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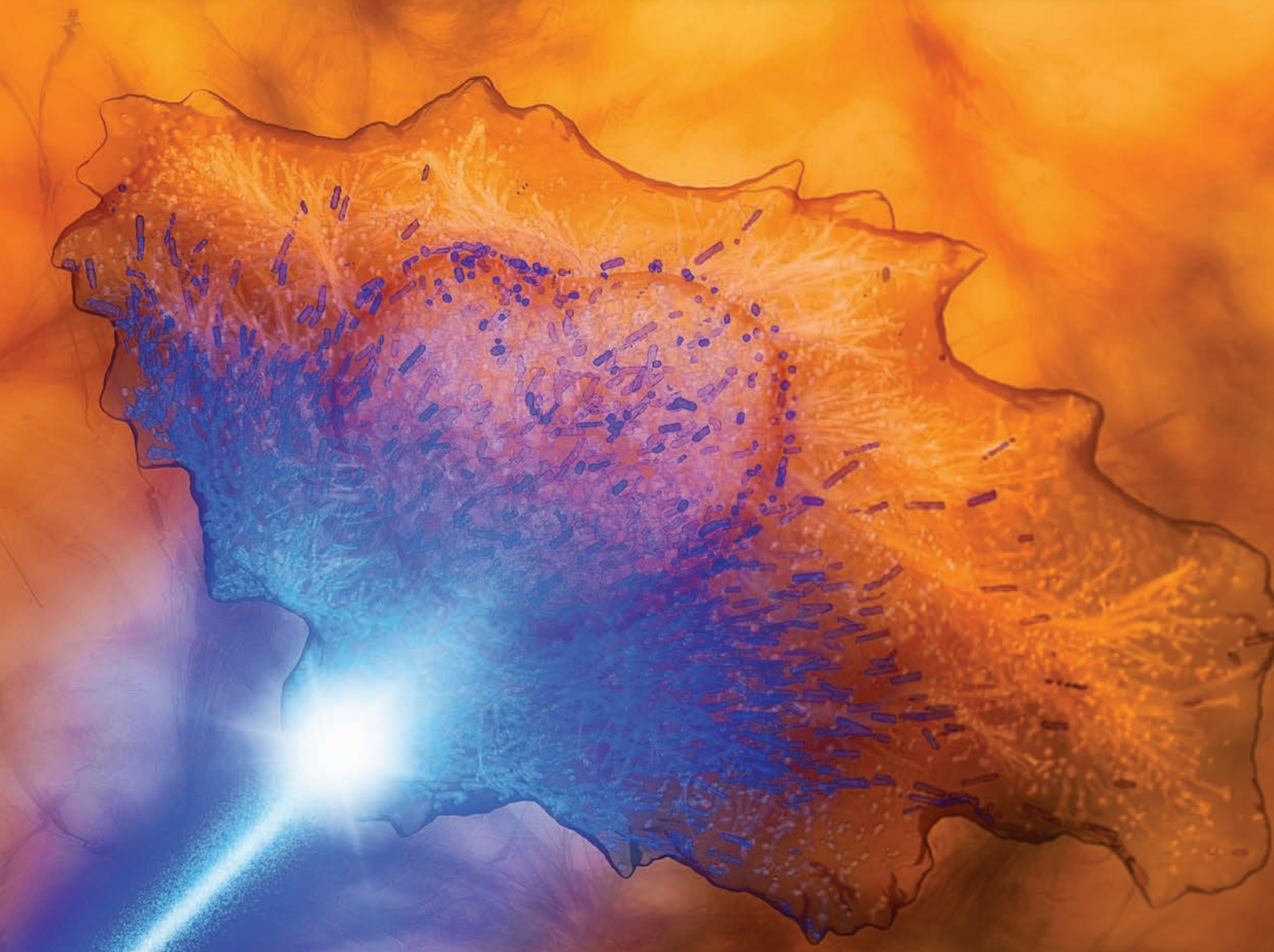
ASBMB TODAY

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



Will optogenetics transform cell biology?

ANNUAL REVIEWS ✻ SPARK A CONNECTION

Annual Review of Microbiology

micro.annualreviews.org · Volume 69 · September 2015

Editor: **Susan Gottesman,** *Bethesda, MD*

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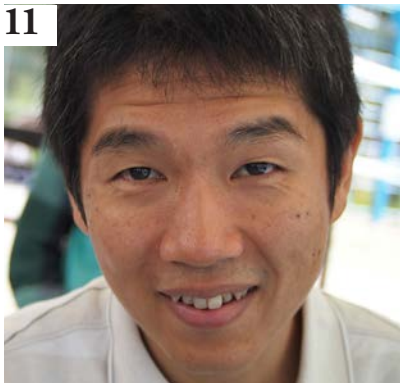

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EDITOR'S NOTE

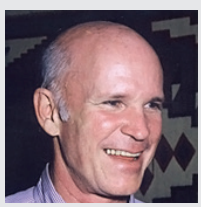
Changing places and perceptions

New series to feature scientists in flux

As we set to work sketching ideas for ASBMB Today's 2015-2016 publishing calendar, we at the magazine keep coming back to your contributions. We love covering our members' achievements, bringing to light new developments that are chronicled in the society's journals or happening in the lab and the classroom, and recording the strides that outreach, minority affairs and policy professionals are making in the name of a stronger and more inclusive scientific community.

On top of all of that, during this last year, when we asked you to share more of yourselves with our readers through our Hobbies and Generations essay series, we were delighted by a particular element of intimacy that made it into the stories you sent our way. Who knew you would be passionate hunters of arrowheads and damselflies? That you'd learned to play the viola as an adult when others said it was too late, or took time you didn't really have to DJ radio shows, or created video homages to your favorite heavy metal bands? We were moved when you told us what it was like to have a baby in graduate school, how your family of big thinkers and healers instilled in you the joy of discovery, or why your hippie past continues to shape the values you hope to pass on to new generations.

Hearing your voices has inspired us to keep you writing and as the Hobbies and Generations series come to a close – we will run the last of the essays in December – we are excited to be introducing two new essay series. Set to start in January and run through December of 2016, the two series, "Coordinates" and "Transition States" will feature your experiences with movement and change. The Coordinates series will focus on place and the effect it has on personal and professional lives and Transition States on what it's like to switch gears for a career change. Check out our advertisement on page 33 for more details about the two series and how and when to submit.



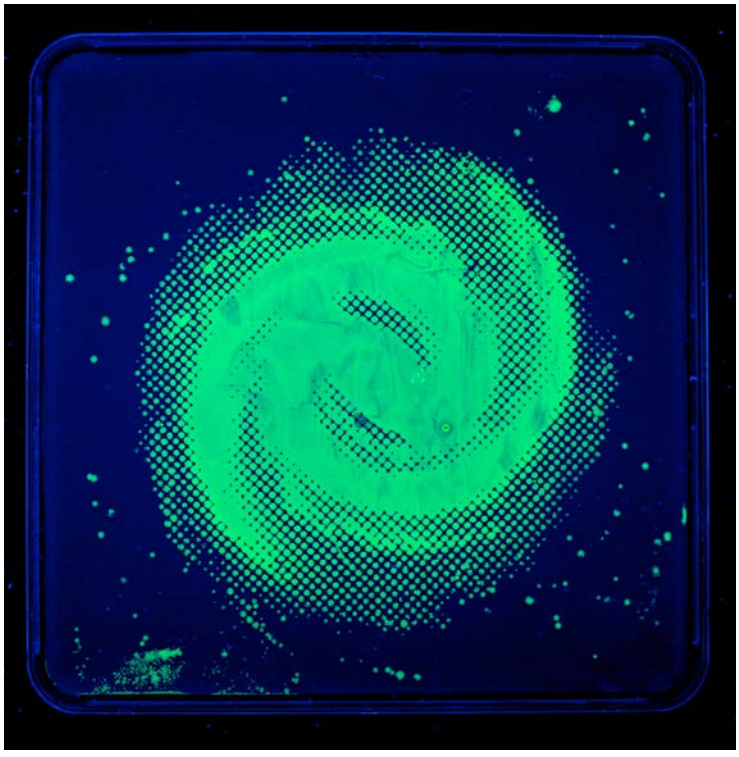
PRESIDENT'S MESSAGE

Steven McKnight's column will resume next month.

Making STEAM

The growing interplay of art and STEM

S – T – E – M. The ubiquity of the STEM acronym – now on the lips of every science outreach professional and educator from K to 20 – has become a sign of commitment to fields that once were perceived to be too dull or difficult for the general population to get behind. President Obama makes liberal use of the four letters, collectively championing science, technology, engineering and math as the country's way forward to a brighter, more competitive future.



ZACHARY COPFER

Part of the hard sell behind STEM, which has taken the form of a "science is fun" mantra, is an attempt to chip away at the misconception that fields involving scientific discovery and technological innovation are full of people who've rejected pleasure – that becoming a scientist, engineer or mathematician means putting oneself at a remove from the revelry and beauty and comparative accessibility of the humanities or the arts.

In the past few years, however, attempts by institutions and individuals to break apart these misconceptions and the academic silos they help to underpin have resulted in a weaving of arts and design into STEM curricula. The resulting integration has its own acronym: STEAM. Champions of STEAM (STEM plus art) talk about the ways in which the artistic and scientific processes echo each other. They emphasize shared values like creativity, experimentation and a desire for discovery, and they suggest that the inherent connections between the two worlds are balanced by enough difference to produce the right tensions for innovation.

STEAM is remaking classroom experiences and creating collaborations between artists and scientists on a professional scale. Bio artists, some of whom have scientific backgrounds, are incorporating living organisms into gallery shows or working with geneticists to produce new life forms for installations. Sculptors are building homages to the magic of kinesis. Professional theater and dance productions are enjoining audience members to experience the drama and beauty of molecular processes by staging them at a macro level. Scientist-musicians are writing symphonies that reflect biological processes or rock lyrics derived from lab trials.

Intermittently, over the course of this next year, we will feature stories about STEAM works that impress and intrigue us. We will talk to the creators about their own processes of creativity, discovery and innovation and delve into the science that underlies their work. We begin this month on page 28 with Zachary Copfer, a former pharmaceutical researcher whose "bacteriographs" have become a bio art hit. If what Copfer is doing reminds you of a STEAM project you've seen recently, get in touch with us. Help us share more of the wonder of these science-inspired artistic experiments.

Lauren Dockett (ldockett@asbmb.org) is the managing editor of ASBMB Today.

American Society for Biochemistry and Molecular Biology

ACCREDITATION & ASSESSMENT *for* B.S./B.A. PROGRAMS IN BIOCHEMISTRY & MOLECULAR BIOLOGY

The ASBMB has launched a national accreditation program for departments and programs offering baccalaureate degrees in biochemistry, molecular biology and other related degrees. Accredited programs gain access to an independently developed and scored examination for assessing student performance that leads to the conferral of an ASBMB-certified degree.

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American Society for Biochemistry and Molecular Biology

A measured response to reproducibility problems

By Chris Pickett

The research enterprise has been enduring a crisis of confidence. Many reports have been published over the past several years suggesting the biomedical research enterprise is generating irreproducible research and wasting billions of taxpayer dollars. In June, the National Institutes of Health released two notices describing new policies and procedures the agency would implement in 2016 to improve reproducibility in research (1, 2). While improving reproducibility in research is a laudable goal, papers that make sweeping generalizations or conduct incomplete analyses about science have the potential to slow the pace of research.

One paper published in June in the journal PLoS Biology suggested the United States spends roughly $28 billion each year on irreproducible research (3). This paper used fairly broad criteria to determine whether research was irreproducible. Using these criteria, the authors suggested that roughly half of all research is irreproducible and then extrapolated to say that roughly half of all money invested in biomedical research is spent on irreproducible findings. The 1:1 correlation between irreproducibility and investment is simplistic and ignores the possibility that many of the findings in a paper are reproducible and useful. By using such a broad definition for irreproducible research, the authors surely mislabel useful findings and inflate their estimate of how much research is irreproducible.

Another paper published in August, in the Proceedings of the National Academy of Sciences, suggested research efficiency, determined by dividing the number of new drugs approved in a year by the NIH dollars spent in that year, has fallen in recent decades (4). This report makes its case on new drug approvals being the primary output of NIH-funded research. However, NIH-funded research can improve human health by more than just the discovery of new drugs. Discoveries that result in new diagnostics that promote early disease detection or technologies that improve drug delivery methods can have profound effects on human health. Additionally, drugs approved for use in humans decades ago can be repurposed to treat different diseases. These benefits of NIH-funded research were not accounted for in this analysis. Thus, this paper undersells the effectiveness of NIH-funded research and the contributions made by the scientific community.

