor of cell biology and genetics and director of the Anderson Center for Cancer Research at Rockefeller University, has won the 2018 Bert and Natalie Vallee Award in honor of her groundbreaking discoveries of the mechanism by which telomeres shield chromosome ends and of the relationship between telomere dysfunction and cancer.

James E. Darnell Jr., Vincent Astor professor emeritus of organismal biology and evolution at Rockefeller University, nominated de Lange for this award. "Titia de Lange has almost single handedly solved a major question in cell biology: How do telomeres protect chromosome ends?" Darnell wrote in his nomination letter. "Given the importance of telomere biology in human disease, de Lange's discoveries have wide implications in the context of human health."

Since the work of Barbara McClintock and Hermann Muller, it has been known that telomeres allow cells to make the distinction between broken DNA and the natural ends of chromosomes. If DNA repair pathways were to act at chromosome ends, it could cause fusion of one chromosome with another, leading to dramatic deleterious effects, such as chromosome rearrangement, when the cell tries to divide. De Lange's lab was the first to identify the protein complex shelterin, which binds to the repetitive telomeric DNA. Composed of six proteins, shelterin protects chromosome ends from inappropriate repair or fusion and prevents the activation of DNA damage signaling pathways. Following the discovery of shelterin, her lab used elegant mouse genetics to tease apart how shelterin and its accessory proteins prevent activation of multiple DNA damage repair pathways to keep the chromosome ends intact. Together with Jack Griffith at the University of North Carolina, she also used electron microscopy to discover the T-loop structure of telomeres, which is formed by shelterin and hides the chromosome end from DNA damage response pathways.

"Our work on telomeres has been a source of excitement and wonder. The mechanism by which shelterin and t-loops solve the telomere end-protection problem combines beautiful simplicity with clever complexity. I am fortunate to have this fascinating subject to study and am deeply honored by this recognition from the ASMB."

— TITIA DE LANGE

As a postdoctoral fellow with Harold E. Varmus, de Lange was the first to observe telomere shortening in cancer. Her lab's exploration of the role of telomere dysfunction in cancer showed that telomere-telomere fusion can lead to catastrophic rearrangement of chromosomes and genomic instability.

Stephen J. Elledge, a professor of genetics at Harvard Medical School and investigator at the Howard Hughes Medical Institute, supported the nomination, writing, "What characterizes Dr. de Lange's work is an instinctual recognition of the unproven assumptions that underlie a field and a daring ability to challenge those assumptions in creative and novel ways. She has truly been a pioneer given to carrying out what on the surface appear to be risky experiments, but what are in actuality a reflection of her tremendous insight into the principles of biology."

De Lange received her Ph.D. from the Dutch Cancer Institute in Amsterdam, where she worked on trypanosomes in Piet Borst's lab, followed by a postdoctoral fellowship at the University of California, San Francisco, studying oncogenes with Varmus.

She joined the faculty of Rockefeller University in 1990 and since has devoted more than 25 years to understanding mammalian telomere function. She was awarded the Leon Hess endowed chair in 1999. She has been elected to the National Academy of Sciences and the American Academy of Arts and Sciences and has won numerous awards and honorary degrees.

De Lange will receive her award during the 2018 ASBMB Annual Meeting. Her award lecture, titled "How telomeres solve the end-protection problem," will take place at 8:30 a.m. April 24 in Room 6C at the San Diego Convention

Amber Lucas (aluca685@gmail.com) is a fourth-year Ph.D. student in the department of biological sciences at Carnegie Mellon University.

ALICE AND C.C. WANG AWARD IN MOLECULAR PARASITOLOGY

Winzeler selected for leadership, antimalarial drug-discovery work

By Mariana Figuera-Losada

The 2018 winner of the Alice and C.C. Wang Award in Molecular Parasitology is Elizabeth A. Winzeler, a professor of pediatrics at the University of California, San Diego. The award honors seminal contributions and cutting-edge research in molecular parasitology. Winzeler is recognized for her groundbreaking work in antimalaria drug discovery.

Winzeler obtained her Ph.D. in 1996 at Stanford University, where she worked in bacterial transcription with Lucy Shapiro. She pursued postdoctoral training in the Ronald Davis laboratory at Stanford, working on yeast genomics and expression. In 1999, Winzeler joined the Novartis Research Foundation's Genomics Institute as a staff scientist, and she continues there as head of the department of cellular biology. She joined the department of cell biology at The Scripps Research Institute in 2000. In 2012, she moved to the University of California, San Diego, as director of translational research at the UC Health Sciences Center for Immunology, Infection and Inflammation and professor in the division of pharmacology and drug discovery.

Winzeler's work involves the use of big data from whole-genome sequencing and genomics to identify novel drug targets and genes that contribute to pathogen drug resistance. Much of her work has focused on the parasite responsible for malaria, Plasmodium falciparum, and, more recently, Plasmodium vivax. Her significant contributions include the development of high-throughput phenotypic assays using P. falciparum asexual blood and liver stages to identify antimalarial agents and the identification of over 10,000 different compounds with anti-malarial activity. One of those compounds is an inhibitor of P. falciparum Na^+-dependent ATPase, PfATP4, and is the first novel anti-malarial chemotype in 20 years to reach human clinical trials. Winzeler also identified the imidazolopiperazine scaffold, which allowed the selection of resistant parasites with mutations in the endoplasmic reticulum protein, PfCARL. These compounds showed potent anti-liver and blood stage activity in a mouse malaria model, and one of them is now part of a drug development campaign. Winzeler also led the efforts that identified tRNA synthetases and a phospholipid kinase, PI4K, as promising anti-malarial drug targets.

"I am incredibly grateful to Alice and C.C. Wang for establishing this award. C.C. Wang was a pioneer in the field of parasitology and I am honored to receive an award that bears his name. The recognition is bittersweet this year as C.C. will not be able to attend the events and enliven them with his humor, and great enthusiasm."

— ELIZABETH A. WINZELER

David A. Fidock, a Columbia University professor of microbiology and immunology, supported Winzeler's nomination, writing, "she is a highly gifted and visionary scientist who has made tremendous contributions to the field of molecular parasitology." Fidock and Winzeler are part of an international, multi-year malaria drug target identification program funded by the Bill and Melinda Gates Foundation. Winzeler was named principal investigator of the program. She is also part of the Medicines for Malaria Venture, a global partnership for anti-malarial drug research and development.

Victor Nizet, a colleague at UC San Diego, commended Winzeler's "brilliant work and intuition for selecting and completing (and publishing) high impact projects," as evidenced by more than 20,000 manuscript citations.

Dyann Wirth, professor at the Harvard T.H. Chan School of Public Health, wrote that Winzeler seeks drugs that can be used to eliminate malaria: "Her own work leads the way in this effort, but she has brought together one of the most successful collaborative projects in the field. Her leadership, vision and scientific acumen are key to this success."

Winzeler will receive her award during the 2018 ASBMB Annual Meeting. She will deliver an award lecture, titled "Using in vitro evolution and chemogenomics to explore the malaria parasite drug-able genome," at 2:30 p.m. April 23 in Room 31B at the San Diego Convention Center.

Mariana Figuera-Losada is a clinical research coordinator at the Montefiore Medical Center.

WALTER A. SHAW YOUNG INVESTIGATOR AWARD IN LIPID RESEARCH

Breakthrough lipid-signaling studies earn Burke praise and recognition

By Stefan Lukianov

John E. Burke, an assistant professor in the department of biochemistry and microbiology at the University of Victoria, has won the Walter A. Shaw Young Investigator Award in Lipid Research from the American Society for Biochemistry and Molecular Biology. The award recognizes his work on the molecular regulation of lipid signaling complexes.

"John Burke has been one of the most outstanding graduate students to have studied under my direction for the Ph.D. degree," former graduate adviser Edward A. Dennis of the University of California, San Diego, wrote in his nominating letter. "I have observed the development of John Burke's early career and feel that his work up to now suggests a very bright and productive future."

Burke's work focuses primarily on the kinases and phosphatases that catalyze the phosphorylation and dephosphorylation of lipid phosphoinositides. Kinases and phosphatases are enzymes that add or remove, respectively, negatively charged phosphate-oxygen groups to other molecules in the cell. This reaction alters the structure of the target molecules, which in turn regulates their function. Burke specifically studies the phosphoinositide 3-kinase and phosphatidylinositol 4-kinase families. These lipid-targeting kinases are under tight regulation, with disruption occurring in many diseases such as cancer, viral infections and inflammation. Accordingly, studying these enzymes could lead to various therapeutics. Indeed, one of Burke's major contributions to science involves the screening of phosphoinositide kinase inhibitors that may yield potential treatments.

"I am tremendously honored to be awarded the Walt Shaw Young Investigator Award in Lipid Research. I am extremely appreciative to the nominators and ASBMB. This award is only possible due to the work and support of my incredible network of mentors, trainees, and collaborators. "

— JOHN E. BURKE

Phosphoinositide kinases are regulated by upstream cell-signaling events. These events occur when specific extracellular molecules bind to receptor proteins in the plasma membrane known as receptor tyrosine kinases and heterotrimeric G-protein-coupled receptors. Virus binding to cognate receptors also can regulate phosphoinositide kinases. Burke's work has been critical to elucidating these cell-signaling pathways and their dysregulation in disease.

Burke's research takes an innovative approach by combining several sophisticated biophysical and biochemical techniques, including hydrogen-deuterium exchange mass spectrometry, X-ray crystallography, surface plasmon resonance, isothermal titration calorimetry and functional assays. These techniques enable Burke and his lab to elucidate the structure and function of the lipid-targeting kinases at the cell's plasma membrane, a complex bilayer of lipids, proteins and carbohydrates that separates the cell's internal space from the external environment.

Roger Williams, Burke's postdoctoral advisor in the division of protein and nucleic acid chemistry at the Medical Research Council Laboratory of Molecular Biology, called Burke "simply one of the best postdoctoral researchers with whom I have worked in the 25 years that I have been a group leader in the Laboratory of Molecular Biology in Cambridge, UK. He is an ideal candidate for ASBMB's Walter A. Shaw Award in Lipid Research."

Burke earned his Ph.D. in chemistry and biochemistry from the University of California, San Diego, in 2008. He conducted his postdoctoral work with Williams at the Medical Research Council until 2014, after which he was appointed an assistant professor in the department of biochemistry and microbiology at the University of Victoria in British Columbia, Canada.

Burke will receive his award during the 2018 ASBMB Annual Meeting in San Diego, where he will deliver an award lecture on probing the structure, dynamics and regulation of lipid signaling enzymes in disease. The presentation will take place at 10 a.m. April 22 in Room 6F at the San Diego Convention Center.

Stefan Lukianov (stefanlukianov@gmail.com) is a Ph.D. candidate at Harvard Medical School and a contributor to ASBMB Today.

ASBMB–MERCK AWARD

Orth a 'scientific trailblazer' in the field of bacterial pathogenesis

By Courtney Chandler

Kim Orth, a professor at the University of Texas Southwestern Medical Center and investigator for the Howard Hughes Medical Institute, has won the 2018 ASBMB–Merck Award for her outstanding contributions in the fields of biochemistry and molecular biology.

In the field of bacterial pathogenesis, Orth has worked to elucidate the activity of bacterial virulence factors on the molecular level, providing insights into how bacteria cause disease and how eukaryotic host cells signal in response to infection. In his letter nominating Orth, Eric Olson, also a professor at UT Southwestern, described her as "an exceptional investigator who has made major contributions to our understanding of the signaling mechanisms involved in bacterial pathogenesis."