Reports such as the two described above do little to improve research reproducibility and efficiency. The American Society for Biochemistry and Molecular Biology is concerned that the hype surrounding these papers and other reports and opinion articles will provoke Congress or research-funding agencies to implement policies that are overly prescriptive. Another concern is the potential misperception by the general public that generating new drugs is the sole purpose of NIH-funded research. This could put pressure on the agency to make a more deliberate transition from funding basic to translational science.

It is important to ensure the research enterprise is producing the best possible research, and the ASBMB long has supported efforts to improve reproducibility and efficiency. Scientists long have been excellent stewards of the taxpayer investment in biomedical research, and the scientific community should constantly be working to ensure it generates useful, well-founded knowledge. But only with measured analyses of the functioning of the research enterprise can policies be made that improve research reproducibility and efficiency.

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Chris Pickett (cpickett@asbmb.org) is a policy analyst at the ASBMB.

Kimble to lead National Medal of Science committee


KIMBLE

President Barack Obama chose Judith Kimble to lead the President's Committee on the National Medal of Science. Kimble is the Vilas professor of biochemistry at the University of Wisconsin–Madison and a Howard Hughes Medical Institute investigator. She served on the committee from 2012 to 2014. According to the National Science Foundation, Congress established the National Medal of Science in 1959 to recognize individuals "deserving of special recognition by reason of their outstanding contributions to knowledge in the physical, biological, mathematical, or engineering sciences." Congress eventually expanded the medal's recognition to include contributions to the social and behavioral sciences. This prestigious award has been given out to nearly 500 scientists and engineers for their contributions to scientific research and development since its inception.

A member of the National Academy of Sciences, Kimble's research explores the fundamental controls of animal development, focusing on stem cells and differentiation.

Written by Erik Chaulk

Mirmira to head diabetes research center


MIRMIRA

Raghu G. Mirmira, Lilly Foundation professor in pediatric diabetes at Indiana University, will direct a new, federally designated diabetes research center at IU. One of 16 such centers in the country, the Indiana Diabetes Center aims to accelerate diabetes and metabolic research and will be funded by a $4.5 million, five-year grant from the National Institute of Diabetes and Digestive and Kidney Diseases. Mirmira says, "This award expresses the confidence of the NIH and NIDDK that we have assembled a world-class program of diabetes research at IU." The center is to support several research cores that will look at microscopy imaging services, insulin-producing cell clusters, new models in swine, and the translation of lab discoveries into human disease understanding. Dr. Mirmira, who is a Herman B. Wells Center for Pediatric Research scientist and professor of medicine and cellular and integrative physiology at IU, earned his M.D./Ph.D. at the University of Chicago. He did his residency and fellowship at the University of California, San Francisco, and received the Physician Postdoctoral Fellowship Award from the Howard Hughes Medical Institute and a Research Career Award from the National Institutes of Health.

Nunnari to edit JCB


NUNNARI

Jodi Nunnari, professor and chair of the department of molecular and cellular biology department at the University of California, Davis, is the new editor-in-chief of the Journal of Cell Biology. She took the helm in August. Nunnari will be the first female editor-in-chief of JCB, a peer-reviewed journal owned by the Rockefeller University Press. A former academic editor of the journal, Nunnari is an internationally recognized leader in the field of mitochondrial dynamics. "Jodi has shown tremendous dedication and enthusiasm as an editor over the past decade to help guide the editorial process and maintain JCB's high standards and reputation," said Susan King, executive director of the press.

Written by Kamalika Saha

Raines wins ACS award


RAINES

Ronald T. Raines won the 2016 Ralph F. Hirschmann Award for Peptide Chemistry from the American Chemical Society. The biennial award recognizes and encourages outstanding achievements in the chemistry, biochemistry and biophysics of peptides.

Raines, professor of biochemistry and chemistry at the University of Wisconsin–Madison, has used synthetic peptides to reveal that an unappreciated force — the n-to-pi* interaction — stabilizes proteins. His team has also used peptides to create hyperstable and large collagens. Raines has made numerous contributions to peptide chemistry. He will receive his award at the ACS annual meeting in March in San Diego.

Tjian to step down as president of HHMI

Citing a desire to return to research, Robert Tjian will leave his post as president of the Howard Hughes Medical Institute at the end of 2016. Tjian, who will continue as an HHMI investigator, became the third president of the institute in April, 2009. The HHMI operates with a $19 billion endowment and is the nation's largest philanthropic funder of academic biomedical research.

During his term, Tjian introduced initiatives to support early-career scientists, expand science communication and emphasize diversity and inclusiveness, especially in how universities teach science. Tjian revamped existing programs including increasing postdoctoral HHMI funds, revitalizing graduate-student awards to include more international students and incorporating voluntary phase-out awards for senior and accomplished investigators. He also collaborated with other foundations, in one case helping to launch the open-access journal eLife.

BARBARA RIES

Robert Tjian

Tjian has been a faculty member at the University of California, Berkeley, since 1979 and will return to his HHMI-supported lab on the Berkeley campus. A member of the National Academy of Sciences, Tjian earned his bachelor's degree at Berkeley and Ph.D. at Harvard University and has done pioneering work on genes. He discovered transcription factors and shined light on how disruptions in the transcription process are involved in diseases like diabetes and cancer. He also operates a lab at HHMI focused on single-cell imaging.

Written by Shaina Hasan

IN MEMORIAM: George R. Waller Jr.

WALLER

George R. Waller Jr., who introduced mass spectrometry to the field of biochemistry, died in March. He was 87.

While a National Institutes of Health fellow at the Nobel Medical Institute in Stockholm, Sweden, Waller assisted in the development of the LKB-9000 gas chromatograph mass spectrometer prototype. The GC/MS, which can identify organic compounds from an unknown sample, was installed at Oklahoma State University in 1965. Waller used it to identify plant compounds and essential oils. It is now part of the Smithsonian collection.

Born in Clinton, N.C., on July 14, 1927, Waller developed an interest in biochemistry as a young boy and raised bantam chickens to fund his formal education. He served in the Navy during World War II, did his undergraduate work in agriculture and biological chemistry at North Carolina State University and received a master's degree in chemistry from the University of Delaware. In 1956 Waller joined Oklahoma State University as an assistant professor in the newly-forming biochemistry department and was named full professor when he completed his Ph.D. Waller published prolifically during his academic career, contributing to more than 400 articles. He was made professor emeritus in 1987.

In the early 1970s, Waller served on a task force that was active in the creation of the Environmental Protection Agency. He helped the state of Oklahoma start environmental education and research programs and shared environmental concerns with his students. In the late 1970s, Waller pioneered work on sustainable agriculture and allelopathy. He served as founder and president of the International Allelopathy Society from 1994 to 2001.

Waller, an avid traveler and photographer who lived on three continents, married Hilda Marie Lominac of Asheville, N.C., in 1947. The couple had three daughters and were married for 64 years until Hilda passed away in 2011.

Written by Sarah Yahoodik

NSF grant to expand ASBMB mentorship program

The National Science Foundation awarded the American Society for Biochemistry and Molecular Biology a grant of $500,000 to support a comprehensive mentoring program for postdoctoral fellows and early-career faculty members. The program focuses on grantsmanship skills and career-development strategies. It also promotes diversity in the scientific workforce by supporting underrepresented minority postdoctoral scientists and new assistant professors in their efforts to secure research funding.

Members of the ASBMB's Minority Affairs Committee started the training program, now called Interactive Mentoring Activities for Grantsmanship Enhancement, as an annual workshop in 2013. Since then, 93 percent of mentees have reported that participation in the workshop increased their confidence in applying for funding, and nearly 56 percent of alumni from the 2013 workshop have obtained funding. The NSF grant will support IMAGE for the next three years.

Marion Sewer, a professor at the University of California, San Diego, and deputy chair of the ASBMB's Minority Affairs Committee, says IMAGE organizers try to create a diverse cohort each year by targeting recruitment of underrepresented minorities. They also look for participants from a variety of geographic locations, try to create a gender balance, and recruit faculty from primarily undergraduate and minority-serving institutions.

Central Michigan University Assistant Professor Benjamin Swarts researches tuberculosis and participated in the program in 2013.

"Inspired by the workshop, I have a living five-year plan document that, in addition to keeping on track with administration, has helped me organize my overarching plans into something that is tangible," said Swarts.

The ASBMB's Minority Affairs Committee expressed confidence that the NSF's support of IMAGE will enrich the scientific community by helping scientists develop the skills they need for long-term professional success. *Written by Allison Frick*

The Center of Translational Medicine seeks a research scientist, Instructor level, with advanced expertise in biochemistry, lipid biology, & mitochondria-based mechanisms of disease as well as experience in the fields of lung biology and fibrosis pathogenesis.

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ASBMB
STUDENT CHAPTERS

T-SHIRT DESIGN CONTEST

Share what being a part of the ASBMB Student Chapters means to you! All chapters can submit a tee-shirt design that exemplifies the Student Chapters' mission of advancing education, research and science outreach. The winning shirt will be sold at the 2016 ASBMB annual meeting in San Diego.

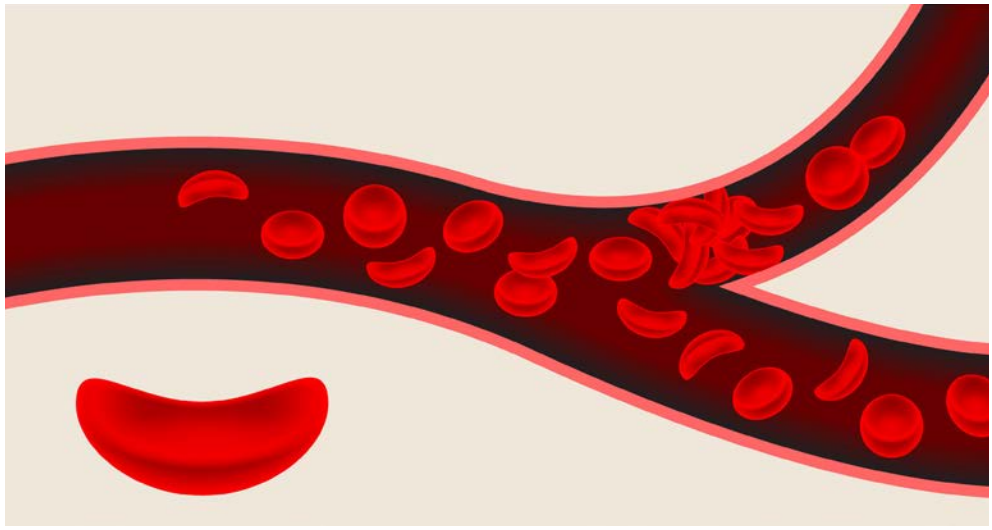
All T-shirt designs must be submitted by Oct. 30, 2015. The winner will be announced in late November 2015.

- Tee-shirts should not include any school's name
- All designs should relate to the Student Chapters' mission
- Designs should not be too specific to one event or institution
- Entries must be designed for the front of the shirt only

All design submissions can be emailed as a high resolution JPEG to education@asbmb.org

Sickened by sickle-cell disease

By Indumathi Sridharan



In 1910, an American physician named James Herrick described a young patient whose red blood cells were elongated and curved like a sickle. Herrick's report was the first clinical description of sickle cell disease in the U.S. Sickle-cell disease, or SCD, is an inherited blood disorder that affects 90,000 to 100,000 people in the U.S., particularly those of African and Hispanic heritage. Current treatments, such as blood transfusions, focus on managing symptoms rather than curing SCD. The American Society for Hematology marks September as "National Sickle Cell Awareness Month" to highlight the need for better treatment options for SCD.

What is a sickle cell?

Red blood cells, or erythrocytes, are typically shaped like discs. They contain the oxygen-carrying protein hemoglobin, which has two alpha and two beta subunits. SCD occurs when a single mutation causes the substitution of valine for glutamic acid in the beta subunit of the hemoglobin molecule. The mutated hemoglobin molecules aggregate into filaments that stretch the cell membrane and create the characteristic sickle shape.

What are the symptoms of SCD?

Sickled erythrocytes have a shorter life span and die quickly. The cells also are too rigid to squeeze through blood vessels. Pain, infections, anemia, organ damage and stroke are brought on as obstructed blood flow leads to poor oxygen levels at the cellular level and cell death. SCD also increases susceptibility to malaria; however, those with only one copy of the mutation in the gene are protected from malarial infections because macrophages of the immune system attack infected sickle cells.

What are the latest approaches for SCD treatment?

Although stem-cell transplantation can cure SCD, the treatment is limited by the availability of compatible donors. Instead of relying on donor stem cells, researchers at the University of California, Los Angeles, reported earlier this year that they had derived stem cells directly from SCD patients. They rectified the mutation in the hemoglobin gene by using enzymes called zinc-finger nucleases, which cut at the site of the mutation. The stem cells' natural repair mechanisms then inserted the correct code at the site. These gene-corrected version of stem cells produced normal erythrocytes (1).