Orth's research originally focused on Yersinia pseudotuberculosis, a bacteria related to the causal agent of the plague. Her work showed that a specific protein secreted by the bacteria is capable of modifying a eukaryotic host protein involved in the innate immune response. This modification promotes survival of the bacteria by blocking inflammation. Her lab also studied a similar protein that can produce the same inflammation-halting effect isolated from Vibrio parahaemolyticus, a bacteria endemic in Southeast Asia and the cause of gastroenteritis. Her findings demonstrated how a bacterial effector protein can act on evolutionarily conserved signal transduction pathways. In his letter, Olson described her work as truly groundbreaking.

Orth has characterized how bacterial effectors manipulate eukaryotic cells through post-translational modifications. She has described how different bacterial proteins can modify host proteins using acetylation, deSUMOylation and deamidation. In one case, she characterized a bacterial effector that acts as an inositol phosphatase to disrupt the host cell actin cytoskeleton connection to the cell membrane, leading to cell death.

"I am extremely honored and thrilled to receive this prestigious ASBMB–Merck Award. To those that have supported my success, including my family, friends, current and former lab members, and colleagues, and to institutes that have so generously sustained our studies, I am deeply indebted. They have enabled me to investigate tools used by bacterial pathogens, aka, mother nature's best chemists and biochemists."

— KIM ORTH

While researching post-translational modifications caused by bacterial proteins, Orth discovered a novel activity of the metabolite adenosine monophosphate, or AMP. Her lab showed that proteins can be modified post-translationally with AMP, changing their activity. Orth and colleagues identified a family of bacterial enzymes that are capable of catalyzing this "AMPylation," highlighting this as an evolutionarily conserved mechanism across pathogens and host cells. Her lab demonstrated that reversible AMPylation is used by host cells to maintain homeostasis. Her research into post-translational modifications has expanded the field of possibilities for regulation of cellular signaling.

Olson described Orth as "one of a diminishing breed of true biochemists able to rigorously dissect complex biological problems in biochemical detail." Her application of traditional molecular and biochemical techniques to microbial pathogenesis research has yielded important insights. Orth is "an exceptionally talented biochemist, scientific trailblazer and role model for female scientists," Olson wrote.

Orth earned her Ph.D. in biochemistry and molecular biology at UT Southwestern. She received the 2010 Norman Hackerman Award in Chemical Research from the Welch Foundation and was a 2011 recipient of the Edith and Peter O'Donnell Award in Science from the Texas Academy of Engineering, Science and Technology. She is a member of the American Academy of Microbiology and received the ASBMB 2012 Young Investigator Award.

Orth will receive her award during the 2018 ASBMB Annual Meeting, where she will deliver an award lecture titled "Black spot, black death, black pearl: tales of bacterial effectors." The presentation will take place at 8 a.m. April 24 in Room 6B in the San Diego Convention Center.

Courtney Chandler (cochandl@umaryland.edu) is getting her Ph.D. in biochemistry at the University of Maryland, Baltimore.

FASEB EXCELLENCE IN SCIENCE AWARD

Maquat celebrated for her service and scientific achievements

By Amber Lucas

Lynne E. Maquat, the J. Lowell Orbison endowed chair and director of the Center for RNA Biology at the University of Rochester Medical Center, is the recipient of the 2018 Federation of American Societies for Experimental Biology Excellence in Science Award. Maquat is being recognized for her outstanding contributions to our understanding of RNA biology and her enthusiastic service to the scientific community.

FASEB established the Excellence in Science Award in 1989 to celebrate outstanding women in science who have made landmark scientific discoveries, shown leadership and a devotion to service in the broader scientific community, and shown dedication to the training of students and postdoctoral fellows.

Jeffrey J. Hayes, chair and Shohei Koide professor in the department of biochemistry and biophysics at the University of Rochester Medical Center, nominated Maquat for the award. "Lynne is a highly esteemed scientist who is a leader in mammalian gene expression and has contributed numerous seminal discoveries elucidating fundamental aspects of mRNA regulation," Hayes wrote in his letter of nomination. "Lynne's innovative work, her unparalleled contributions to science, her record of unselfish service to the scientific community and her efforts fostering future scientists' careers, clearly indicate that she is an outstanding choice for the FASEB Excellence in Science Award."

Maquat's research on RNA decay pathways focuses on nonsense-mediated mRNA decay, or NMD, and how disruption of this pathway can lead to disease in humans. The NMD pathway targets mRNAs with premature stop codons for degradation, protecting against the potentially deleterious effects caused by expression of the truncated proteins encoded by these mRNAs. Maquat's discovery and understanding of the NMD mechanism has been instrumental in the fundamental understanding of RNA biology, how disruption of RNA regulation can lead to diseases and how manipulation of this pathway could be used to treat those diseases.

"It is an honor to receive the FASEB Excellence in Science Award. I look forward to meeting many Experimental Biology 2018 participants, especially those just starting their careers. Even after establishing my own lab, I wasn't sure that I would be a successful scientist. A career in science can have many unpredictable twists and turns. However, if you chip away in a steady and thoughtful way, you may be surprised at what you can accomplish."

— LYNNE E. MAQUAT

Maquat also has been an outstanding role model for the scientific community outside the lab. In 2003, she established the University of Rochester Graduate Women in Science program to offer mentorship for women scientists and provide them with opportunities for professional and personal development. As president of the RNA Society, she also initiated networking and mentoring, and she is a constant advocate for diversity in the sciences.

Maquat earned her Ph.D. from the University of Wisconsin-Madison and decided to stay there for her postdoctoral work at the McArdle Laboratory for Cancer Research. Since joining the University of Rochester, she has published more than 135 papers in peer-reviewed journals and has been recognized with numerous awards including the Canada Gairdner International Award, the Vanderbilt Prize in Biomedical Science, an NIH MERIT Award, the International RNA Society Lifetime Achievement in Service Award, the International RNA Society Lifetime Achievement in Science Award and the Wiley Prize in Biomedical Sciences. She also has been elected to societies such as the National Academy of Sciences, the National Academy of Medicine, the American Academy of Arts and Sciences, and the American Association for the Advancement of Science.

Maquat will receive her award during the Experimental Biology 2018 meeting in San Diego, where she will deliver an award lecture titled "Nonsense-mediated mRNA decay and human disease: genome guardian and executor." The presentation will take place at 9 a.m. April 22 in Room 6B in the San Diego Convention Center.

Amber Lucas (aluca685@gmail.com) is a fourth-year Ph.D. student in the department of biological sciences at Carnegie Mellon University.

ASBMB AWARD FOR EXEMPLARY CONTRIBUTIONS TO EDUCATION

Craig commended for his 'remarkable and inspirational' work with undergrads

By Adriana Bankston

Paul A. Craig, professor of biochemistry and head of the School of Chemistry and Materials Science at the Rochester Institute of Technology, has won the American Society for Biochemistry and Molecular Biology Award for Exemplary Contributions to Education for his work promoting hypothesis-driven thinking in the undergraduate biochemistry lab.

"Paul's work with students is remarkable and inspirational," Lea Vacca Michel, a Rochester colleague, wrote in Craig's nomination letter. Vacca noted that she seeks to follow in Craig's footsteps by taking undergraduates into her group, seeking out those from underrepresented groups and reaching out to struggling students.

Among his many accomplishments, Craig created the Bachelor of Science in biochemistry degree at the Rochester Institute of Technology, upgraded and published on the school's biochemistry teaching lab, and obtained a National Science Foundation grant for an open-ended project-based biochemistry lab on six campuses, as Robert Bateman detailed in his nomination letter.

Bateman, a longtime friend and professor of biomedical sciences at William Carey University, also noted Craig's contribution to funding at the Rochester Institute of Technology in the form of NSF and National Institutes of Health grants and travel awards, all of which are related to biochemistry education. Craig also has 31 peer-reviewed publications and has given 38 national or international presentations.

Craig has been an ASBMB member since 1998 and is an active participant in the society. Judith Voet, a professional colleague and emeritus professor in the department of chemistry and biochemistry at Swarthmore, supported Craig's nomination, calling him a "major guru of biochemistry software development, molecular visualization techniques and bioinformatics education." Voet specifically noted Craig's educational software that simulates polyacrylamide gel electrophoresis, which was valuable to her laboratory. As part of an ASBMB digital library initiative, Craig created Biomolecules Alive, a website to establish a "peer-review method for software and web applications that would give faculty members journal citations for their work in those areas." He also contributed bioinformatics exercises for biochemistry textbooks, which are freely available.

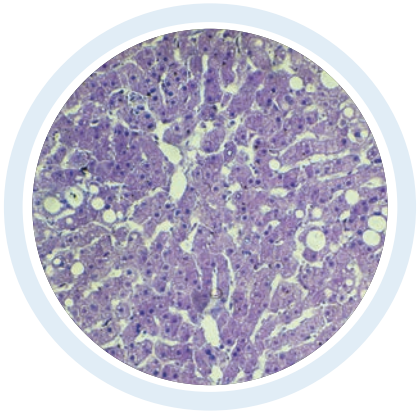
"It has been my privilege to work with remarkable colleagues and, most notably, outstanding students. I started as a professor in 1993 with some ideas about using computers in biochemistry education, but it has been the efforts of my students, mainly undergraduates, who have embraced these ideas and converted them into resources that others can use. Undergraduate students are capable of MUCH MORE than we imagine."

— PAUL A. CRAIG

Craig earned his Ph.D. at the University of Michigan and then held a postdoctoral position in biophysical chemistry at the Henry Ford Hospital in Detroit. He worked as an analytical biochemist at BioQuant Inc. in Ann Arbor, Michigan, and was a visiting scholar at the San Diego Supercomputer Center.

Craig will receive his award during the 2018 ASBMB Annual Meeting in San Diego, where he will deliver an award lecture titled "Promoting hypothesis-driven thinking in the undergraduate biochemistry lab." The presentation will take place at 2:30 p.m. April 22 in Room 6C in the San Diego Convention Center.

Adriana Bankston is a former bench scientist with a passion for improving training and policies for junior scientists. She is also a member of the board of directors at the nonprofit organization Future of Research.



MILDRED COHN AWARD IN BIOLOGICAL CHEMISTRY

Joshua–Tor recognized as 'one of the top scientists in her field'

By Alexandra Nail

Leemor Joshua–Tor, an investigator and professor at the Howard Hughes Medical Institute at Cold Spring Harbor Laboratory, has won the 2018 Mildred Cohn Award in Biological Chemistry from the American Society for Biochemistry and Molecular Biology. Named for the first female president of the ASBMB, the award is given to scientists who have used pioneering approaches to understand biological chemistry. Joshua–Tor is recognized for her work in resolving the structures of proteins involved in gene silencing, DNA replication and gene regulation in yeast.

Bruce Stillman, a colleague at Cold Spring Harbor, nominated Joshua–Tor for the award, writing that her "structural and biochemical insights have provided significant breakthroughs to our understanding of important cellular processes."

Joshua–Tor began her scientific career working for the Israel Defense Forces in research and development. As a graduate student, she worked in the lab of Joel Sussman at the Weizmann Institute of Science where she mastered X-ray crystallography and studied abnormalities in DNA structure. During her postdoctoral work at the California Institute of Technology, she focused on hexameric compartmentalized proteases called bleomycin hydrolases.

Joshua–Tor's major contributions have focused on structural characterization of proteins in RNA-mediated silencing; helicase mechanisms in DNA replication; and galactose, or GAL, protein interactions in yeast-gene regulation. Her lab was the first to identify Argonaute as the protein in the RNA-induced silencing complex that carries out the cleavage of mRNA for gene silencing. Later collaborations with Greg Hannon at Cold Spring Harbor showed that only Argonaute and silencing RNA were needed for cleavage of mRNA targets and effective RNA interference.

"I'm so thrilled to be honored with this award named after such an incredible trail blazer as Mildred Cohn. What an inspiration!"

— LEEMOR JOSHUA–TOR

Joshua–Tor's group also has investigated the mechanism of DNA translocation by DNA helicases and how helicase is able to unwind DNA during the replication process. John Kuriyan, a professor of molecular and cell biology at the University of California, Berkeley, supported Joshua–Tor's nomination for the Cohn award, writing of this work, "In one swoop, this paper showed how helicase recognizes DNA and how ATP binding and hydrolysis results in a spiral staircase that reptates around the DNA."

Joshua–Tor and her team solved the structure of the transcriptional repressor GAL80, which binds to and represses the GAL4 activator protein important for galactose utilization in yeast. Before her work, it was not known how GAL80 was able to dissociate rapidly from GAL4 to allow for galactose metabolism.

Joshua–Tor's lab now focuses on mechanisms of RNAi and DNA replication, including the regulation of the important miRNA let-7. Her lab has also recently solved the structure of the human origin recognition complex, using combined X-ray crystallography and cryo-electron microscopy to create three-dimensional images of proteins.

Joshua–Tor has received numerous awards over the years, including the American Council on Education Women's Network Women in Science and Education Leadership Award, the Dorothy Crowfoot Hodgkin Award from the Protein Society, and the Beckman Young Investigator Award from the Arnold and Mabel Beckman Foundation.

Joshua–Tor will receive her award during the 2018 ASBMB Annual Meeting in San Diego, where she will deliver an award lecture titled "The origin recognition complex: where it all begins." The presentation will take place at 8:30 a.m. April 23 in Room 6B in the San Diego Convention Center.

Alexandra Nail (alexandra.gjevre@uky.edu) is a Ph.D. candidate in the department of microbiology, immunology and molecular genetics at the University of Kentucky.

HERBERT TABOR RESEARCH AWARD

Hart honored for glycobiology breakthroughs

By Dawn Hayward

Many proteins are not physiologically active after translation. In fact, many have small chemical groups such as sugars or phosphates added later in what are called post-translational modifications. One such suite of modifications, glycosylation, was long thought to be added only in the secretory pathway or at the cell surface. Glycobiologist Gerald Hart debunked this myth when he showed that a modification called O-linked beta N-acetylglucosamine, or O-GlcNAc, was added to intracellular cytoplasmic and nuclear proteins. For this and other contributions, Hart, a professor and director of biological chemistry at the Johns Hopkins University, has won the American Society for Biochemistry and Molecular Biology's 2018 Herbert Tabor Research Award.

Hart began his work in glycobiology as a graduate student in Gary Conrad's laboratory at Kansas State University where he studied sugar modifications to proteins including proteoglycans and glycosaminoglycans. While a postdoctoral fellow at Johns Hopkins in William Lennarz's laboratory, Hart experimentally determined the protein amino acid sequence required for the enzyme oligosaccharyltransferase to add a sugar moiety. As an independent investigator at Johns Hopkins, Hart continued studying glycosylation, looking at the addition of sugars to the nitrogen of certain amino acids, termed N-linked glycosylation. A collaboration with Paul Englund's laboratory at Johns Hopkins led to determining the pathway necessary to add a phospholipid, glycosylphosphatidylinositol, to proteins attached to the plasma membrane.

Members of Hart's lab discovered the addition of O-GlcNAc to cytoplasmic and nuclear proteins in the 1980s. This modification is a monosaccharide sugar and is not elongated further. Its cycling on and off of proteins is similar to phosphorylation, with one enzyme adding the sugar and another removing it. In addition, the donor used to generate O-GlcNAc is made by redirecting incoming glucose to a different pathway. Hart's group characterized and cloned the enzymes involved in the O-GlcNAc addition and investigated the interplay between O-GlcNAc and phosphorylation. They determined that the O-GlcNAc modification is added to proteins involved in signaling and transcription and that its generation is a nutrient sensor, as a substantial amount of glucose is siphoned away from glycolysis to generate the modification.

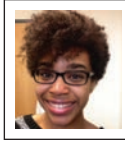
"Receiving the Herb Tabor Award is a special honor for me personally. I have admired Dr. Tabor since I was a graduate student. Not only because he is a first-rate scientist, but also because of his devotion in leading the premiere biochemistry journal for such a long time. He handled complex and contentious issues in a manner that always treated people with respect and civility. Herb is an amazing scientist, a nice human being, and an incredible citizen of our field. He serves as a role model that we can all aspire to."

— GERALD HART

Hart has served on the National Institutes of Health common fund glycoscience panel and the Howard Hughes Medical Institute review panel. He was founding editor-in-chief of Glycobiology from 1989 to 2001. He is an associate editor of the Journal of Biological Chemistry and Molecular & Cellular Proteomics and the president-elect of the ASBMB.

In his letter nominating Hart, Kevin Campbell, professor of molecular physiology and biophysics at the University of Iowa, wrote that Hart "created an entirely new field by demonstrating (the O-GlcNAc modification) occurs in both the nucleus and cytoplasm of mammalian cells." A.L. Burlingame, a professor of pharmaceutical chemistry at the University of California, San Francisco, and editor of Molecular & Cellular Proteomics, supported the nomination, noting that this honor fits Hart's work: "considering the achievements of Herb Tabor and his towering stature in reporting and molding the progress of biological chemistry through JBC, Jerry Hart is the perfect candidate for consideration of this award."

Hart will receive his award during the 2018 ASBMB Annual Meeting in San Diego, where he will deliver an award lecture on nutrient regulation of signaling and transcription. The presentation will take place at 8 a.m. April 22 in Room 6B at the San Diego Convention Center.



Dawn Hayward (dhaywar5@jhmi.edu) is a graduate student at the Johns Hopkins University School of Medicine.

EARL AND THRESSA STADTMAN YOUNG SCHOLAR AWARD

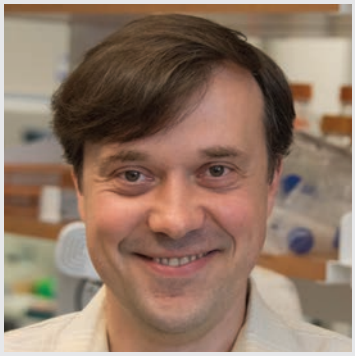
'Astonishing advances' in ribosome research earn Korostelev recognition

By Lauren Borja

Andrei Korostelev, an associate professor of biochemistry and molecular pharmacology at the University of Massachusetts Medical School, has won the 2018 American Society for Biochemistry and Molecular Biology Earl and Thressa Stadtman Young Scholar Award in recognition of his contributions to the understanding of ribosome structure and translation.

Korostelev's research focuses on capturing minute structural changes in ribosomes as they translate RNA into proteins. He uses methods such as X-ray crystallography and cryogenic electron microscopy to take snapshots of the ribosome during translation. Nominating him for the award, Joachim Frank, a professor at Columbia University who received a 2017 Nobel Prize for the development of cryo-EM, wrote that Korostelev's work represents "astonishing advances, both of methodology and biological knowledge — taking advantage of the most recent toolset of cryo-EM — which would have been impossible only a few years ago."

Korostelev captures high-resolution snapshots of ribosome movements during translation of RNA into proteins. Because he can make molecular movies with a resolution of a few angstroms, his experiments reveal minute details about the fundamental dynamic mechanisms governing translation. Korostelev's work includes investigations into how viruses or diseases change the initiation, elongation and termination of the translation process. Recently, he and his collaborator Nikolaus Grigorieff of the Howard Hughes Medical Institute visualized the mechanism through which the ribosome ensures accuracy during translation. According to Grigorieff, "This process is at the core of ribosome function and is therefore an outstanding achievement in his field."



"Scientific research is immensely rewarding on its own. Being recognized by the ASBMB as an Earl and Thressa Stadtman Scholar is empowering, as it strengthens the motivation of my lab to explore the unknowns of translation—a puzzling and complex aspect of the cellular world. It also motivates me to excel both as a scientist and as a mentor, reaching for the standard set by Earl and Thressa. I thank my mentors and my lab members with whom I've had the privilege to work."

— ANDREI KOROSTELEV

Korostelev started studying ribosome biology early in his career, as a Ph.D student in Michael Chapman's lab at Florida State University. For his doctorate, Korostelev developed computational methods for analyzing images derived from X-ray crystallography or cryo-EM data. These methods have been pivotal in the field of structural biology for creating high-resolution atomic models of ribosomes and other macromolecular (protein and nucleic acid) structures.

Korostelev continued his work as a postdoctoral fellow under Harry Noller at the University of California, Santa Cruz. There, he produced high-resolution images of ribosomes using X-ray crystallography. These images allowed further insights into the ribosome translation mechanism, some of which altered how scientists understand translation termination.

In 2010, he joined the faculty at the University of Massachusetts in Worcester. Since establishing his own research group, he has published more than 20 papers.

"I believe Andrei, who has now joined the growing ranks of cryo-EM practitioners, is one of the most promising young investigators," Frank wrote.

Grigorieff supported the nomination, describing Korostelev as "a fantastic collaborator who is willing to take risks and cross boundaries into new areas of research." Korostelev also helped establish the New England High-Resolution Cryo-EM Facility, which is shared jointly between the University of Massachusetts Medical School and Harvard Medical School. Since it opened in late 2016, researchers from around the world have had access to cryo-EM techniques.

Korostelev will receive his award during the 2018 ASBMB Annual Meeting in San Diego, where he will deliver an award lecture on visualizing translation by ensemble cryo-EM. The presentation will take place at 9 a.m. April 23 in Room 6B in the San Diego Convention Center.

Lauren Borja (laurenborja@gmail.com) is a postdoc at the University of British Columbia.

AVANTI AWARD IN LIPIDS

Voelker's discoveries and integrity draw praise

By Stefan Lukianov

Dennis R. Voelker, director of research of the pulmonary division in the department of medicine at National Jewish Health and a professor of biochemistry and molecular genetics at the University of Colorado, Denver, will receive the Avanti Award in Lipids from the American Society for Biochemistry and Molecular Biology. The award recognizes his work on lipid metabolism, nonvesicular phospholipid trafficking and phospholipid regulation of innate immunity.

Voelker has made "seminal contributions" to the field of lipid biology, George M. Carman of Rutgers University wrote in his nomination letter, adding that he has collaborated several times with Voelker "because of his expertise and keen insight into the molecular genetics and biochemistry of lipids."

The Voelker group has focused for 37 years on such topics as phospholipid-protein interactions, lipid metabolism, lipid transport and lipid enzymology, using a variety of techniques in virology, biochemistry and molecular biology. His early research provided insight into the mechanisms of phospholipid transport between organelles, especially between the endoplasmic reticulum and mitochondria. Phospholipids are major constituents of cell membranes, consisting of a hydrophilic head group linked by a phosphodiester to a hydrophobic segment containing esterified fatty acids. The amphipathic nature of phospholipids enables them to spontaneously form bilayer structures, which are the hallmark of biological membranes. Using biochemical and genetic approaches, Voelker's group has identified genes and proteins important for the phospholipid aspect of membrane assembly.

"It is an honor to receive the Avanti Award in Lipids, and I am indebted to my mentors, Ten-ching Lee, Fred Snyder and Eugene P. Kennedy for providing exceptional training. I also must recognize the students and fellows whose insights and dedication have been an essential part of my laboratory."