Fetal globin is a form of hemoglobin that has a better affinity for oxygen. Earlier this year, a study demonstrated that fetal globin production can be induced in erythroid cells using genome editing. The method introduces a mutation that increases the activity of TAL-1, an activator of the fetal globin promoter sequence. The increased TAL-1 activity concomitantly increased fetal globin production (2).

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Indumathi Sridharan (sridharan.indumathi@gmail.com) did her Ph.D. in molecular biochemistry at the Illinois Institute of Technology, Chicago and her postdoctoral work in bionanotechnology at Northwestern University.

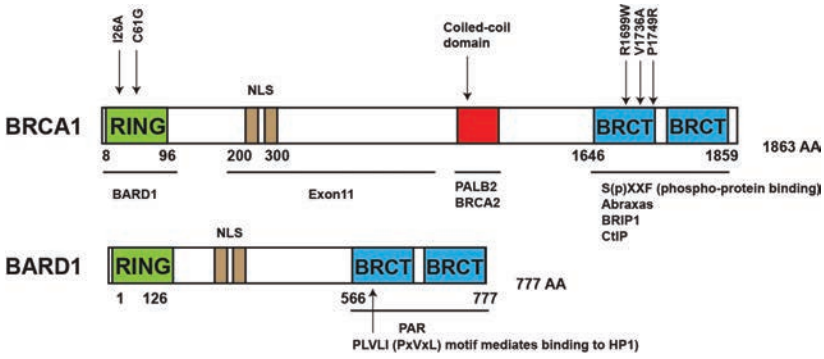
The normal function of BRCA1

By Caitlin Hanlon

After learning she was a carrier for the breast cancer susceptibility gene 1, actress Angelina Jolie opted for a preventative double mastectomy and later wrote an essay for the New York Times about her decision. The widely read and disseminated article, published in the spring of 2013, helped BRCA1 enter the common lexicon and gain recognition as a leading risk factor for breast and ovarian cancer. However, the normal function of BRCA1 often is missing from these discussions. In "Deciphering the BRCA1 tumor suppressor network," a recent minireview in the **Journal of Biological Chemistry**, Qinqin Jiang and Roger A. Greenberg of the Abramson Family Cancer Research Institute at the University of Pennsylvania discuss the role that BRCA1 and its associated proteins play in noncancerous cells.

BRCA1 is well studied for its involvement in DNA damage response. At its C-terminus, BRCA1 contains two BRCA C-terminal domains, which enable its binding to proteins involved with DNA repair. With its partner protein, which is called BRCA associated RING domain 1, BRCA1 is able to bind to nucleosomes and localize to damaged regions of DNA. BRCA1 then facilitates homology-directed DNA repair, an error-free method that restores DNA to a nonmutated state.

BRCA1 is a member of three separate protein complexes that each play a role in DNA repair. BRCA1 interacts with the tumor-suppressor protein Abraxas, and this complex then binds ubiquitylated lysine residues at DNA double-strand breaks. In a separate complex, BRCA1 interacts with BRCA1 interacting protein C-terminal helicase 1, a DNA helicase that is required for DNA crosslink repair. The third complex is BRCA and C-terminal binding protein interacting protein, an endonuclease also known as retinoblastoma-binding protein 8. This complex speeds end resection, the process of removing bases around a double-strand break so that homologous-directed repair can occur.



Domainstructure of BRCA1-BARD1 and key interacting partners in the BRCA network.

BRCA1 and its binding partners often are located at transcriptionally active sites and at regions of replication fork stress. The authors point out that BRCA1 is influencing genome stability for the cell itself and its daughter cell by localizing to these regions.

Mutations in BRCA1 cause failures in homology-directed DNA repair and prompt the cell to use more error-prone repair methods. In BRCA1 mutant cells, blocking these error-prone pathways using molecular inhibitors causes an accumulation of cytotoxic complexes and results in cell death. Inhibition of these pathways is a popular therapeutic target since it specifically favors cancer cell death. Because cancer cells are developing resistance to the current class of inhibitors, the authors discuss alternate repair pathways that may be viable therapeutic targets. Two examples are Rad52, a protein involved in single-strand annealing repair, and Polθ, which is involved in micro-homology-mediated end joining. Additional targets include proteins that increase replication stress, which already is heightened in BRCA1 mutant cells. Further development of these therapies represents a step forward for the treatment of breast and ovarian cancer.

Although an enormous amount of knowledge has been generated from studying BRCA1 mutations, much work remains to be done to understand fully what endogenous BRCA1 is doing. For example, it is not fully known why BRCA1 mutations specifically cause a susceptibility to breast and ovarian cancer. Moreover, the exact mechanism for what BRCA1 is doing during DNA repair remains unknown. Understanding BRCA1's molecular function may lead eventually to better methods for treating BRCA1 mutations.

Caitlin Hanlon (chanlon3@jhmi.edu) earned a BS from Ursinus College and a Ph.D. from the Department of Cell Biology at the Johns Hopkins School of Medicine.

Baba wins Tabor Award for transcription research

By Erik Maradiaga

Takashi Baba, an assistant professor at Kyushu University in Japan, is the recipient of the **Journal of Biological Chemistry** Herb Tabor Young Investigator Award for his research on the function of the transcription factor Ad4BP/SF-1 and its significance for the regulation of metabolism.

Baba has shown that Ad4BP/SF-1 regulates overall metabolic processes at the transcription level. In genome wide experiments, he both identified all of the target genes of Ad4BP/SF-1 and discovered that each gene involved in glycolysis and cholesterol biosynthesis was regulated by Ad4BP/SF-1.

Baba earned his bachelor's degree and Ph.D. at Tohoku University in Japan, where he studied the gene regulation involved in xenobiotic metabolism, also known as drug modification, by the aryl hydrocarbon receptor. During a postdoc at the National Institute for Basic Biology in Japan, he continued researching the aryl hydrocarbon receptor by analyzing the protein in knockout mice. After finding that AhR cooperates with Ad4BP/SF-1 in the regulation of a gene involved in estrogen synthesis, he became intrigued by the unique function of Ad4BP/ SF-1, which had already been discovered to regulate all genes involved in steroid hormone synthesis.

Takashi Baba received the Tabor Award from the JBC interim editor-in-chief, F. Peter Guengerich of Vanderbilt University at the 19th International Conference on Cytochrome P450 in June in Tokyo, Japan.

Baba will continue his work with Ad4BP/SF-1 at Kyushu University and plans to further elucidate the significance of the orchestration of metabolism regulation by a single transcription factor.

Erik Maradiaga (em3914a@student.american.edu) is a biology major at American University.

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Why are some recluse spider bites much worse than others?

Substrate specificity of toxins offers clues

By Mollie Rappe

Brown recluse spiders are common in the southern United States and have potent venoms. Bites from this family of spiders can cause necrotic ulcers and, in rare cases, the destruction of red blood cells, kidney failure and death.

In a recent **Journal of Biological Chemistry** paper, Matthew Cordes, a biochemistry professor at the University of Arizona, and co-workers uncovered why recluse spider venoms are so complex.

"The venom is really like a complicated cocktail – like a martini with five different brands of gin and vermouth in it," Cordes explained. "Not only is it a particular kind of ingredient in the venom cocktail that makes brown recluse bites harmful to people, it seems that certain 'brands' of that ingredient are more likely than others to be poisoning people."

A BROWN RECLUSE SPIDER. IMAGE COURTESY OF CENTERS FOR DISEASE CONTROL AND PREVENTION'S PUBLIC HEALTH IMAGE LIBRARY

Brown recluse spider venom contains many toxins, including a variety of phospholipase D enzymes, which attack the phospholipid cell membrane. Daniel Lajoie, a graduate student and the first author on the JBC paper, and co-workers discovered why recluse spider venoms have so many different phospholipase D enzymes: Some of the toxins have evolved to attack sphingomyelin, which is common in mammals and some insects, while other toxins have evolved to attack ethanolamine-containing sphingolipid, which is not found in humans but is common in insects the spiders prey on.

Figuring out the substrate specificity for the different toxins is only one step in the path to understanding why some recluse spider bites are much worse than others. Where the spider bite is located, the age of the person bitten, how much venom is injected and the composition of the venom are all important factors that affect how severe the bite is. Interestingly, Greta Binford, a biology professor at Lewis & Clark College, discovered that in addition to the species of the spider, the spider's age and sex affect the precise composition of venom.

There is still work to be done to understand and treat brown recluse spider bites. For instance, it's still a mystery how cleaving the headgroup off of the fatty acid portion of the phospholipid and forming a cyclic ceramide phosphate triggers a cascade of events leading to cell death.

However, stopping the toxins from attacking the cell membrane or preventing the downstream cascade triggered by their products are possible methods for treating recluse spider bites. This new research undertaken by the Cordes lab sheds light on the complexity and redundancy of the venom, informing future work toward treating brown recluse bites.

One interesting spinoff from this research is a new idea for an insecticide. One of the toxins found in the six-eyed sand spider is very effective at attacking ethanolamine-containing sphingolipid, a phospholipid common in insects but not found in humans.

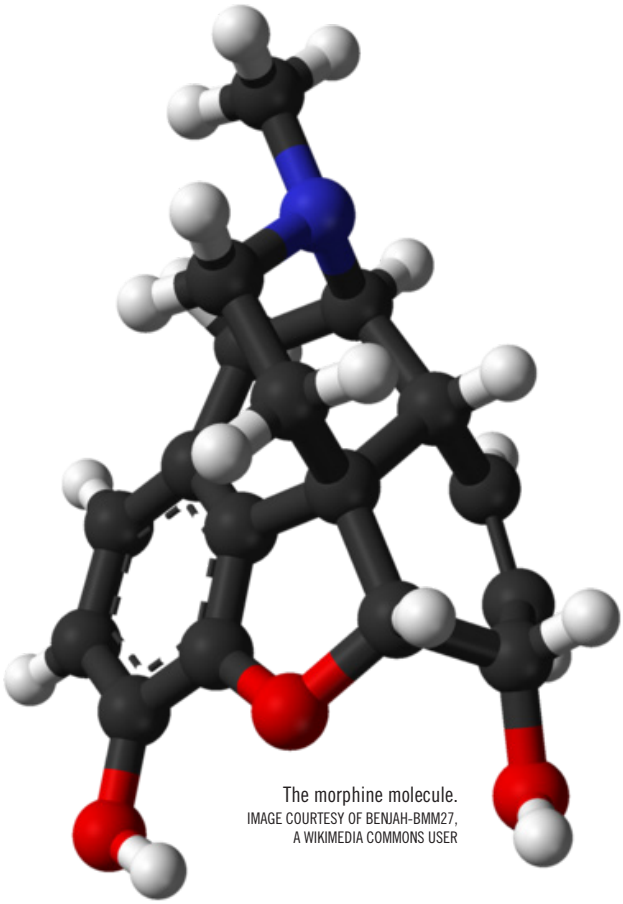
Mollie Rappe (mollie.rappe@gmail.com) earned her Ph.D. in biophysics at the Johns Hopkins University. She will begin writing for Sandia National Laboratories shortly.

Exploring the effects of morphine on the nerve synapse

By Alexandra Pantos

Morphine is a highly effective pain reliever that acts on opioid receptors in the brain to calm pain-signaling nerve cells. But it is also notoriously addictive. A recent paper in the journal **Molecular & Cellular Proteomics** looks at how addiction to morphine affects the brain at the protein level.

When Lakshmi Devi, who is at the Icahn School of Medicine at Mount Sinai in New York City, wanted to learn more about how the brain remembers a drug-induced experience of pleasure, she began to think along the lines of changes that occur in the brain during relapse from addiction. Morphine was of particular interest because it remains the painkiller of choice in hospitals despite its addictive properties.



The morphine molecule.
IMAGE COURTESY OF BENJAH-BMM27, A WIKIMEDIA COMMONS USER

Devi says that there were two main issues with morphine that warranted investigation. One issue was whether relapses into addiction were essentially memories of an addiction flaring up in the brain. Could it be that a relapse occurs when someone's brain recalls at the molecular level how it felt to take the drug? This notion suggests that changes brought about by an addictive substance could occur at the synapse at the molecular level.

The other issue was tied to the first one: Little had been done to explore the molecular changes that occur in the synapse during memory. The limitations of existing technology made it difficult to isolate the details of what happens at synapses during memory recall.