— DENNIS R. VOELKER

Most recently, the Voelker lab has made important advances in understanding how phospholipids inhibit innate immune processes and respiratory viral infections. The lab found that there are high-affinity interactions between anionic phospholipids and enveloped respiratory viruses, such as respiratory syncytial virus and influenza A virus, that inhibit viral infection. These phospholipids also bind to Toll-like receptors, which are crucial for triggering inflammatory processes of the innate immune system. This interaction inhibits the inflammatory response that accompanies infection and injury, thereby protecting the lungs from the damaging effects of prolonged inflammation.

In addition to Voelker's outstanding research, Carman mentioned his superb mentorship. Several of Carman's students worked with Voelker, whose "guidance in research excellence and communication propelled their careers in academia or the pharmaceutical industry," Carman wrote.

Richard J. Martin, chair of the department of medicine at National Jewish Health, described Voelker in a letter supporting the nomination as an integral member of their research community. "At National Jewish he is highly regarded by faculty, fellows and students for his scientific acumen, integrity and insight," Martin wrote, adding that Voelker's presentations there are "heavily attended and reach all researchers from basic to clinical in an engaging and enlightening scientific manner."

Voelker earned his Ph.D. from the University of Tennessee-Oak Ridge National Laboratory Graduate School of Biomedical Sciences in 1978. He completed his postdoctoral training at Harvard Medical School in 1981, afterward becoming an assistant professor in the department of biochemistry, biophysics and genetics at the University of Colorado Health Sciences Center as well as an assistant faculty member in the department of medicine at the National Jewish Center for Immunology and Respiratory Medicine. Voelker was promoted to full professor in 1994.

Voelker will receive his award during the 2018 ASBMB Annual Meeting in San Diego, where he will deliver an award lecture on phospholipid regulation of inflammatory processes and viral infection. The presentation will take place at 8 a.m. April 23 in Room 6B at the San Diego Convention Center.

Stefan Lukianov (stefanlukianov@gmail.com) is a Ph.D. candidate at Harvard Medical School and a contributor to ASBMB Today.

WILLIAM C. ROSE AWARD

Clarke stands out with seminal discoveries in protein methylation and inspired teaching

By Nathalie Gerassimov

Steven Clarke, distinguished professor of chemistry and biochemistry at the University of California, Los Angeles, has won the 2018 William C. Rose Award for illuminating how protein modifications by methyl groups regulate fundamental biological processes.

Christine Hrycyna, who earned her Ph.D. in Clarke's lab and now heads the chemistry department at Purdue University, nominated him for the award, writing, "Not only has he sustained a highly impressive level of novel research in biochemistry and molecular biology over the past nearly forty years, but he has also been instrumental in mentoring and launching the careers of entire generations of scientists."

One of many scientific insights emerging from Clarke's laboratory is that protein damage repair is a fundamental cellular process and a response to aging. It is well appreciated that DNA undergoes damage and repair throughout an organism's lifetime. However, prior to Clarke's seminal work, it was less appreciated that damaged proteins can be recognized and repaired by specific enzymes.

Clarke and his student Philip McFadden discovered the first example of a protein repair methyltransferase in 1982. Two amino acid residues, asparaginyl and aspartyl, can react spontaneously with the protein backbone, leading to a kink in the protein that can render it nonfunctional. This kink (isoaspartyl residue) can be modified by a widely conserved methyltransferase, leading to regeneration of the normal aspartyl residue. The deletion of this repair methyltransferase affects the lifespan of organisms including worms, flies and mice, which indicates its fundamental role.

"It is such an honor to be named for this award emphasizing both science and mentorship. I am grateful to have had so many wonderful scientists in my laboratory and as collaborators. I hope I have learned well from my own mentors, including James E. 'Skip' Skinner, Neal Cornell, Guido Guidotti, Daniel E. Koshland Jr. and David Sigman."

— STEVEN CLARKE

Subsequent work in the Clarke laboratory has pioneered bioinformatic approaches to find candidate methyltransferases from genomic data and uncovered their diverse roles of methylation reactions in biology. These include the protein phosphatase 2A C-terminal leucine methyltransferase, the ribosomal protein histidine methyltransferase and the N-terminal X-P-K methyltransferase. In addition, in collaboration with other laboratories, he and his students identified the C-terminal isoprenylcysteine methyltransferase and found the first protein arginine methyltransferase and additional members of its family. Finally, he and his students discovered small-molecule methyltransferases involved in the repair of age-damaged S-adenosylmethionine (a cosubstrate involved in methyl group transfers and other reactions), yeast invasive growth, and resistance to the cantharadin toxin produced by blister beetles.

David Eisenberg, professor of molecular biology at UCLA, wrote in support of the nomination of Clarke's "sustained, highly original contributions to biochemical and molecular biological research," and Jamil Momand, a professor of biochemistry at California State University, Los Angeles, wrote, "At the research level … Steve is head and shoulders over the majority of independent scientists. He is a pioneer in the areas of aging and protein processing; and in the field of protein methylation, he is the top expert."

The Rose Award also recognizes outstanding commitment to scientific education. Clarke has published 290 papers during his 39 years at UCLA, the majority of which have his graduate and undergraduate students as first authors. Forty-seven graduate students have completed their Ph.D. with Clarke and have gone on to become professors and scientists in industry and academia as well as to have careers in law and finance. Another aspect of Clarke's scientific

education legacy is his work since 1988 as the director of the National Institutes of Health-funded UCLA Cellular and Molecular Biology Training Program, where he has developed research integrity training and worked to increase the diversity of Ph.D. candidates.

Zhaohui Sunny Zhou, a professor of chemistry and chemical biology at Northeastern University, wrote that Clarke is defined by his attitude of collaboration and dedication as a mentor. "Because of Steve's model as a generous leader," Zhou wrote, "the whole field has been much more collaborative, and as a result, more productive." And Mary Beth Mudgett, professor of biology at Stanford University, wrote, "An impactful scholar like Steve never stops mentoring. He is forever inspirational!"

Harvey Herschman, a distinguished research professor at the David Geffen School of Medicine at UCLA, wrote that Clarke's seminars are "always engaging, informative, well organized, delivered with astonishing enthusiasm, inspiring, and — above all — clear." Clarke's lecturing can be experienced on the UCLA YouTube channel or live at the American Society for Biochemistry and Molecular Biology award ceremony.

Clarke will receive his award during the 2018 ASBMB Annual Meeting in San Diego, where he will deliver an award lecture titled "What can protein methylation tell us about biology? Histones, ribosomes, translation factors and cancer." The presentation will take place at 8:30 a.m. April 25 in Room 6C of the San Diego Convention Center.

Nathalie Gerassimov (nathalie.gerassimov@gmail.com) is a Ph.D. student at Johns Hopkins School of Medicine.

SPECIAL EVENTS AND WORKSHOPS

SATURDAY, APRIL 21

8:30 a.m. to 4:30 p.m. | **Graduate Student and Postdoc Career-Development Event**

1 p.m. | **Undergraduate Poster Competition**

4:45 p.m. | **Careers Speed Networking**

6 p.m. to 7 p.m. | **Tang Prize Award Lecture**
Feng Zhang, McGovern Institute for Brain Research, MIT

7p.m. to 8:30 p.m. | **EB Welcome Reception and Science Outreach Activity Posters**, Sails Pavilion

SUNDAY, APRIL 22

12:15 p.m. to 2:15 p.m. | **Poster Sessions and Meet the Speakers**, Exhibit Hall
View the posters, network with your peers, and meet with world-renowned scientists during the midday poster sessions for an informal scientific discussion.

12:30 p.m. to 2 p.m. | **Advocacy Town Hall**, Room 6A

5:30 p.m. to 6:15 p.m. | **Organizing a Successful ASBMB Student Chapter**, Room 31C

5:30 to 7 p.m. | **Workshops**

- *The Art of the 3-D Cell Culture, from Organoids to Organs-on-a-Chip*, Room 31B
- *Cryo-EM and Cryo-ET: Step-by-Step*, Room 31A
- *Your Data, Magnified: Success in Scientific Publishing*, Room 30E
- *Storytelling and the Art of Giving a Good Presentation*, Room 6B
- *Strategically Building Your CV at Every Career Stage*, Room 6A

7 p.m. to 8:30 p.m. | **ASBMB Annual Meeting Networking Reception**, foyer outside Rooms 30A-E

7 p.m. to 9 p.m. | **Student Chapters Advisers Networking Reception** (by invitation)

MONDAY, APRIL 23

12:15 p.m. to 2:15 p.m. | **Poster Sessions and Meet the Speakers**, Exhibit Hall

5:30 p.m. to 7 p.m. | **Workshops**

- *Optogenetics and Molecular Sensors: Tools and Applications*, Room 31B
- *Supported Lipid Membranes and Nanodiscs*, Room 30D
- *Molecular Visualization*, Room 6A
- *Turning Science Research into Science Outreach*, Room 6B

9 p.m. to 11 p.m. | **Young Experimental Scientists (Y.E.S.) Mixer**, Hilton Bayside in Aqua ABC

TUESDAY, APRIL 24

12:15 p.m. to 2:15 p.m. | **Poster Sessions and Meet the Speakers**, Exhibit Hall

5:30 p.m. to 7 p.m. | **Women Scientists Mentoring and Networking Event**, Room 6A

WEDNESDAY, APRIL 25

11:45 a.m. to 2 p.m. | **Poster Sessions** and Meet the Speakers, Exhibit Hall

MCP to spotlight systems biology and proteomics

By Saddiq Zahari

Molecular & Cellular Proteomics will sponsor a session on systems biology and proteomics at the 2018 American Society for Biochemistry and Molecular Biology Annual Meeting. Leading researchers in the field will discuss state-of-the-art systems biology and proteomic techniques applied in a number of areas, including virus infection, biomarker discovery and validation, and drug response.

The session will begin at 10 a.m. April 23 in Room 6E of the San Diego Convention Center.

10 A.M.

Protein localization and interaction partners

Knowing where a protein resides within the cell and what other proteins it interacts with is crucial to understanding its molecular functions. MCP Deputy Editor Steven Carr of the Broad Institute will present new approaches for studying subcellular localization of proteins and their interaction partners with high spatial resolution. Carr will describe the proximity labeling technique, where the protein of interest is fused to a promiscuous biotin ligase to enable the identification of its interacting partners using mass spectrometry. His talk will focus on how the technique has been used to investigate fundamental biological questions, such as mapping mitochondrial matrix proteins and defining the proteomes of synapses of living neurons. He also will describe new work on developing genomic locus proteomics, a technique that combines proximity labeling, genome targeting and quantitative mass spectrometry to identify proteins that occupy specific genomic loci.

CARR

10:30 A.M.

Proteome organization during viral infections

Viruses remodel host cellular organelles, such as mitochondria, to suppress host defense and promote viral replication. Session organizer Ileana Cristea of Princeton University will give a talk on how her laboratory integrates experimental studies, mathematical modeling and inference methods to study the proteome dynamics of host cells during viral infections. Cristea, an MCP editorial board member, will describe how methods such as live-cell microscopy and mass spectrometry-based proteomics have been used to discover the dynamic changes that occur in organelle composition and subcellular localization in response to viral infection. She will highlight how integrative -omic technologies can help paint a picture of the pathogen's life cycle and aid in the future development of antiviral therapies.

CRISTEA

11 A.M.

Building an operating system for cancer

With systems biology comes big data. A challenge to advancing precision medicine to treat cancer is how to integrate massive data sets and studies to translate to actionable information for patients. Kevin White of the University of Chicago will talk about building an operating system for cancer. He will discuss the steps that have been taken to develop technological solutions and novel approaches to the challenge of integrating massive data sets and validating discoveries. He will describe his efforts to engineer and industrialize a systematic solution to allow physicians to treat patients using a real-time machine learning system that condenses petabytes of data into actionable information matched uniquely to each patient.

WHITE

11:30 A.M.