But proteomics technology had matured enough to allow Devi and her team to identify minute quantities of proteins in the brains of rats, which might reveal effects of the drug. The team administered an increasing dose of morphine to lab rats over a few days, long enough for the rodents to become dependent on the drug. The rats were then euthanized and regions of their brains subjected to cellular fractionation and analysis by mass spectrometry. Proteins that were identified by the mass spectrometric analyses were further studied by using bioinformatics approaches.

Some of the proteins identified by Devi and colleagues were notably more abundant in morphine-treated rats, including ones associated with the ubiquitin-proteasome system. The finding surprised Devi and her team, because it showed that ubiquitination occurring at the synapse could affect protein function. These results add to emerging evidence that ubiquitination as a post-translational modification is more about signaling than simple protein degradation.

The next step is to conduct a study similar to the one already done, except this time the investigators will look at the synaptic changes after taking the drug away for a while and then reintroducing it. Discoveries from these studies could be vital in identifying new therapeutic targets for debilitating pain. Even if morphine itself cannot be made less addictive, these findings could aid in the development of new drugs that can manage pain in a nonaddictive way.

Alexandra Pantos (apantos@asbmb.org) is an intern at the ASBMB and a senior biology student at the University of Maryland.

Compartmentalizing the complex system of acyl-CoA metabolism

By Ulli Hain

A recent minireview in the **Journal of Biological Chemistry** dives into the complexity of the metabolism of fatty acids, important biomolecules used for energy storage and production, formation of membrane phospholipids and signaling.

Fatty acids derived from a fatty meal, synthesized de novo within the cell or hydrolyzed from triacylglycerol, or TAG, must be linked to coenzyme A, or CoA, to form acyl-CoAs before the cell can use them. From here,

"(A)n acyl-CoA molecule faces many possible fates..."

an acyl-CoA molecule faces many possible fates, including breakdown through β-oxidation to provide energy, esterification to form phospholipids or storage as TAGs.

How does the cell correctly partition acyl-CoAs into these pathways to meet the physiological needs of the whole organism? Daniel Cooper and colleagues at the University of North Carolina at Chapel Hill make the case that in order acyl-CoA metabolism is compartmentalized to organize and increase efficiency of this complex system.

Metabolism of acyl-CoAs occurs at distinct locations in the cell: Elongation and desaturation of fatty acids, TAG synthesis, and esterification occur at the endoplasmic reticulum, while β-oxidation for production of the energy carrier adenosine triphosphate, or ATP, and thermogenesis occur within the mitochondria matrix.

The location of long-chain acyl-CoA synthetase, or ACSL, isoforms, which convert free long-chain fatty acids into fatty acyl-CoA thioesters, appears to help define these pathways. For example, when ACSL4 was overexpressed at the mitochondria rather than the ER, there was a 50 percent reduction of its downstream product, the lipid phosphatidylinositol, or PI. This suggests that the interaction of ACSL4 with PI enzymes located at the ER is important for PI synthesis and that acyl-CoAs produced elsewhere in the cell are not freely available to pathways at other sites.

While many downstream proteins for acyl-CoA metabolism have well-defined positions in the cell, the authors note that location can change in response to stimuli, such as insulin.

They also point out that more work needs to be done to characterize both the location and function of the ACSL enzymes. Current methods are problematic, as fractionation experiments can be contaminated with other organelles, while overexpression analyses may mislocalize proteins and overwhelm downstream metabolic pathways.

The minireview, titled "Physiological consequences of compartmentalized acyl-CoA metabolism," also describes key aspects of acyl-CoA regulation. Studies suggest that ACSL isoforms have different substrate preferences, subcellular locations and functions. Complicating this is the observation that the location and function of a particular isoform may vary in different tissues and cell types.

The mRNA levels of several ACSL isoforms are regulated by peroxisome proliferator-activated receptors, or PPAR, transcription factors, which are activated by particular endogenous and exogenous fatty acids and acyl-CoAs. The substrate specificity of PPARs also appears to be cell-type specific, affording another level of complexity for fine-tuning metabolism. Due to this complexity and the contrasting results found in similar cell lines, the authors argue for the importance of studying acyl-CoA metabolism in primary cells.

Even at a particular site in the cell, multiple pathways can compete for acyl-CoAs. For example, glycerol-3-phosphate acyltransferase 1, or GPAT1, needed for synthesis of the signaling molecule lysophosphatidic acid, and carnitine-palmitoyltransferase 1, or CPT1, needed to translocate fatty acids into the mitochondria, are both present on the outer mitochondrial membrane. The relative levels of these enzymes, which control this partitioning, are regulated by the transcription factors SREBP1 and ChREBP for GPAT1 and PPARα for CPT1.

The authors bring to bear several remaining questions in the field: How are exogenously derived fatty acids transported from the cytosolic face of the plasma membrane to specific sites within the cell? How do multienzyme metabolic assemblies associate and disperse in response to changing nutrient and energy availability? What is the role of post-translational modifications?

It is vital to understand how acyl-CoA metabolism is regulated, the authors assert, as it "represents a critical node for understanding whole-body pathophysiology."

Ulli Hain (hain.ulli@gmail.com) is a Ph.D. graduate in biochemistry from Johns Hopkins School of Public Health, a freelance science writer, and a science policy fellow with Research America.

The pivotal role of phospholipases

By Lauren Dockett

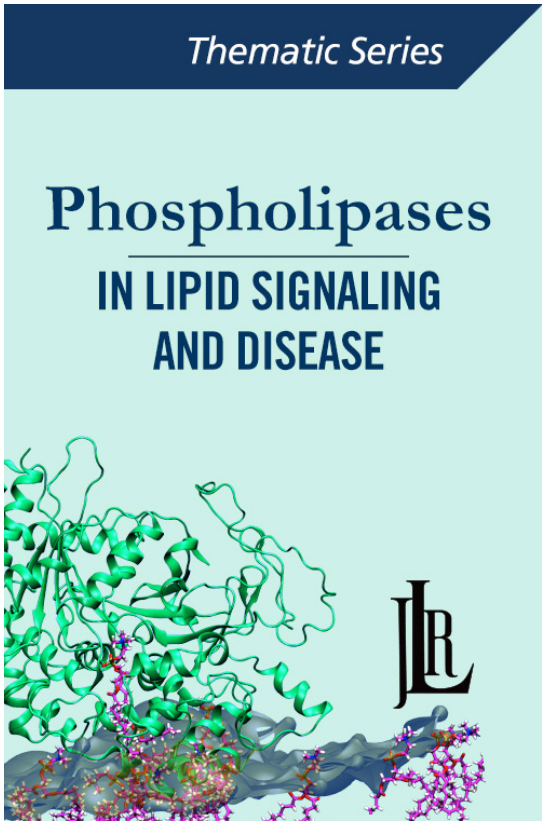
The digestive enzymes known as phospholipases are critical to most physiological processes and play a central role in lipid signaling and disease.

Edward Dennis, editor-in-chief of the **Journal of Lipid Research**, has pulled together a thematic review series about the influential enzymes. He says, "Phospholipases constitute a surprisingly large class of enzymes that includes specific enzymes for all of the hydrolytic targets of phospholipids including the two acyl groups, the phosphodiester bonds on both sides of the phosphate, and even the phosphates on the inositol ring of polyphospho phosphatidylinositols. One or more phospholipases seem to be implicated in virtually all diseases in some manner including cardiovascular disease, diabetes, mitochondrial disease, cancer and certainly inflammation."

Despite their omnipresence, phospholipases have not been easy to study. They challenge investigators, says Dennis, "because they act on phospholipids associated with membranes rather than on substrates free in solution."

Eleven reviews that focus on what we do know about the enzymes will appear in the series "Phospholipases in Lipid Signaling and Disease." An introduction and eight reviews are currently available in the journal. Additional articles on phospholipase A1 and phospholipid remodeling are expected to appear before the series is complete.

Lauren Dockett (ldockett@asbmb.org) is the managing editor of ASBMB Today.



Introduction to Thematic Review Series: Phospholipases: Central Role in Lipid Signaling and Disease
Edward A. Dennis, University of California, San Diego

Cytosolic phospholipase A2: physiological function and role in disease
Christina C. Leslie, National Jewish Health, Denver

A new era of secreted phospholipases A2 (sPLA2)
Makoto Murakami, Hiroyasu Sato, Yoshimi Miki, Kei Yamamoto and Yoshitaka Taketomi, Tokyo Metropolitan Institute of Medical Science

Destructive effects of iPLA2-derived lipid signaling: a beta-cell perspective
Sasanka Ramanadham, Tomader Ali, Jason W. Ashley, Robert N. Bone, William Hancock and Xiaoyong Lei, University of Alabama at Birmingham

Phosphoinositide-specific phospholipase C (PLC) in health and disease
Lucio Cocco, Matilde Y. Follo, Lucia Manzoli and Pann-Ghill Suh, University of Bologna, Bologna, Italy

Physiological and pathophysiological roles for phospholipase D
Rochelle K. Nelson and Michael A. Frohman, State University of New York, Stonybrook

Lipid phosphate phosphatases and their roles in pathophysiology
Xiaoyun Tang, Matthew G. K. Benesch and David N. Brindley, University of Alberta

Autotaxin, a lysophospholipase D with pleomorphic effects in oncogenesis and cancer progression
Lorenzo Federico, Kang Jin Jeong, Christopher P. Vellano and Gordon B. Mills, M.D. Anderson Cancer Center, University of Texas, Houston

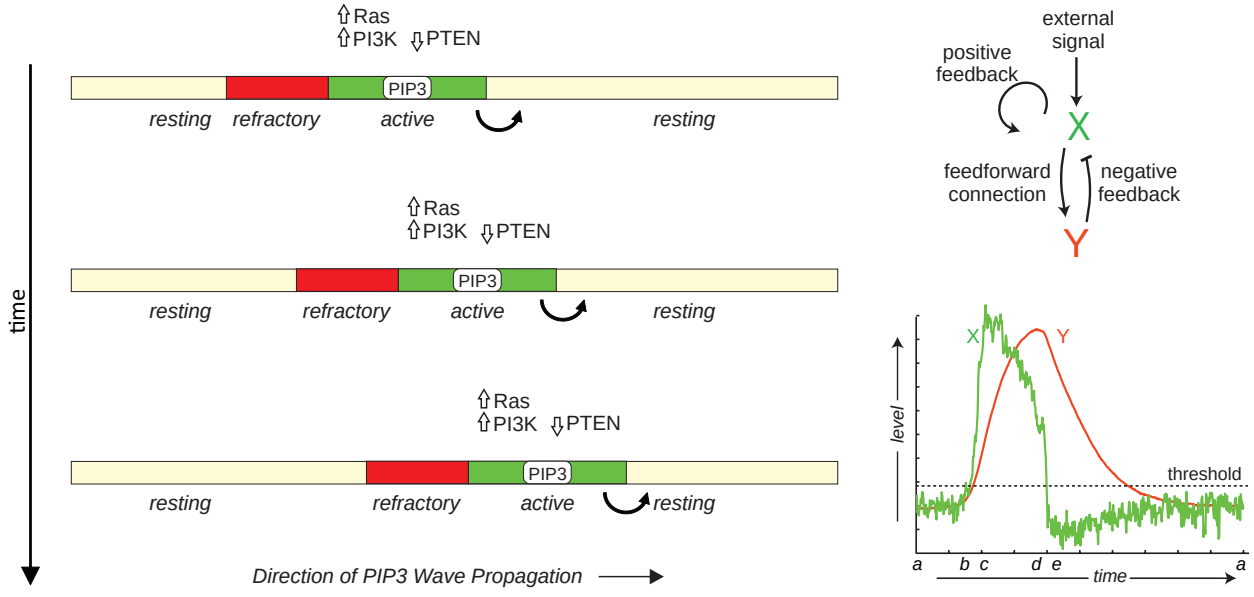
Phosphatidylinositolphosphate Phosphatase Activities and Cancer
Simon A. Rudge and Michael J. O. Wakelam, The Babraham Institute, Cambridge, UK

Reaction-diffusion waves of phosphoinositides in the membrane

By Chuan–Hsiang Huang and Peter N. Devreotes

Phosphoinositides, phosphorylated forms of phosphatidylinositol, or PI, are minor components of the membrane lipids yet play important roles in the signaling of a broad range of cellular processes including cell migration, phagocytosis, cell-cycle regulation and membrane trafficking. Derangements in phosphoinositide signaling are implicated in diseases ranging from congenital malformations and metabolic syndromes to cancers. The various forms of phosphoinositides differ in the number and position of phosphate groups on the inositol ring of PI and can be interconverted by lipid kinases and phosphatases. For example, PI-4 kinases add a phosphate on the 4-position of the inositol ring to generate PI(4)P, which can be phosphorylated further at the 5-position by PIP5Ks to generate PIP(4,5)P2, often referred to as PIP2. Phosphorylation of PIP2 on the 3-position by PI3Ks generates PI(3,4,5)P3 or PIP3, whereas the lipid phosphatase PTEN catalyzes the reverse reaction to convert PIP3 back to PIP2. Tamas Balla has provided a comprehensive review on phosphoinositide chemistry and biology (1).

An extraordinary new view of the dynamic spatiotemporal regulation of phosphoinositides is emerging from advances in fluorescent biosensors and imaging. For example, propagating waves of a PH-domain that binds to PIP3 were found at phagocytic cups and the basal surface of migrating cells including Dictyostelium (2) and human neutrophils (3). These activities are closely aligned with reports of the activities of other signaling proteins, such as Ras and Rac, and with waves of markers for the actin-based cytoskeleton described earlier (4 – 7). PTEN dissociates from the active zone of the wave, contributing to the local increase in PIP3. Importantly, cells devoid of cytoskeletal turnover



In migrating cells, propagation of PIP3 and signaling proteins across the membrane has features of reaction-diffusion waves in an excitable medium including all-or-none activation followed by a refractory period. The phenomenon can be modeled by the coupling between an autocatalytic activator (X) and a delayed inhibitor (Y).

still display these spontaneous signaling events, indicating that they drive the cytoskeletal network to generate protrusions (3, 7 – 9). Guidance cues, such as chemoattractants that bias the signaling activities, direct cell migration (3).

A prominent feature of these signaling waves is their annihilation upon collision, suggesting that they are reaction-diffusion waves in an excitable medium. The term "excitability" often is associated with the action potential of neurons, which is characterized by large responses to suprathreshold stimuli, followed by a refractory period of unresponsiveness to further stimuli. When the reactants diffuse in the medium, activated species trigger neighboring elements in succession, leading to wavelike propagation of responses. These waves leave behind a zone of refractoriness such that the medium becomes unresponsive in both directions when two waves collide, leading to the annihilation. In support of their excitable nature, the signaling activities of Dictyostelium and neutrophils also display all-or-none and refractory characters (3, 7).

The molecular basis of this excitability is not known. In general, excitable systems are thought to contain an autocatalytic process that becomes activated fully when a threshold is crossed as well as a delayed inhibitor that not only turns off the response but also makes the system transiently refractory. Based on this scheme, several mathematical models have been proposed (5, 8 – 10). Molecularly, Ras and PIP3 form a positive feedback (7), and a Ras-TorC2-PKB negative feedback loop has been described (11). However, cells without PIP3 can still migrate, albeit less efficiently, suggesting redundancy in the signaling network. Further studies also are required to understand how the signaling network couples to the cytoskeletal machinery. Answers to these questions not only will reveal fundamental insights into cell migration but also will open up new opportunities for the treatment of human diseases, such as metastatic cancers.

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Chuan-Hsiang Huang (chuang29@jhmi.edu) is a researcher in the cell biology department at the Johns Hopkins University School of Medicine.

Peter N. Devreotes (pnd@jhmi.edu) is director of the cell biology department at the Johns Hopkins University School of Medicine.

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LET IT SHINE

Is optogenetics ready to cause a revolution in cell biology?

By Rajendrani Mukhopadhyay

"No one lights a lamp in order to hide it behind the door: the purpose of light is to create more light, to open people's eyes, to reveal the marvels around." – **NOVELIST PAULO COELHO**

The light-based technique optogenetics has revealed marvels in neuroscience. In the past 10 years, researchers have used the technique to, among other things, make lab animals stop binge drinking, forget bad memories and elicit the flight-or-flight response, all on command.

The method has been hailed as a revolution in neuroscience. In 2010, the journal Nature Methods declared optogenetics to be the method of the year. In 2013, the prestigious Grete Lundbeck European Brain Research Prize went to six researchers whose work is considered to have laid the foundations for the technique (see box). Optogenetics even made its way into the Obama administration's BRAIN Initiative and the pages of the New Yorker.

Now some scientists want to see if optogenetics can repeat its magic in understanding how cells, beyond the ones in the brain, work. "The hope is that optogenetics is going to enable transformations in cell biology as it's already enabled in neuroscience," says Orion Weiner at the University of California, San Francisco.

Biologists are starting to test out optogenetics to understand the nuances of basic cellular processes, such as migration, polarity, transcription and signal transduction. "We've seen an explosion of interest in the idea of controlling biological activity with light," says Michael Lin of Stanford University, whose laboratory is creating light-controlled proteins to study nucleotide exchange and protease activities.

As recognized by the Brain Prize, several groups contributed to the development of optogenetics. But most people mention a 2005 Nature Neuroscience paper as the one that launched a thousand optogenetics experiments. (There are more than 1,100 papers in PubMed with the word "optogenetics.")

The Nature Neuroscience paper, authored by Ed Boyden, now at Massachusetts Institute of Technology, Karl Deisseroth at Stanford University and others, described the introduction of a gene for an algal ion channel called channelrhodopsin-2 into rat hippocampal neurons. The light-sensitive ion channels opened up when researchers shone light on the neurons and triggered synaptic transmission. The investigators effectively were in control of when the neurons fired.

The work made neuroscientists sit up: This was a way to selectively control neurons of their own choosing, which they couldn't do with other approaches. After watching experiment after experiment come out in neuroscience based on optogenetics, Jared Toettcher at Princeton University says, cell and molecular biologists "looked at all that success and reasoned, if you can activate specific neurons in a large population, maybe… you can also activate a specific signaling protein in a large complicated network that acts within a cell."

Like needle-nose pliers

It has been tough to understand the contributions of individual components in complicated molecular networks. While many experimental perturbations of cells have yielded important information about biology, in most cases their mode of action is much like that of a hammer smashing the entire cell.

Electrodes for electrical stimuli poke into cells; the mere poking can trigger a response even before the experiment begins. Some chemical stimuli can bind indiscriminately to untargeted molecules and often are

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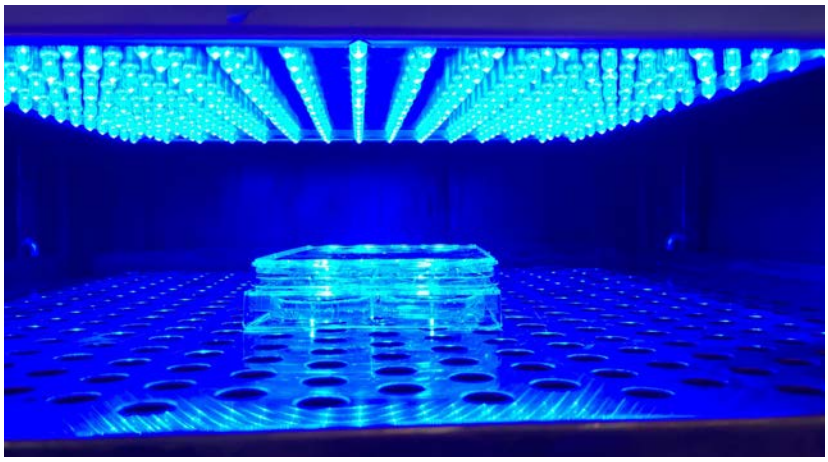


LAURA B. MOTTA-MENA, ELIZABETH ORTH AND KEVIN H. GARDNER, CITY UNIVERSITY OF NEW YORK, ADVANCED SCIENCE RESEARCH CENTER

Human cells grown in 6-well plate for an optogenetics experiment in an incubator fitted with an LED panel.

CONTINUED FROM PAGE 19

irreversible. Gene knockouts permanently prevent production of related proteins, sometimes causing dramatic effects that aren't physiologically relevant. Knockout experiments also are slow, allowing cells time to compensate for the missing gene before scientists can characterize the effects of the knockout.

Light is different. Researchers can place a light source a distance away from the experimental system, eliminating the effects of touch. Most importantly, with lasers and LEDs, researchers can control the amount of light and the duration of light exposure, which lends greater precision to protocol measurements. Light exposure also is reversible, as researchers can switch back and forth between light and dark.

When researchers combine light, with all these useful attributes, with the expression of specific genes in cells, they get a technique with the exactness of a pair of fine-tipped, needle-nose pliers: Researchers make a group of cells artificially express photosensitive proteins. When these cells are exposed to light, photosensitive proteins activate, allowing researchers to see directly what effects these proteins have on a set of cells or even a whole animal.

The technique "is such a different way of approaching science than just knocking proteins out or overexpressing them with a green fluorescent protein tag on them," says Weiner. It "enables us to plug in the intermediate steps of a cascade so we can isolate a given module with spatial and temporal control."

The ability to reach in and play with a single molecule among a mishmash of hundreds of molecules is one of optogenetics' most appealing attributes. Because light beams can be directed to specific locations in the cell, optogenetics gives scientists the ability to investigate the influence of a protein's coordinates. Experts interviewed for this story cited the ability to study cell dynamics as another major appeal.

Information on location and timing of cellular events makes optogenetics different from other light-based analytical methods. In optogenetics, light acts "more as the actuator than as the sensor," driving the pace and place of the experiments, says Chandra Tucker at the University of Colorado. "You really can't do that through any other approach. That's where I feel optogenetics has a lot of power." Other light-based approaches rely on the light for sensing, in that fluorescent reporter molecules passively emit photons, reporting cell behavior.

Experts interviewed for the story point to experiments that have been hard to do or impossible by other means but that now seem doable with optogenetics. Toettcher gives the example of p53, a well-known tumor suppressor that's turned on in response to several stimuli. But researchers realized that the protein doesn't turn on and stay on in response to a particular stimulus. For something like ionizing radiation, p53 fluctuates in pulses over time. In fact, the number of pulses of p53 is proportional to the amount of damage the cell receives. Unfortunately, most molecular biology techniques gloss over the time-dependent expressions of proteins. Western blots simply detect the average expression of pro-

teins, and gene knockout experiments annihilate all expression or artificially jack up expression.

"There is a much more sophisticated code at work in cell biology than people originally thought," says Toettcher. "That's really where these optogenetic tools in cell signaling are going to make a big impact. They allow us, for the first time, to dissect the contributions of different dynamic responses."

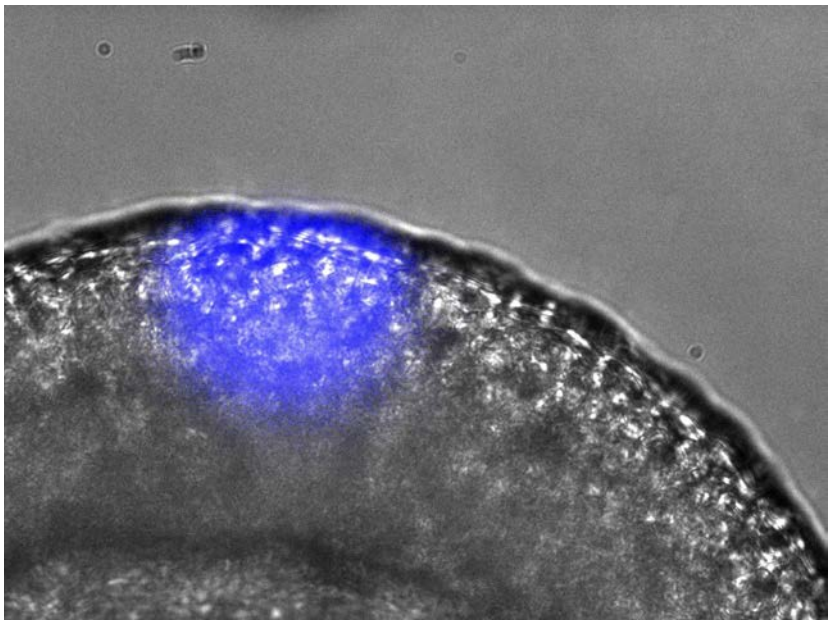
LOV and more

At the core of optogenetics are the genes for light-sensitive proteins that researchers plop into cells. The field heavily relies on photosensitive molecules, such as channelrhodopsins and other opsins, derived from microorganisms and plants. One set of molecules has come from the light-oxygen-voltage-sensing domains, better known as LOV domains, which are found in plants, algae, fungi and bacteria.

Kevin Gardner at The City University of New York Advanced Science Research Center and colleagues have engineered a bacterial LOV-containing protein called EL222. When illuminated with blue light, EL222 binds to DNA in less than 10 seconds in several mammalian cell lines and intact zebrafish embryos.

This timescale of seconds is important. "When you knock proteins down or out, (the experiment) takes on the order of days, weeks or months to perform. Cells have ways of upregulating compensatory pathways," notes Weiner. "But if you can take them out on a timescale of seconds, you can see phenotypes that are invisible with the slower perturbations."