Virion display technology to characterize GPCRs

G-protein coupled receptors, or GPCRs, are a family of membrane-bound receptors that are notoriously difficult to study because they must be embedded in a membrane to maintain native conformation. Heng Zhu of the Johns Hopkins University School of Medicine will describe the development of a virion display array technology, VirD, where GPCRs are displayed in the membrane envelope of virions to maintain their native conformation. Zhu, who is also an MCP editorial board member, will discuss how the VirD approach has been used to characterize orientation, ligand-binding activities and protein targets of the GPCRs. He plans to illustrate the utility of VirD technology as a high-throughput platform for screening of drugs, affinity reagents, ligands and more.

ZHU

Saddiq Zahari (szahari@asbmb.org) is the editor for manuscript integrity at Molecular & Cellular Proteomics.

Make room for sessions beyond the science

By Danielle Snowflack

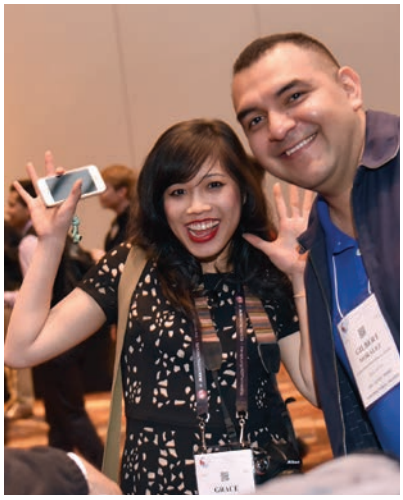
A question for graduate students and postdocs: How are you preparing for the annual meeting?

I remember pouring over the abstract book with my lab mates before my first scientific conference. What scientific sessions did I want to attend? What techniques did I want to learn? How would they inform my research? I carefully planned my days around my science.

As my career progressed, I realized that scientific meetings offer more than just research talks. These meetings provide amazing opportunities for professional development, hosted by experts from around the country. Now, when I plan my schedule for a meeting, I pencil in some time for these exciting, interactive events that focus on career growth beyond the lab. Whether this is your first meeting or your tenth, I suggest you do the same. To help, I've broken the 2018 American Society for Biochemistry and Molecular Biology Annual Meeting into four main categories for you to explore.

Education

While your main focus is on your research, chances are you spend some time in the front of a classroom. Paul Craig of the Rochester Institute of Technology, winner of this year's ASBMB Award for Exemplary Contributions to Education Lecture (see his profile on page 41), will discuss his work, "Promoting hypothesis-driven thinking in the undergraduate biochemistry lab." This lecture will show you how to help your students engage with traditional biochemistry lab experiences. You also can learn more about active learning in biochemistry and molecular biology during the Education Spotlight Session.



Communication

Regardless of your career stage or goals, communication skills are critical. The more compelling your message, the more likely you are to impact your students, publish a paper or even get a job. Several panels and workshops will provide tips and tricks for communicating with expert and nonexpert audiences. One session I'm excited about is a workshop on "Storytelling and the Art of Giving a Good Presentation" led by Public Outreach Committee members Thomas Baldwin and Teresa Evans. In this interactive session, you'll learn how to create a compelling narrative with your research. These skills are used by journalists and professional communicators every day — so why not put them to work for you?

Outreach

The importance of science outreach continues to grow as we work to combat misinformation and present science as a human endeavor. Outreach can be as simple as sharing your research with a friend or neighbor, or as complex as hosting a multiday science fair. To learn more about how outreach can be inspired by your work in the lab, be sure to attend the "Transforming Science Research into Science Outreach" workshop organized by the ASBMB Public Outreach Committee. Let outreach professionals help you expand, improve or even start your own public engagement activity.

Career development and networking

Have you looked at your CV lately? Does it truly reflect your background and training? Learn more about using your unique experiences to market yourself by attending "Strategically Building your CV at Every Career Stage" organized by the ASBMB Education and Professional Development Committee. You'll get advice from a diverse panel of experts on how to present yourself in the best possible light to employers to achieve your career goals.

On the facing page, you'll find handy schedules that you can cut out and carry with you so you don't miss any of these great sessions.

And remember — while several networking events are scheduled at the annual meeting, every interaction has the possibility to be a networking experience. Don't be afraid to seize the moment. Bring business cards to share with people you meet. These cards can contain links to your LinkedIn page, your science communication portfolio, any resources you want a potential mentor or collaborator to access. (Pro tip: Be sure to use a professional-sounding email address.)

Danielle Snowflack (dsnowflack@asbmb.org) is the director of education, professional development and outreach at the ASBMB.

EDUCATION

CREST (Connecting Researchers, Educators and Students) Conversations
12:15–1:15 p.m. Sunday, April 22, in the ASBMB lounge (near ASBMB booth, #1316, in exhibit hall)

ASBMB education award lecture
Sunday, April 22, 2:30–3:45 p.m. in Room 6C
"Promoting hypothesis-driven thinking in the undergraduate biochemistry lab" — Paul Craig, Rochester Institute of Technology

Workshop | Molecular Visualization
5:30–7 p.m. Monday, April 23 in Room 6A

Spotlight Talks: Active Learning
4–5:15 p.m. Monday, April 23, in Room 31C

Education poster session
12:15–2:15 p.m. Monday, April 23, in the exhibit hall

OUTREACH

Science Outreach Poster Session
7–8:30 p.m. Saturday, April 21, in Sails Pavilion

Workshop | Storytelling and the Art of Giving a Good Presentation
5:30–7 p.m. Sunday, April 22, in Room 6B

Workshop | Transforming Science Research into Science Outreach
5:30–7 p.m. Monday, April 23, in Room 6B

CAREER DEVELOPMENT AND NETWORKING

Spotlight Talks: Advancing Successful Careers
4:15–5:15 p.m. Sunday, April 22, in Room 31C

Workshop | Constructing your Elevator Pitch
Noon–1 p.m. Monday, April 23, in Exhibit Hall D, Career Resources Center Room 2

Session and panel discussion | Strategically Building Your CV at Every Career Stage
10 a.m.–noon Sunday, April 22, in Room 6A

Workshop | Strategically Building Your CV at Every Career Stage
5:30–7 p.m. Sunday, April 22, in Room 6A

Education poster session
12:15–2:15 p.m. Sunday, April 22, in the exhibit hall

COMMUNICATION

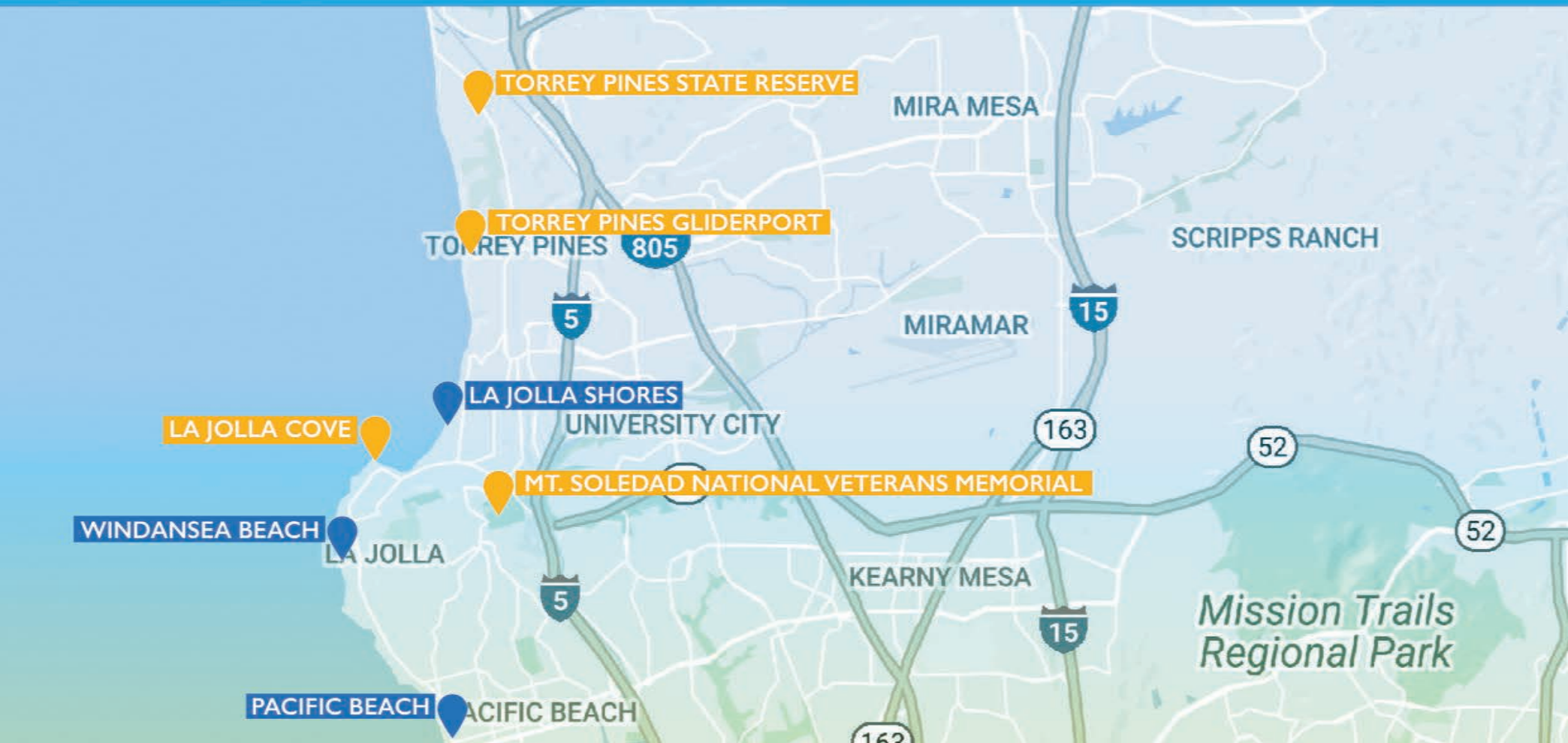
Workshop | Storytelling and the Art of Giving a Good Presentation
5:30–7 p.m. Sunday, April 22, in Room 6B

Workshop | Your Data, Magnified: Success in Scientific Publishing
5:30–7 p.m. Sunday, April 22, in Room 30E
Sponsored by Journal of Biological Chemistry

Session and panel discussion | Communicating Scientific Ideas to Novice Audiences
10 a.m.– noon Monday, April 23, in Room 31C

Meet the Speakers
2:30–3:30 p.m. Monday, April 23, in the ASBMB lounge (near ASBMB booth, #1316, in exhibit hall)
Learn more about the ASBMB's "Art of Science Communication" course from members of the society's Public Outreach Committee

WELCOME TO SAN DIEGO




BELMONT PARK
MISSION BAY
MISSION VALLEY
OLD TOWN SAN DIEGO
OCEAN BEACH
OCEAN BEACH
LIBERTY STATION
BALBOA PARK
SUNSET CLIFFS
San Diego
POINT LOMA
CORONADO BEACH
CORONADO ISLAND
CABRILLO NATIONAL MONUMENT
National City
La Mesa
Lemon Grove
Bonita
RANCHO DEL REY
Imperial Beach
805
8
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15
125
San Diego Air & Space Museum
USS MIDWAY
HORTON PLAZA
GASLAMP QUARTER
SEAPORT VILLAGE
OLD TOWN TROLLEY TOUR
CONVENTION CENTER
Hilton Diego
ASBMB '18
ANNUAL MEETING
SAN DIEGO | APRIL 21–25

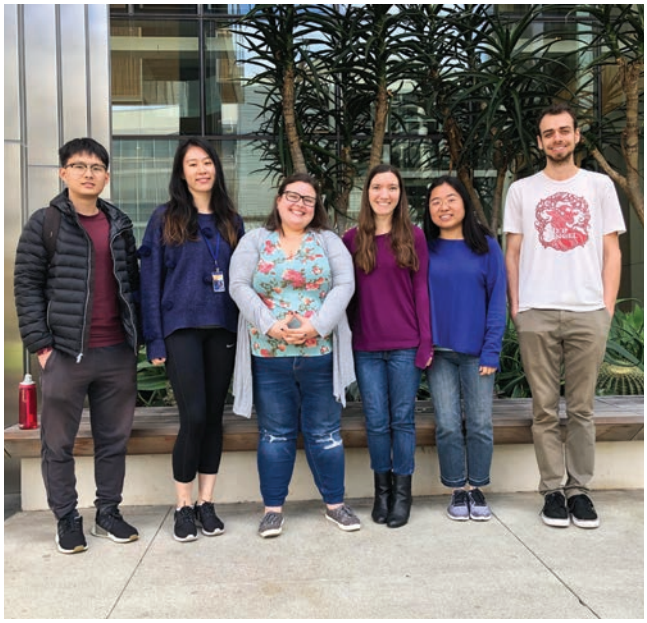
WELCOME TO SAN DIEGO

By Terri Clister

To make your stay a little easier, here are some recommendations from the Zhang Lab at the University of California, San Diego, for local places worth checking out. This advice comes to you from eight graduate student, postdocs and project scientists who have lived here at most three years; it's meant to be necessary and sufficient, though by no means exhaustive. Every place listed has been visited at least once by one person (N=1).