LOV domains also have been used to study the influence of place. Lukas Kapitein at the University of Utrecht and his team showed that LOV domains could be used to attach cytoskeletal motor proteins to peroxisomes, mitochondria and recycling endosomes to move them around to



ANNA READE, STEPHANIE WOO AND ORION WEINER, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO.

Gene expression can be spatially controlled by optogenetics in the zebrafish embryo.

different parts of cells. For example, Kapitein and colleagues demonstrated that the local positioning of recycling endosomes influenced the growth of neurons.

Another optogenetics approach is to turn a protein that's oblivious to light into a version that responds to light. Klaus Hahn at the University of North Carolina and his group did just that in 2009 with photoactivatable Rac. "Instead of harnessing the functions of naturally occurring molecules, molecules can now be manipulated to do things that nature never engineered them to do," says Hahn.

The GTPase Rac regulates the actin cytoskeleton. The photoactivatable version of Rac changes conformation when illuminated with light and becomes active. Researchers now can see in detail how photoactivated Rac influences different parts of the actin cytoskeleton. Because Rac controls cell movement, researchers have been able to use photoactivatable Rac to guide living cells to precise positions inside living animals and to start to work out how cell placement influences phenomena such as development and the trafficking of immune cells in and

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out of tumors. Inspired by the photoactivatable Rac, researchers have made other proteins light sensitive, such as kinases and G-protein–coupled receptors.

With these engineered light-sensitive proteins, explorations inside cells become more sophisticated. Weiner gives the example of the Ras/MAP kinase cascade, which regulates a range of biological processes, such as cell differentiation, proliferation and arrest. Researchers have been puzzled by how one cascade can regulate such different biological outcomes. But with optogenetics, researchers can drive the activation of the cascade directly and begin to figure out how sustained and transient activations and dosages regulate cell biology.

In 2013, Weiner, along with Toettcher, who was his postdoctoral fellow at the time, and UCSF's Wendell Lim, used the plant Phy-PIF system to delve deeper into the Ras cascade. Phy, a phytocytochrome, photoswitches between two different states; PIF binds to one of those two states. The investigators attached Phy to the membrane and fused PIF to various activators, such as a protein called SOS, of the Ras pathway in the cytoplasm. When they hit Phy with a red light, it was able to interact with PIF; when they hit Phy with infrared light, the interaction went away.

By playing around with different doses and timed pulses of light, the investigators determined, for example, that the transcription factor STAT3 is activated by only a particular part of the cascade after photoactivatable Ras is active for more than an hour.

Removing the kinks

For all their enthusiasm for optogenetics, experts recognize the glitches. "The initial hope with optogenetics was it was going to be as easy as GFP. You just slap it on the end of your favorite molecule and regulate its activity," says Weiner. "It turns out it's harder than that."

One reason optogenetics has been less plug-and-play in molecular biology than it has been in neuroscience is that every neuron is "activated by the exact same kind of stimulus, which is membrane depolarization," says Toettcher, but, in other cells "it's not at all the case that every signaling protein is activated by the same kind of input."

Another problem dogging the field is inconsistency: One LOV domain may work like gangbusters in a particular cell line or on a particular protein but drop dead in another. "I hate to say it, but there's a ton of variability right now," says Gardner. "Those of us who are developing these tools and are the first adopters really need to start thinking about addressing this a little more comprehensively."

Gardner applauds colleagues who have published papers, which he describes as "not sexy," that systematically work through different photosensitive proteins to see what exactly they can do. Some of the proteins "work great everywhere. Some work great in some cell lines in some settings and not others," says Gardner. "Some have been tough to adopt by people not born out of the discoverer's lab."

Then comes the question of physiological relevance. As with any method that is based on changing the cell, how do researchers know that they are not rendering the system useless by the simple act of introducing a foreign light-controlled protein? "You have to make sure you're not altering the physiology of the cells before you turn on the light," says Hahn. "That's challenging."

There is also the issue known as "leakiness." That's when a light-sensitive protein is residually active without light, causing changes in the cell even before the experiment begins. Hahn says the issue can be addressed by measuring the level of activity of the protein as it gets different doses of light so a researcher knows how much activity is present in the absence of

light or, better yet, can build a protein that has a large difference in activity when lit and when not lit.

Once researchers are armed with better photosensitive modules, the aim will be to integrate several of them into a single experiment. The multiplexing aspect "in theory, sounds great because there are already proteins out there with different colors," says Hahn. But it hasn't been possible so far because "none of them are really perfect." Hahn and others state that improving the proteins so that they turn on and off cleanly with a specific wavelength of light is valuable, but grunt, work.

Investigators using optogenetics in molecular biology say the kinks will be ironed out as more people try out optogenetics in their experimental systems. They say no special skills are needed, although engineering new optogenetics approaches does require specialization in protein engineering and optics. Some savviness with cloning and protein expression, a bit of microscopy savoir faire, and you're able to harness the powers of optogenetics. There isn't even a need for highly specialized microscopes or complicated lasers.

Experts are willing to lend a helping hand. Weiner puts out the welcome mat: "I hope people interested in using optogenetics will fly out to our lab for a few days or a week to learn how it works. It's much easier to learn and take back the technique from our lab than reading protocols and trying to troubleshoot over the phone."

Adopters of optogenetics feel that the effort invested into the technique will pay off simply because it allows nuanced, delicate measurements within complicated systems. Besides the ability to tease out the effects of place and timing, researchers can analyze the effects of doses of protein activity by exploiting the amount of light fed into an experimental system. "That's one thing the field isn't taking much advantage of yet is the fact that it's titratable," says Weiner. "You can not only acutely control signals in time, but you can dose them in a titratable, reversible fashion for more quantitative biology."

So experts feel their enthusiasm for optogenetics is warranted. "The number of applications is just screaming for attention. A lot of people are getting very creative here," says Gardner. There is no doubt in his mind that the next five years "will be an interesting period."

Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the chief science correspondent for the American Society for Biochemistry and Molecular Biology. Follow her on Twitter at twitter.com/rajmukhop.

The Brain Prize

The Grete Lundbeck European Brain Research Prize, also known as the Brain Prize, recognizes original and influential advances in any area of neuroscience. In 2013, the prize went to Gero Miesenböck, Ernst Bamberg, Peter Hegemann, Georg Nagel, Ed Boyden and Karl Deisseroth. The award announcement cited these six men for laying the foundations of optogenetics.

The prize recognized Bamberg, Hegemann, Miesenböck and Nagel for making the fundamental observations and discoveries about light-sensitive molecules and developing them so they could be introduced into specific types of neurons. It acknowledged Boyden and Diesseroth for developing the technique further and getting it to work in live animals.

Colin Blakemore, chairman of the foundation's selection committee, said in a press release: "Optogenetic control of nerve cells is arguably the most important technical advance in neuroscience in the past 40 years. It offers a revolution in our understanding of the way in which circuits of neurons carry out complex functions, such as learning and controlling movement. And it could provide an entirely new approach to the restoration of function in blindness or brain degeneration, and to the treatment of a variety of other neurological and psychiatric disorders."

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The American Society for Biochemistry and Molecular Biology announces a new online course for mastering science communication: "**The Art of Science Communication**."

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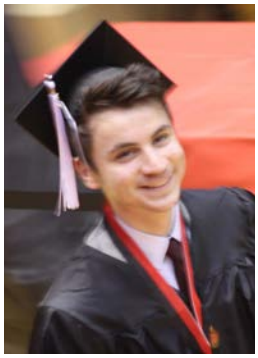
Teenage college grad is determined to help others

By Allison Frick



Last spring, at the age of 17, Ismail Gunacar graduated from the University of Cincinnati with a degree in biochemistry. Gunacar started taking college classes when he was 13, and according to UC, is the second-youngest student ever to earn a bachelor's degree from the university.

Ismail Gunacar moved with his family from his native Turkey to Cincinnati when he was 5 years old and says it was his passion to help others and his exuberant love of learning that powered him through advanced coursework at such a young age. Known to friends and family as "Ish," Gunacar says he is "taking a break" after his senior year. So far during this break he's studied for and taken the MCAT, applied early decision to UC's medical school, and celebrated his eighteenth birthday.

Our interview with him has been edited for length and clarity.

When did you know you wanted to pursue more advanced school work?

It got to the point where, in middle school, it was just not challenging anymore … I was already looking up higher level math concepts for myself just out of pure interest. One of my dad's friends is a professor, and he told us about the Postsecondary Enrollment Options Program (now called the College Credit Plus program), and I thought it would be pretty good for me … I took some placement exams at the University of Cincinnati Blue Ash College. I applied to that program, and I placed into calculus just from studying myself. And that was sort of like the first door … After that, I just sort of branched out, started looking more into sciences and stuff.

What did your parents think about all this?

My parents have always been very supportive. My dad always has emphasized the importance of education. Ever since I was little, probably his biggest advice was "Make sure you really pay attention. Make sure educa-

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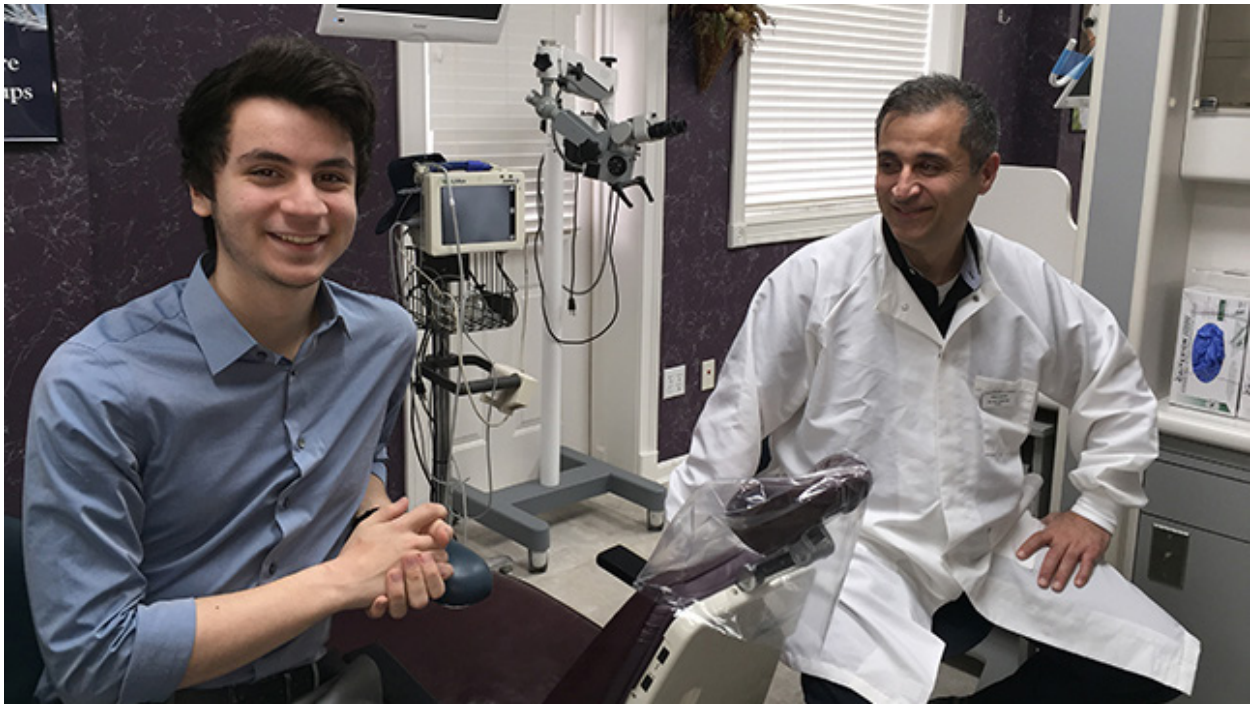

IMAGES COURTESY OF ISMAIL GUNACAR

Ismail and his father, Guy Gunacar, in his father's dental office in Ohio

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tion is the most important thing." The power behind knowledge is his biggest piece of advice to me.

What was it like to be so much younger than your classmates at UC Blue Ash?

I always tell this story, and it's quite funny. My mom actually led me to the class. The professor was kind of shocked, like, "Are you the student? Or he's the student?" And my mom told him, "He's the student; I'm just dropping him off." Once I started getting more comfortable starting up conversations, some of my friends would tell me, "You know, Ish, the first time that you sat down in that class, I thought that you had a parent or something – your mom or something was taking a class and she couldn't find a babysitter."

Did you ever find it challenging to be in a different age range?

Not at all. The community of University of Cincinnati and especially the Blue Ash Campus – I'm so thankful to them. It's such a warm community there. Everybody just adopted me as their younger brother.

What inspired you to study biochemistry?

I sort of got to biochemistry by just exploring different things … But eventually I started looking at DNA and big macromolecules. Lipids are very interesting to me. Nucleotides, proteins, amino acids – just very interesting stuff. I would go past the required reading a lot of times, and I just stuck with it.