A note about transportation: San Diego is a city of neighborhoods (well, duh). Unlike some cities, however, it can be difficult to navigate between neighborhoods without a car. I've structured this list such that places closer to the San Diego Convention Center are listed first, and you can easily fill any free time with things downtown. Buses and the trolley system are accessible from downtown/convention center, but they don't reach all the cool places. So, if you find yourself with more free time and want to venture farther out, know that San Diego has both Uber and Lyft ridesharing options.

The local attractions listed here and beaches are noted on the locator map on pages 42 and 43.



Members of Jin Zhang's lab at UC, San Diego, who contributed to this feature include, from left, Shawn Chen, Simin Li, Danielle Schmitt, Terri Clister, Xin Zhou, Chris Booth. Not pictured are Gary Mo and Brian Ross.

15 THINGS TO DO TO FILL YOUR FREE TIME

1 Old Town Trolley Tour

www.trolleytours.com/san-diego

The Old Town Trolley Tour is a great way to see San Diego and learn about local history. Options are for a one-day or two-day pass with hop-on/hop-off privileges for stops at or near many of the places listed here. The Seaport Village or Horton Plaza stops are the closest to the convention center, 0.6 mile each.

2 5th Avenue in Gaslamp Quarter

www.gaslamp.org

All along this street are restaurants and bars to try. If you're looking for a bar with a club vibe, check out Vin de Syrah *(901 Fifth Ave., 0.6 mile)*, which has a hidden entrance and a cool atmosphere.

3 Seaport Village

849 W. Harbor Dr, 0.6 mile

www.seaportvillage.com

Just around the corner from the convention center is Seaport Village with many shops and restaurants along the water. Check out Aaron Chang Art Gallery for world-famous surfing photography displayed in a unique way. And if you're hungry, Puesto (*789 W. Harbor Dr.*) has really good Mexican food, especially the tacos.

4 USS Midway

www.midway.org

910 N. Harbor Dr., 1 mile

Just beyond Seaport Village is the decommissioned USS Midway aircraft carrier, now a museum ship. Exhibits and tours give insight into the ship's involvement in post-WWII action.

5 Horton Plaza

324 Horton Plaza, 0.6 mile

www. westfield.com/hortonplaza

Need to do some shopping? Horton Plaza is close to the convention center and has many common retail stores.

6 Balboa Park

www.balboapark.org

A staple of San Diego, Balboa Park offers many activities. Museums? Check. Gardens? Check. Hiking/walking paths? Check. International houses? Check. An artist's village? Check. Special Earth Day events on April 22? Yep. (Actually, the "largest free environmental fair in the world.") The Old Town Trolley stops in Balboa Park; otherwise the easiest way to get there is by rideshare. Museums offer student discounts, so bring your student ID.

7 Coronado Island
www.coronadovisitorcenter.com
The trolley stops at the historic Hotel del Coronado. You also can catch the ferry at the convention center to the island for $4.75 one way. The hotel has a nice restaurant and beach access, both open to the public.

8 Old Town
www.oldtownsandiego.org
Both the green line trolley ($2.25 one way or $7 day pass) and Old Town Trolley have a stop in Old Town, which has many museums and restaurants. The Old Town market is a great place to get Mexican souvenirs. Check out Miguel's (*2444 San Diego Ave.*) for a great Taco Tuesday special.

9 Liberty Station
www.libertystation.com
The former naval training center has been redeveloped with multiple restaurants and shops, including artist storefronts. If you're into local craft brews, check out Stone Brewing.

10 Cabrillo National Monument
www.nps.gov/cabr
A beautiful location with a lighthouse and tide pools during low tide. (Plan your visit accordingly if you want to check them out, and wear good shoes.) The monument, at the end of a peninsula in the bay, commemorates the first European to arrive in San Diego. From the monument are some fantastic views of the city. This is a national park with a $15/vehicle fee or $7/person fee if you walk in.

11 Sunset Cliffs
www.bit.ly/OBSunsetCliffs
In a neighborhood called Ocean Beach (call it "OB" if you want to sound like a local), this place is exactly what it sounds like: cliffs right above the ocean with beautiful sunset views and walking paths. Maybe you'll even see the rare green flash.

OH, YOU JUST WANT TO GO TO THE BEACH?

If you want to brave the water, be aware that different sections of beach are designated for swimmers and for surfers.

Ocean Beach
www.oceanbeachsandiego.com/attractions/beaches
Great place to watch the sunset. Lots of bars to grab a beer and hang out.

Pacific Beach
www.pacificbeach.org
Very cool bars; if you want to catch a game, there's a bar for your team. You can watch surfers from the piero or walk along a boardwalk that extends into Mission Beach.

Mission Beach
Same beach, continues south of Pacific Beach.

Belmont Park
www.belmontpark.com
A small amusement park. Has a roller coaster, mini golf, laser tag and other activities.

Coronado
www.sandiego.org/explore/things-to-do/beaches-bays/coronado
Voted one of the best beaches in the United States. (Most restaurants have happy-hour specials.)

La Jolla Shores
www.lajolla.com/guides/la-jolla-shores-guide
Many small restaurants are nearby on Avenida de la Playa.

Windansea Beach
www.sandiego.com/beaches/windansea-beach
South of La Jolla Cove and less touristy. (May be rockier than other beaches, depending on tide and time of year.) Check out The Promiscuous Fork (*6984 La Jolla Blvd.*), a tiny/hole-in-the-wall café with good food.

12 Mount Soledad
www.soledadmemorial.com
A park/veterans memorial overlooking the city with a beautiful view of the bay, the ocean and mountains.

13 Torrey Pines Nature Reserve
www.torreypine.org
A great place for a longer hike, though be warned there is a long, steep hill to climb before panoramic ocean views on any of multiple paths.

14 Torrey Pines Gliders Port
www.flytorrey.com
Active gliding club on a cliff overlooking the ocean, with a small café.

15 La Jolla Cove
www.lajolla.com/guides/la-jolla-cove-guide
A popular tourist destination to see sea lions and walk along cliffs by the ocean, with many restaurants and shops to check out nearby.

Terri Clister (tclister@ucsd.edu) is a graduate student in Jin Zhang's lab at the University of California, San Diego, working toward a Ph.D. in molecular biology.

LOTS OF THINGS TO EAT

By Terri Clister & the Zhang Lab

QUICK BITES

The Food Shop ($ & vegan)
465 Fifth Ave. (0.3 mile from the San Diego Convention Center)
Vietnamese
(619) 359-8894

Oscar's Mexican Seafood($)
927 J St. (0.5 mile)
www.oscarsmexicanseafood.com
Serving almost exclusively fish tacos (depending whom you ask, best tacos in San Diego).

The Taco Stand($)
645 B St. (0.9 mile)
www.letstaco.com
Surprise, surprise: sells tacos (depending who you ask, best tacos in San Diego).

Tender Greens ($)
110 W. Broadway (0.9 mile)
www.tendergreens.com
SoCal chain offering good, fresh food, salads and sandwiches.

CASUAL DINING

The Broken Yolk Cafe ($$)
355 6th Ave. (0.3 mile)
www.thebrokenyolkcafe.com
SoCal-based chain restaurant, great place for breakfast/brunch.

Sab Lai Thai Kitchen ($$)
500 5th Ave. (0.3 mile)
www.sablaithaikitchen.com
Awesome Thai.

Breakfast Republic ($$)
707 G St. (0.6 mile)
www.breakfastrepublic.com
Great for breakfast/brunch.

Puesto ($$)
789 W. Harbor Dr. (0.6 mile), by Seaport Village
www.eatpuesto.com
Mexican food with great tacos.

Neighborhood ($$ & vegan)
777 G St. (0.6 mile)
Beer and good food.

Tajima ($$)
901 E St. (0.9 mile)
www.tajimasandiego.com
Delicious ramen.

The Crack Shack ($$)
2266 Kettner Blvd. (1.7 mile)
www.crackshack.com
The best fried chicken in a casual outdoor seating restaurant.

FROM SLIGHTLY ABOVE CASUAL DINING TO FANCIER OPTIONS

Fleming's Prime Steakhouse and Wine Bar ($$$)
www.flemingssteakhouse.com
380 K St. (0.2 mile)
Excellent steak.
(619) 237-1155

Double Standard ($$)
695 Sixth Ave. (0.5 mile)
www.dskrestaurants.com
Delicious Italian kitchenette.
(619) 795-8880

Cowboy Star Restaurant and Butcher Shop ($$$)
640 Tenth Ave. (0.7 mile)
www.cowboystarsd.com
Best steak in San Diego.
(619) 450-5880

Ironside ($$)
1654 India St. (1.3 miles)
www.ironsidefishandoyster.com
Fresh seafood and great cocktails ($1.50 oysters during happy hour).
(619) 269-3033

Barbusa ($$)
1917 India St. (1.5 miles)
www.barbusa.com
Really good Italian food.
(619) 238-1917

Cloak & Petal ($$$)
1953 India St. (1.5 miles)
www.cloakandpetal.com
Japanese in a beautiful atmosphere.
(619) 501-5505

CHEAP EATS

By Ana Maria Barral

Experimental Biology takes place in the San Diego Convention Center, which is in close proximity to the historic Gaslamp Quarter (full of restaurants, bars, and clubs), the Marina and Seaport Village. All touristy and beautiful, and food options often seem to be between upscale and fast food. Here are suggestions for good and affordable food in walking distance or a short Uber/Lyft ride away from the convention center. Sources were local recommendations and Yelp.

Richard Walker's Pancake House
520 Front St. (2-minute walk)
www.richardwalkers.com
American breakfast and brunch. Not the healthiest but for sure filling!

The Field Irish Pub
544 5th Ave. (4-minute walk)
www.thefield.com
Irish pub and restaurant. Irish atmosphere. Often live music.

Barleymash
600 5th Ave. (8-minute walk)
www.barleymash.com
American sports bar good for breakfast and brunch.

Hub Market and Deli
748 6th Ave. (12-min walk)
www.hubmarketanddeli.com
Deli with great sandwiches.