What was it like working in the lab?

Of course, I have to thank University of Cincinnati again for that, especially Dr. Pat Limbach. They were

very supportive, very trusting in my abilities. They saw my potential, and he let me come and work in his lab, and it was a phenomenal experience … just being in there, working in the lab … was a huge advantage for me.

How did it feel to graduate from college at 17?

My last year was the freshman year of the kids that I grew up with, so I was in college my senior year with all of my old friends. It was a very different experience to interact with people my own age. I had to graduate while they get to continue on and just have fun together. But I definitely don't regret it. Some people say that I won't ever experience the true college experience, but I think that I did really, because I got very involved. I was on campus a lot of the time. My first three or four years, I couldn't even get off campus until my mom picked me up, because I couldn't drive, so I definitely did get a college experience … I got to experience something that I think very few people have ever experienced. I'm very thankful for that. I wouldn't change anything.

Why did you choose med school?

My father has always been a person that I looked up to. He's a dentist, and just seeing him work, seeing how he interacts with patients, his character, his integrity were very inspiring to me, so I always had that health care idea in my head. Then volunteering in hospitals, volunteering in schools, tutoring, trying to help the community as much as I could and shadowing doctors, I really developed the passion that I really do want to do medicine instead of anything else.

What lies ahead for you?

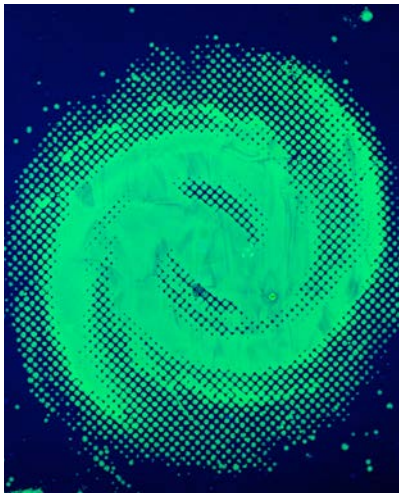
The biggest goal is to get into medical school, and the long-term goal is to graduate. I think I'd be 22 at that point, so I guess that'd make me pretty young. I don't know the exact standing, but that'd make me a pretty young MD.

Gunacar poses for a graduation photo last May with his father, Guy Gunacar, and mother, Aygen Gunacar, at the University of Cincinnati.

What do you do when you're not studying?

Work isn't really work to me … because it's very enjoyable. I really do like doing all the things that I do, whether it is studying or learning or doing research or my hobbies. My whole life is free time that I'm really enjoying.

Allison Frick (africk@asbmb.org) is the ASBMB's print and digital media specialist.



A Milky Way of E. coli

The bacteria show

By Nicole C. Woitowich

Irradiating bacteria into cool shapes. Making E. coli with GFP-encoding plasmids glow under fluorescent light. These are not the late-night shenanigans of a couple of bone-weary lab mates. In the hands of popular bio artist Zachary Copfer, they are the tools of creation.

A self-titled "microbiologist masquerading as an artist, or an artist masquerading as a microbiologist," Copfer has gained popularity in the world of bio art by doing unique work with bacteria. Coper makes "bacteriographs," images of iconic scientists and celebrities that look, on first inspection, like pop-art altered photographs or lithographs but are in fact colonies of bacteria manipulated on agar plates.

COPFER

In his "My Favorite Scientist" collection, Albert Einstein and Charles Darwin receive the bacteriographic treatment, their faces appearing in tan agar against a background of maroon Serratia marcescens. Individual colonies of the bacteria dot the periphery of the plates as if ready to be plucked up by an inoculating loop. S. marcescens produces the tripyrrole pigment prodigiosin and gives the images their deep red color.

Another of his collections, entitled "Star Stuff" as a nod to Carl Sagan, features images taken from the Hubble telescope that are grown in E. coli containing GFP-encoding plasmids. When visualized under ultraviolet light, the Milky Way comes to life in fluorescent spirals of E. coli. The single colonies appear as neighboring stars against the night sky.

"People can be passionate about art and science and be interested in both," says 33-year-old Copfer, who has degrees in biology and fine arts and worked as a pharmaceutical researcher until his passion for art, theater and photography won out.

"When I first went to (fine arts) grad school I put science on the shelf for a while," he says. But while brainstorming ideas for a project, Copfer came across Sagan's television series "Cosmos" on Netflix.

"The introduction to the first episode is beautiful and amazing," he says. "(It shows that) science can be poetry. I've always been amazed by that and tried to figure how to get that into my art."

Bio artists like Copfer are often champions of scientists and of communicating science to the general public. "Science is very creative and that is something that people who aren't in science wouldn't expect," he says. "They think of it as dry, people in lab coats crunching numbers, very removed and sterile, when it couldn't be more of the opposite! People are excited and emotional about their research."

Copfer says when he first started making bio art he was most interested in sharing the beauty in science. That intention is still there, but it's shifted a bit over time. Now he's also trying to have fun with science.

Choosing bacteria as a medium has

The Einstein bacteriograph

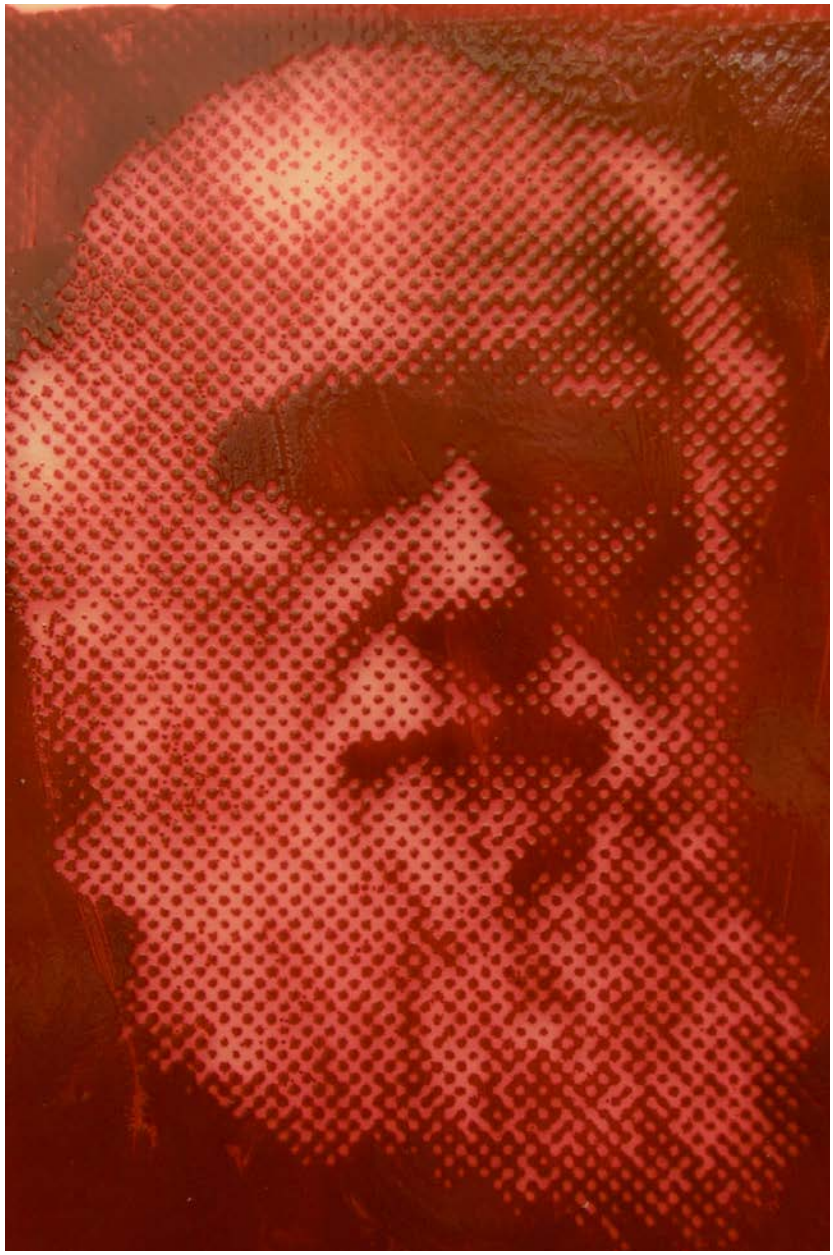
kept things fun. "(Bacteriography) is so much more rewarding than regular photography; by looking at it, you realize that this image is living," he says.

But inventing a means of growing a live photograph wasn't easy. There was a significant period of trial and error before the bacteriographic process really gelled. "The only thing I had to go from was dark room photography. No one had ever done this," he says.

Copfer uses halftone images of his subjects as a type of negative that he places above a full plate of bacteria. He then irradiates the negative and plate with short-wavelength ultraviolet light that kills any bacteria left exposed by the halftone image and leaves the bacteria in the shadow to grow. This results in bacteriographs that look like pixelated photographs of his subjects. Copfer has made bacteriographs of Pablo Picasso, Leonardo da Vinci, the British actor Stephen Fry, celebrity mathematician Carol Vorderman and the queen of England.

Challenges are similar to those found in a lab: determining optimal growth temperature, time and concentrations of growth media ingredients. In stark contrast with regular photographs, Copfer's bacteriographs require extensive preservation methods, which he says was one of the biggest technical blocks to creating this kind of art. It was tricky finding an appropriate resin to preserve but not dehydrate the bacteria and agar so that the plates could be safe to handle and display. After significant experimentation, Copfer found ideal sealants that he applies after he's irradiated a piece's remaining bacteria. This allows his art to travel nationally and internationally to science expos and galleries.

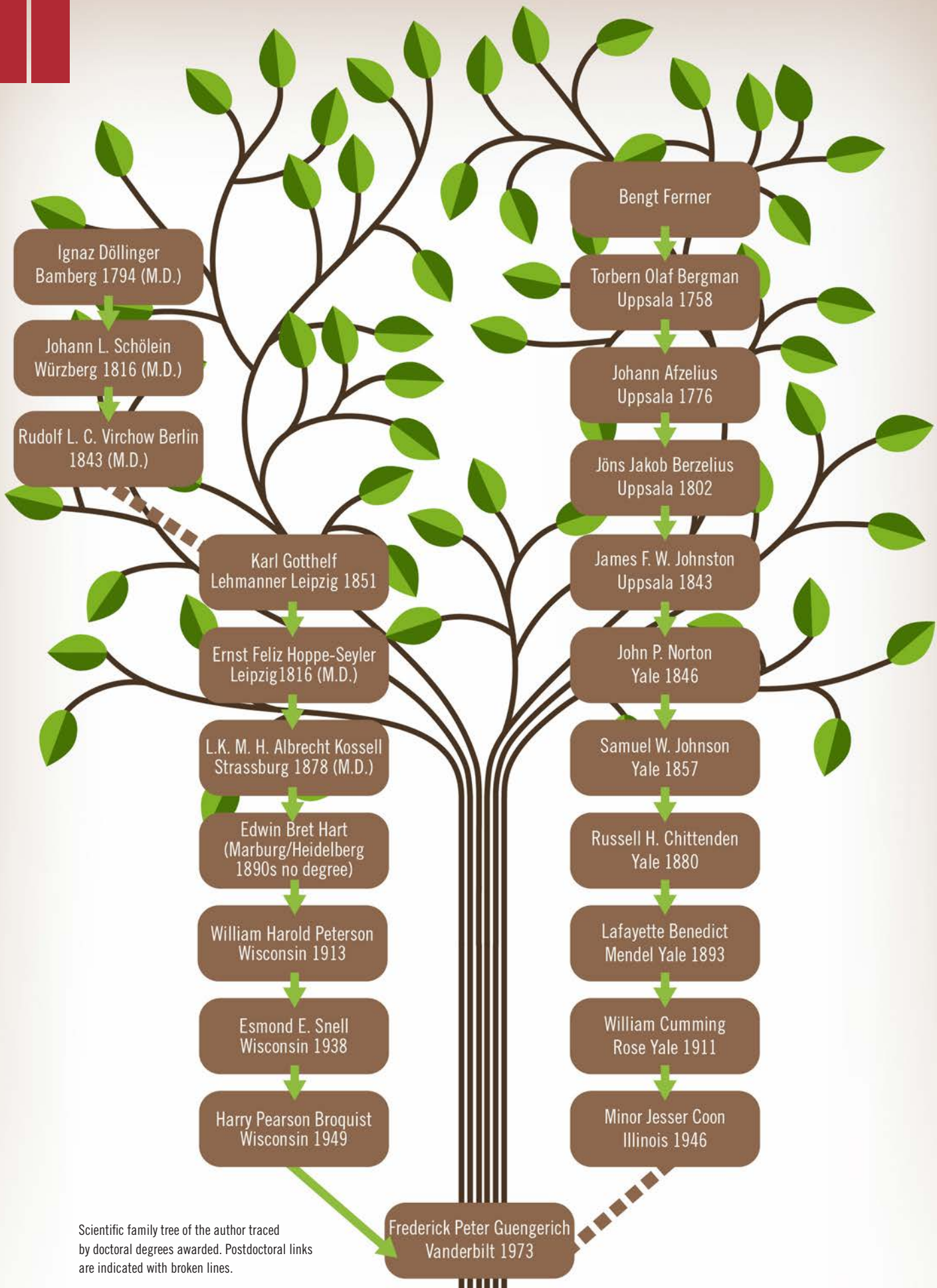
Copfer doesn't see himself as an art-world anomaly. He believes that scientists are intrinsically artistic in nature and can find the creative process therapeutic. "Most good research isn't cut and dry. It requires creativity," he says. While art "allows people who are struggling or stuck in a routine a great outlet … (and a chance) to look at things differently and to put things in a different context."