Bud & Rob's New Orleans Bistro
815 F St. (14-minute walk)
www.budandrobsbistro.com
Cajun/creole (New Orleans) food.

Pokez
947 E St. (19-minute walk)
www.pokezrestaurant.com
Mexican, vegetarian/vegan. Funky place.

Hodad's Downtown
945 Broadway (19-minute walk)
www.hodadies.com
Hodad's burgers are cult classics.

Ryan Bros Coffee
1894 Main St. (21-minute walk)
wwwryanbroscoffee.com/location-mainst.htm
Coffee and sandwiches. Coffees on tap!

Mariscos Mi Gusto Es
1531 Broadway (25-minute walk)
Mexican. Food truck!

Las Cuatro Milpas
1875 Logan Ave. (29-minute walk)
This is a local gem. Come early, as the lines get long. Closes at 3 p.m.

Ana Maria Barral (abarral@nu.edu) is an assistant professor at the National University in Costa Mesa, California, a member of the ASBMB's Public Outreach Committee and a member of the ASBMB Today editorial advisory board.

SOMETHING SWEET

Donut Bar ($, VG)
631 B St. (0.9 mile)
www.donutbar.com
Donuts! There will be a line, but it moves fast.

Extraordinary Desserts ($–$$)
1430 Union St. (1.1 miles)
www.extraordinarydesserts.com
Delectable desserts with sit-down or to-go options (they also serve non-dessert food). There's usually a line.

CRAFT BREWERIES

See **www.asbmb.org/asbmbtoday.com.**

Sacrifice and a strong network help build a research career

Adela Cota–Gomez talks about how her parents' sacrifice motivated her to pursue a career in research and how her professional network helped her get on her chosen career path.

Tell us about your current career position.

I am an associate professor in the department of medicine and division of pulmonary sciences and critical care medicine at the University of Colorado-Anschutz Medical Campus. I am also the coordinator of the undergraduate summer research program Graduate Experience for Multicultural Students, or GEMS.

What key experiences and decisions enabled you to reach your current position?

Many experiences have shaped who I am today, but by far the greatest one was witnessing my parents sacrifice for the future of their children. When I was 9 years old, my parents made the difficult decision to uproot us from Mexico, our home country, and immigrate to the United States for the sole purpose of giving me and my siblings greater opportunities to develop the potential they saw in us. I was old enough to understand their sacrifice. Seeing how hard it was for them to leave their own families behind in order to give us a chance at a better life was life-transforming. I resolved, then and there, to go as far as I possibly could, make them proud, make their sacrifice count and lead as full, happy and rewarding a life as I could. Every decision since then has been with that goal in mind, and I'm glad to report that I have done it. I can't think of a more exciting and rewarding career than mine, and I lead the life that I resolved to over 35 years ago.

COURTESY OF ADELA COTA–GOMEZ

Adela Cota-Gomez was able to find a satisfying research position with the help of her network.

How did you first become interested in science?

As a child, I was always intrigued by nature, especially living things. In junior and senior high school, biology and chemistry were my favorite subjects, so when I went to college I majored in biology. Like the vast majority of biology majors, I thought medicine was the most obvious career choice. However, when I started shadowing doctors in clinics and hospitals, I quickly realized that I hated patient interactions; medicine was most definitely not for me. I was scared and disappointed in myself and had no idea what else one could do with a biology degree. Luckily, I had a great college counselor who pointed me in the direction of research. The following summer I had a summer undergraduate research fellowship, or SURF, and that was when I fell head-over-heels in love with research. I have not stopped doing it since.

Were there times when you failed at something critical to your path? If so, how did you get back on track?

At the end of my postdoctoral training, I was offered a tenure-track faculty position in a primarily teaching university that was attempting to increase their research portfolio. I was attracted to the idea of developing new programs that I thought would open a lot of doors for me, so I accepted the position. Three years into that position, I realized that I was not able to pursue the research I wanted to do because the university did not have the research infrastructure and grant-processing office I needed to perform translational research. Also, the teaching load was very heavy and the release time was not sufficient for the intensity of research I aspired to. While I thoroughly enjoyed teaching, I was not willing to do it at the expense of research. I realized that I had deviated far away from my original career path. Luckily, I was able to regroup and get

back on track largely due to the commitment of the professional network I had built over the years. Thanks to those connections, I secured a tenure-track position at the University of Colorado-Anschutz Medical Campus and have since risen through the ranks. I'm grateful for the caring and supportive network that helped me get back on path.

What advice would you give to young people from underrepresented backgrounds who want to pursue a career similar to yours?

As early as possible, find a mentor or mentors who will help you navigate the challenges and stumbles along the career path and who will also celebrate your successes. Think of them as your professional parents; they should be the center of your support network. Stay in touch with them always, use them as a grounding stake and allow them to help you.

What are your hobbies?

I love books and movies, in that order. My favorite way to unwind after a long grant-writing period or a particularly unsuccessful lab day is to curl up with a book and a glass of wine. My favorites are fiction novels, especially science fiction and fantasy. My favorite author is Stephen King — I can get lost in his worlds for hours.

What was the last book you read?

"The Gunslinger," the first book in the "Dark Tower" series by Stephen King. I read it ahead of the theatrical release of the "Dark Tower" movie.

Do you have any heroes, heroines, mentors or role models? If so, describe how they have influenced you.

I admire all my colleagues and collaborators; I feel a strong kinship and solidarity with them, and they are the ones who best understand my motivations, drive and struggles.

What is it that keeps you working hard every day?

The satisfaction of my research discoveries — the idea that no one else in the world is doing exactly the same thing that I do.

About the Research Spotlight

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

25 years of inspiring the next generation

Teens get hands-on experience at UT Southwestern Science Day

By Amanda Goldner, Brittany Johnson & John Corbett

A graduate student at the University of Texas Southwestern Medical Center explains to a group of high school students why people in the same family can have straight or curly hair, weaving the central dogma of biology and Mendelian genetics into the explanation. After absorbing the information, one teenager has a lightbulb moment, saying, "Oh, that's why my grandma has curly hair but the rest of us have straight hair!"

That straight-haired student was one of about 180 Dallas-area high schoolers exposed to information about careers in medicine and biomedical research at the 25th anniversary of the annual Health Professions Recruitment and Exposure Program, or HPREP, at UT Southwestern.

Stuart Ravnik, associate dean of the university's graduate school and a member of the American Society for Biochemistry and Molecular Biology's Public Outreach Committee, helps organize the event. "The initial idea was to create hands-on science activities to demonstrate how scientists might address a scientific question," he said.

Science and medicine originally were covered in a single day, but three years ago the high school students suggested more time be dedicated to science. A committee of three graduate students helped plan Science Day from the start and modified activities to better emulate scientific experiments and to demonstrate important scientific principles, such as hypothesis formulation, data processing and results interpretation. More than 400 high school students from underrepresented backgrounds applied for the program. Participants were selected based on their career interests, according to Dawn Cureton of the Office of Diversity and Inclusion at UT Southwestern.

PHOTOS COURTESY OF STUART RAVNIK

Pictured with adviser Stuart Ravnik (second from right) at the HPREP Science Day at UT Southwestern are the authors of this article, (from left) John Corbett, Amanda Goldner and Brittany Johnson.

The day introduced the students to diverse topics in biomedical science. Genetic inheritance was explained and tested using paper coated with phenylthiocarbamide, or PTC, which tastes bitter to those carrying the dominant gene for PTC tasting, TAS2R38. At another station, graduate students showed mutant phenotypes in fruit flies and zebra fish as examples of model organisms in the lab.

"I've never seen anything like this before," one high school student said.

Dallas-area high school students look through microscopes, learning about neurological and cardiac histology, during the HPREP Science Day at UT Southwestern.

Dallas-area high school students taste phenylthiocarbamide paper to determine whether they carry the dominant gene for PTC tasting, TAS2R38, during the HPREP Science Day at UT Southwestern.

"We learn about genetic differences in our biology class but don't get firsthand experience of how these differences are expressed."

To demonstrate visual cortex neuroplasticity, students repeatedly tossed bean bags at a target while wearing a patch over one eye, which altered their perception of the target location and distance. Throws were initially inaccurate, but the high schoolers quickly adapted to the eye patch and soon matched their two-eyed proficiency.

Nora-Guadalupe Ramirez was one of the graduate student coordinators. "The goal of Science Day is to give meaningful glimpses into the different topics and techniques used in biomedical research," she said. "We wanted to ensure more hands-on activities in order for the students to get a feel for research and also understand how each technique can be used to answer impactful questions."

Planning for next year's Science Day already has begun. Organizers expect even more applicants and believe exposing more high school students to science will motivate more individuals from underrepresented groups to pursue careers in biomedical research and related fields.

Amanda Goldner (Amanda.Goldner@UTSouthwestern.edu) is a third-year graduate student in the Green Center for Systems Biology at the University of Texas Southwestern Medical Center. She studies the material properties of embryonic tissue under the cell and molecular biology graduate program.

Brittany Johnson (Brittany.Johnson@UTSouthwestern.edu) is a third-year graduate student in the department of molecular genetics at the University of Texas Southwestern Medical Center. She is currently in the biochemistry graduate program elucidating molecular mechanisms underlying the regulation of sterol and nonsterol isoprenoid flux in mammalian cells.

John Corbett (John.Corbett@UTSouthwestern.edu) received his Ph.D. in biomedical engineering in 2017 and is currently a research associate in the department of ophthalmology at the University of Texas Southwestern Medical Center, where he investigates how mechanical behaviors of corneal fibroblasts are regulated by both biochemical and biophysical stimuli.

The GRE hurts graduate schools — and science

By Alexander Shames

When I arrived to take the Graduate Record Examinations this past January, it was hard to tell whether I was in a testing facility or an airport security line. After submitting my identification and placing all my belongings in a locked drawer, I was waved over by a security wand and instructed to turn out my front and back pockets, shake out my sweatshirt hood and lift up my pant legs. I recalled the MTV movie about six teenagers who conspire to steal the SAT answer key. During the 3½ hour exam, my fellow test takers and I were under constant video surveillance and permitted to leave only once, for 10 minutes, provided we signed in and out. We were allowed to write on only official GRE scratch paper, which seemed suspiciously identical to normal paper, except for the text printed at the top reminding us that cheating was, as a matter of fact, forbidden. All these security measures reminded me of the time my friend Maggie opted for eight simultaneous ibuprofens rather than seeing a doctor about her swollen ankle.

I had to take the GREs, protracted and belittling though they may be, because I could not become a biochemist without them. According to U.S. News and World Report, of the top 10 biochemistry graduate programs in the United States, only one, the University of California, Berkeley, is test optional, and, historically, a low GRE score means no admission to any graduate program, in or out of the sciences. The logic, according to the website of the GRE's administrative company, Educational Testing Service, or ETS, is that the GRE is "a proven measure of an applicant's readiness for graduate-level work" and "gives you more opportunities for success."

This description seems reassuring, as the future of biochemistry rests in the hands of graduate students who have passed through the GRE. But what kinds of students tend to do well on the test? According to Robert J. Sternberg, a professor of human development at Cornell University, mostly rich, white and male ones. Sternberg, talking to The Atlantic magazine, refers to decades of research from Stanford University, New York University, the University of Florida and the University of Missouri showing that women and racial minorities consistently underperform on the GRE compared with their white male counterparts. A 2014 Nature article by Casey Miller and Keivan Stassun supports Sternberg's claim, stating, "in simple terms, the GRE is a better indicator of sex and skin colour than of ability and ultimate success."

GRE results fail to predict performance in future academic courses, an area where even the notoriously biased SAT is somewhat effective. In 1997, Sternberg and Wendy M. Williams, another Cornell professor, published data in American Psychologist suggesting high GRE scores fail to correlate with any metric of graduate school success beyond first-year grade point average — and this correlation held for only the analytical section of the GRE and for only male students. My own adviser, now a tenured professor of molecular biology and biochemistry, initially was rejected from graduate school because her GRE math scores were too low.

Even though its irrelevance has been clear for more than 20 years now, the GRE survives because ETS, a self-styled "mission-driven, not-for-profit organization" that has not paid federal taxes since 1949, uses the exam to enrich its executives. Robert Murley, the ETS chairman, has no

CONTINUED ON PAGE 54

GRExit or retain

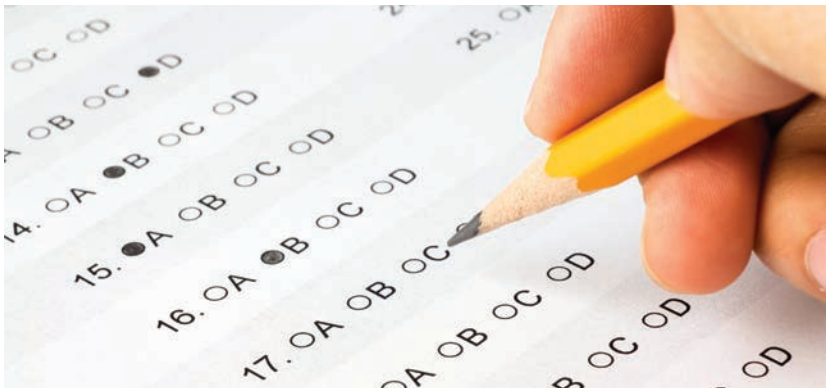
The growing debate over standardized test scores in graduate admissions

By Rajini Rao

For almost 70 years, the Graduate Record Examination, or GRE, has been a rite of passage toward a doctoral degree in the United States. Introduced in 1949, the GRE is a standardized test that seeks to assess verbal, quantitative, critical thinking and analytical writing skills, all of which are undeniably important for success in graduate school. Of late, however, the GRE has come under increasing criticism from students and educators alike and appears to be falling out of favor.

Since 2015, the National Institutes of Health no longer requires GRE reporting for institutional training grants and individual fellowships, and the popular National Science Foundation Graduate Research Fellowship Program stopped asking for GRE scores in 2010. A growing number of top-notch graduate programs (at the University of California at San Francisco and Berkeley, the University of Michigan, Emory University) have dropped the GRE requirement from their applications. Other graduate programs are paying attention: Once a critical mass of #GRExiters is reached, schools will have to decide whether to join the exodus or risk a significant loss of applicants who choose not to take the exam.

Many old-timers, myself included, may have strong reservations about abandoning a long-held gold standard for admission. The GRE potentially offers equal opportunity for applicants who otherwise would be difficult to compare across widely disparate college and grade standards. This is especially true for international students: With no context for my college grades from India and no comparable research experience, the GRE was my only ticket to graduate admission in the U.S. So I read the Oxford English Dictionary from A to Z, aced the tests and voila — the admission offers came rolling in. This was in 1983; today, admissions criteria are tougher and programs even more competitive. Surely a standardized test is the great leveler? The data, however, say otherwise.



Let's start with convincing evidence that GRE scores are poor predictors of graduate school success. A 2017 study by Joshua D. Hall and others at the University of North Carolina Medical School found no correlation between GRE scores and productivity in terms of publications within a cohort of 280 students who matriculated into the umbrella biomedical sciences program at UNC at Chapel Hill between 2008 and 2010. Nor was there statistical difference in time-to-degree or even degree completion with respect to GRE scores.

Similarly, from an analysis of 683 Vanderbilt University biomedical graduate students, Liane Moneta-Koehler and researchers at Vanderbilt concluded that GRE scores were not useful in predicting success in graduation rates or times, obtaining fellowships, passing qualifying exams or publishing first-author papers, although test scores were moderate predictors of graduate GPA. Based on these and other studies, reliance on GRE scores as a quantitative admissions metric may seem imperfect but harmless. Why not keep the scores as part of a more holistic approach to application reviews?

Unfortunately, more insidious problems may exist with standardized testing. Many studies show that GRE scores track best with socioeconomic status: It is well known that practice makes perfect, but taking — and retaking — the GRE is not cheap (about $200 each time), and the cost of courses or tutors for test preparation can run to thousands of dollars, well beyond reach for many economically disadvantaged students.

Equally troubling, GRE scores reflect bias against women and minorities. Data from the Educational Testing Service, or ETS, the company that administers the test, show that women score 80 points lower on average than men and African-Americans

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background in education, holding a B.A. in politics and master's degrees in business administration and economics. According to its IRS form 990, a publicly available document that federal tax exempt organizations must fill out yearly, ETS had revenues of about $928 million, $1.2 billion and $1.1 billion in 2015, 2014 and 2013, respectively, in addition to more than $600 million in assets. Greater than 85 percent of that revenue came from "Program Services," including test-prep courses and practice books that ETS promotes on its website, as well as the $205 fee to take the GRE, which amounts to more than 20 hours of work at my on-campus job (low-income students can pay half that). Since 2011, ETS has allocated more than $240 million of its income to salaries and wages, plus an additional $13.9 million for "executive compensation." The Washington Post reported that, in 2015, some ETS board of directors members worked approximately two hours a week for almost $1,000 an hour, totaling $103,000 that year. Meanwhile, the average graduate student in the U.S. earns less than $30,000 a year, and most professors are in a near-constant scramble for funding. What kind of science would be possible if researchers had even half the amount of money ETS sees on a yearly basis?

The GRE still exists not because it provides an accurate assessment of graduate school readiness, not because it allows across-the-board comparison among applicants from various schools and not because it creates educational opportunities but because business executives with no interest in science or education can earn huge sums of money from the proliferation of a discriminatory exam and because universities are complicit in that effort. Each time a graduate program requires applicants' GRE scores, it is dissuading low-income, female and minority students from becoming scientists. The fields of molecular biology and biochemistry have probably lost thousands of creative, hard-working, curious individuals by demanding they participate in an outdated, discriminatory examination system that exploits students to enrich those at the top. All graduate programs affiliated with the American Society for Biochemistry and Molecular Biology should remove their GRE requirement as soon as possible.

When I finally was released from the exam, a woman waiting at the bus stop recognized me from the testing center. I asked her what she thought of the exam. "It was OK," she replied. "It's my second time taking it, so I knew what to expect. But I didn't score high enough, so I'll have to take it again sometime. Maybe during spring break."

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score 200 points lower than white Americans in the quantitative test. Using score cut-offs could disproportionately eliminate women and minorities. While the ETS implements statistical measures to eliminate bias in the questions, many factors are beyond their control, including stereotype threat and socialized behavior in risk-taking (guessing). Studies have shown that marking gender and ethnicity in standardized tests like the GRE risks confirming a negative stereotype associated with a minority group that undermines their performance. A consequence of socialization, stereotype threat often is overlooked, yet it can be quantified in real time by physiological stress responses that include increased anxiety and hypervigilance about making mistakes, which negatively impact working memory. Whatever the reason, Casey Miller and Keivan Stassun conclude in a 2014 essay in Nature, "The misuse of GRE scores to select applicants may be a strong driver of the continuing underrepresentation of women and minorities in graduate school."

For years, GRE scores were a quick and easy way for busy faculty, who often rotate through graduate admissions committees, to screen hundreds of applications. There is no easy solution or time-saving shortcut that can substitute for a holistic review of strengths and weaknesses in the application. While no perfect predictor for success exists, perhaps it's time to retire the GRE as an admissions criterion for graduate school.

What do you think?

Should graduate programs continue to require the GRE? If so, why? If the GRE is retired, what (if anything) should take its place? Send your thoughts, in 500 words or fewer, to asbmbtoday@asbmb.com. We hope to publish responses to these essays in a future issue.

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Medicine for emotions

By Stefan Lukianov

Emotions provide a richness and depth to life that is uniquely human. Compellingly warm emotions envelop me when I view a Mark Rothko painting, attend a Latin Tridentine Mass or dance to a favorite DJ at a club. We realize how precious emotions are when we cannot experience them normally. When there are no emotions, or too much of any emotion, the imbalance interferes with living a healthy and fulfilling life. Emotional dysregulation is a symptom of many psychiatric disorders.

As a patient, I can attest to the havoc of unchecked emotions. I began experiencing symptoms of severe depression and anxiety about 12 years ago, at age 22. At the time, I was a first-year biochemistry Ph.D. student at Harvard Medical School. A few months before starting school, my fiancée had left me for someone else. Everything inside me felt disordered, empty and dark, and it was not going away. I sought help from a psychologist who was a family friend, but a much greater struggle was in store.

Four years later, having withdrawn from Harvard because I didn't have a thesis lab, I was in an ambulance traveling from a hospital in Marlborough, Massachusetts, to McLean Hospital in Belmont, Massachusetts, about 30 miles away. I was in an overmedicated fog, so the trip is a bit hazy. I think I joked with the paramedics, but I can't be sure. At McLean, I was unloaded from the ambulance and led to the locked inpatient depression unit.

After about a week in the psychiatric unit at Marlborough, the staff hadn't known what was wrong with me. My family hoped that McLean, considered the best psychiatric hospital in the world, could figure me out. Thankfully, my intake psychiatrist offered to work with me after I was released from the unit about two weeks later. I was diagnosed with bipolar disorder, though I do not know at what point during my stay, and the next several years involved an arduous recovery.

Bipolar disorder is a psychiatric illness consisting of manic and depressive episodes. Mania is elating and full of grandiose thoughts, whereas depression flattens affect and makes you feel worthless. For me, mania consists of racing thoughts and a reduced need for sleep. Conversely, depression ruins my self-esteem and self-confidence and promotes social isolation. In either case, my emotions run dangerously out of control. As part of my recovery, I use medication and therapy for safety and proper functioning.

I ultimately came to rely on three medications for my mental health: citalopram (Celexa), lamotrigine (Lamictal) and aripiprazole (Abilify). Citalopram is an antidepressant of the specific-serotonin reuptake inhibitor family, which works by blocking a transporter protein that removes serotonin from the synaptic cleft between neurons, thus keeping serotonin in the cleft for prolonged action. Lamotrigine is a sodium channel blocker that initially was used as an anticonvulsant for epileptics but found its way into psychiatric clinics as a great mood stabilizer. Aripiprazole is an atypical antipsychotic that partially activates dopamine signaling in the brain and is used to treat a variety of diseases including bipolar disorder.

It confuses me to think about how these diverse medications are helping balance my brain biochemistry. How do they act in concert with my body to stabilize, and thereby help me truly experience, my emotions? They have such different mechanisms of action, and the brain is so complex, that I do not think a full explanation is possible. What I do know is the emotional and behavioral effect they have on me when used together. I'm able to sleep and eat normally, and the full range of healthy emotions is open to me at appropriate times. I stop withdrawing from other people, and I am able better to identify what bothers me without spiraling into oblivion. These medications don't calm the storm of life, but they do give me control of my ship.

There is no single cause of bipolar disorder, but genetic and environmental factors are believed to increase risk. This lack of a single cause occasionally agitates me. I wish my psychiatrist could point to a single malfunctioning molecule in my brain to explain what's wrong with me, but that is impossible. I do take comfort in the fact that the disease definitely has a brain biochemistry component. This is evidenced by the many successful psychiatric medications that have returned the lives of so many patients. I am thankful that such medications exist and that I am able to take them without any side effects. Finding the right regimen for me took years of psychiatric help, but the work was well worth it. I have my life back and the emotions to prove it.

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