Charles Darwin emerges from Serratia marcescens. IMAGES COURTESY OF ZACHARY COPFER

His advice for anyone with a background like his who is interested in pursuing the arts? "You can't be afraid to screw up or pursue every dumb idea. It is about having fun, letting go and being absorbed by the things that make you excited … Don't see it as a waste of time. Give it the same time and energy that you would give your research because it is just as valid and just as important."

Nicole C. Woitowich (nicole.woitowich@my.rosalindfranklin.edu) is a member of the public outreach committee and a Ph.D. candidate at Rosalind Franklin University of Medicine and Science.



Scientific family tree of the author traced by doctoral degrees awarded. Postdoctoral links are indicated with broken lines.

My scientific lineage

A biochemist traces his academic geneaology

By F. Peter Guengerich

When considering scientific influences, one can talk about genealogies of background or of training. None of my own relatives were scientists, so my science lineage is composed primarily of who trained who in my academic history. In recent years, the creation of academic family trees, which trace the influence of an academic's mentors and degrees granted at institutions, has grown in popularity. They are more common in chemistry than biochemistry, but I was curious about my own and consulted some electronic search tools (see box) that helped me put a tree together fairly easily (Fig. 1). It extends back 200 years and crosses continents.

The tree begins with my two outstanding mentors for my graduate and postdoctoral training, Harry "The Chief" Broquist and Minor J. "Jud" Coon. Beyond them, it branches back through a few American schools (mainly Illinois, Wisconsin and Yale) and then crosses the Atlantic Ocean to Germany and Sweden. My research gleaned interesting details about these individuals and showed me that some individuals — and institutions — can have remarkable influences in the lives of many people in this world of science.

First, let me consider the Ph.D. thesis side, beginning with Broquist, who contributed research in the areas of folic acid, lysine, carnitine and alkaloid biosynthesis. He was a Wisconsin graduate and my mentor first as an undergraduate at Illinois and then in graduate school at Vanderbilt University. Broquist was a graduate student of Esmond Snell, the pre-eminent researcher in pyridoxal chemistry at the University of Wisconsin. Snell had received his Ph.D. at Wisconsin with William H. Peterson, who received his Ph.D. at Wisconsin with Edwin B. Hart. Hart spent some time training in Germany in the 1890s in several labs, particularly with Nobelist L. K. M. H. Albrecht Kossel in Marburg and Heidelberg.

Hart, it seems, never received a doctoral degree, because Kossel moved from one institution to another. Nevertheless, he became a professor at Wisconsin, trained 46 Ph.D. students, and was a member of the National Academy of Sciences — achievements I do not think it would at all be possible today without a doctorate. Working with his student Harry Steenbock at Wisconsin, Hart determined that iodine deficiency was the cause of goiter.

Researching Kossel meant discovering links to Europe. An M.D. from Strasbourg, Kossel received the Nobel Prize in physiology or medicine for his discovery of the nucleic acid bases. This is of note in light of my own interest in this area, i.e. DNA polymerases and DNA adducts.

Kossel was a student of Ernst F. Hoppe–Seyler (Leipzig), who may be considered one of the fathers of German biochemistry. He published extensively on hemoglobin and founded what was then the leading German biochemical journal, Hoppe-Seyler's Zeitschrift für Physiologische Chemie, which is today published as Biological Chemistry. Hoppe–Seyler, an M.D., had trained with Lehmann in Leipzig and also later with Rudolf L. C. Virchow. Virchow, widely acclaimed as the father of modern pathology, wrote more than 2,000 papers; founded several journals; wrote textbooks; and first described the diseases leukemia, chordoma, ochronosis, embolism and thrombosis. His colleagues in Berlin referred to him as the "pope of medicine." Virchow, in turn, trained with Johann Schölein (Berlin). Schölein was physician to Frederick William IV, discovered the cause of ringworm and named tuberculosis. He trained in Würzburg with Ignaz Döllinger, who obtained an M.D. (Würzburg) in 1794 and made early contributions to comparative anatomy.

The other side of my scientific lineage is traced through my postdoctoral adviser, Jud Coon. Coon is best known for his pioneering research in amino acid metabolism and cytochrome P450 enzymology. He received his Ph.D. from Illinois with William Rose, who discovered threonine and elucidated the requirements for amino acids in rats and humans. The American Society for Biochemistry and Molecular Biology's Rose Award is named for him. I was fortunate to receive this award in 2005, as did Coon and Snell before me.

This branch of my lineage then

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goes through Yale University for several generations. Rose received his Ph.D. with Lafayette Mendel, a prominent biochemical nutritionist (the American Institute of Nutrition awards the Osborne–Mendel Award each year). Mendel received his Ph.D. (Yale) with Russell Chittenden, sometimes referred to as the father of American biochemistry. Chittenden received his Ph.D. (Yale) with Samuel Johnson, a pioneering agricultural scientist, who received his Ph.D. at Yale with John Norton. Norton, also an agricultural science pioneer with a Ph.D. from Yale, trained with James Johnston.

Crossing the Atlantic on this side, now to Sweden, Johnston received a Ph.D. from Uppsala working with Jöns Jakob Berzelius, who is generally considered a father of modern chemistry, along with Robert Doyle, John Dalton and Antoine Lavoisier. He discovered the elements cerium and thorium and also developed the table of atomic weights. Another of Berzelius's students was Friedrich Wöhler, who first synthesized urea in 1828. Thus, one can see that our biochemical ancestors were trained in medicine and chemistry; they more or less invented biochemistry.

Berzelius received his degree with Johann Afzelius (Uppsala), who had trained with Torbern Bergman, considered the first analytical chemist in Sweden.

Bergman received his Ph. D. (Uppsala) working with Bengt Ferrner, an astronomer. I was able to trace his lineage back for at least five more generations (not shown) to learned men mostly in the areas of mathematics and physics from all over Europe including Basel, Switzerland, Leiden, the Netherlands, Jena, Germany and Paris, France. At this time, our own field was little advanced beyond alchemy — or perhaps we should call it "albiochemy."

A few universities dominate in my tree — Vanderbilt, Illinois, Wisconsin, Yale, Uppsala and Würzburg — and my lineage underlines the European roots of the sciences in the United States.

If one considers more details of the 20 individuals on this list (Fig. 1, not including Ferrner or me), it is really remarkable how much they contributed to science in terms of advancing the field we now call biochemistry. Chittenden was one of the founders of the ASBMB (then the American Society of Biological Chemists, or ASBC, which is what it still was when I became a member in 1978) and our first president. Mendel, Rose, Snell and Coon were also presidents of the society. Kossel was a Nobel laureate (1910). Snell, Hart, Coon, Rose, Mendel, Chittenden and Johnson were (are) members of the U.S. National Academy of Sciences.

Important applications in fields including agriculture, nutrition and drug metabolism are part of my lineage. Isaac Newton said, "If I have seen a little further, it is by standing on the shoulders of giants." This applies here and probably to the family trees many of you will find if you ever do this. Another important point to make is that these people were undoubtedly good mentors, or this lineage would not exist. I know from firsthand experience that Broquist and Coon certainly were, and I have tried to emulate them.

This is not just boring history about some old guys. It is evidence that we should all make the most out of our opportunities in science. What we do is important in the scheme of things. Twenty people created a heritage that will last for centuries in terms of the influence they had in science and in training others to do science — science that truly matters in the lives of everyday individuals. We are not just treading water until we can collect our pensions. Individuals and institutions can make a difference in the lives of others. We can be part of a legacy that changes the world.

F. Peter Guengerich (f.guengerich@vanderbilt.edu) is the Tadashi Inagami professor of biochemistry at Vanderbilt University. He is interim editor-in-chief of the Journal of Biological Chemistry, and in 2005, received the ASBMB's William Rose Award.

Academic geneaology resources

The author pulled together his academic family tree with the help from online sources, including:

- The Chemical Genealogy Database
- The University of Illinois at Urbana–Champaign's geneaology resources
- The University of Texas at Austin's academic geneaology of chemistry faculty
- Wikipedia

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- examine how where you are or where you came from influences who you are or who you will become, and
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Added challenge: Given the significance of coordinates to the study of structural biology, we will give special consideration to submissions that artfully connect the dots between molecular structure and personal coordinates.

TRANSITION STATES

While physical location will anchor the "**Coordinates**" series, the "**Transition States**" series will examine instances when scientists made (or decided to make) career changes. Scientists switch gears every day: They move into or out of academia or industry, abandon bench science, become managers and administrators, gain independence and responsibilities, begin and grow their families, start businesses, create or join nonprofits, enter government service and take on a variety of other roles. This series will scrutinize the many feelings, processes and influences associated with such transitions.

We welcome submissions of personal essays, short features, interviews, photos, artwork and poetry that achieve one or more of the following:

- offer a glimpse the period before, during and/or after a career change,
- counsel those considering career changes,
- describe the emotions and thought processes leading up to and resulting from changes,
- acknowledge unexpected outcomes of upheaval,
- reflect on the role of family when things were in flux, and
- take into account logistical and financial considerations of particular importance.

Guidelines: Written work and art must be unpublished, between **300** and **1,000** words and submitted through **asbmbtoday.submittable.com/submit** by **Nov. 30, 2015**. Please include a brief cover letter with the title of your piece, complete contact information, a headshot, and an author bio of no more than **100** words.

The 1,200-pound dance partner

By Alexandra Pantos

Getting a Ph.D. in molecular and cellular biochemistry doesn't leave you with much free time. But Sarah Martin, a newly minted Ph.D. with a policy fellowship at the American Society for Biochemistry and Molecular Biology, found a way to make time between lab hours and piles of research for what she loves most: dressage.

Dressage, which means "training" in French, is sometimes referred to as horse ballet. Horses learn a series of dancelike movements like trotting in place with hoofs high, moving sideways and pirouettes.

"It's considered the highest form of training of the horse," says Martin. "Originally it was cavalry maneuvers for warhorses, so a lot of the things we do are to show the agility and the athleticism of the horse and your ability to communicate with the horse seamlessly."

Martin grew up in Lexington, Kentucky, or, as she calls it, "horse country." She had a horse mobile over her crib as a baby, and as soon as she could sit up, her mother put her on a horse that knew voice commands. She remembers riding him for hours at a time.

But Martin says the riding life was never forced upon her. "I was always pestering my parents to get me (a horse)."

Martin began her riding career as a hunter-jumper but switched to dressage when she grew very tall, eventu-

Sarah Martin and her horse, Garth.

ally reaching a height of six feet and one inch. Being tall is not great for "the kind of person who goes over fences," says Martin. But in dressage, "being tall is useful. Your legs hang down longer on the horse, and you can control them better."

Martin made the switch to dressage at age 14. The change of focus was a relief to her mother, who wasn't happy watching her daughter occasionally fall during increasingly higher jumps.

Martin's horse competes as SRC Parrot Bay, but that isn't the name he was given when he was born. Martin calls him Garth, which is a Nordic name that means "quiet brook" or "meadow." She chose the name because he is half Friesian, which is a Nordic breed, and because he is quiet but attentive. She talks about Garth as one would about a human dance partner. She does her best to make sure his gaits are presented well but says sometimes this gets complicated. "Your 1200-pound dance partner never agrees with what you have to say," she says.

IMAGES COURTESY OF EMILY HUFF

Martin and Garth at his new home in Maryland. Martin blogs about science and dressage at equestrianbiochemist.wordpress.com.

Garth and Martin currently are focused on getting back into shape after taking some time off so Martin could finish up her dissertation. The break gave Garth some much-needed relaxation, as the two had competed through most of Martin's time in graduate school. Among their most recent wins are the American Warmblood Society 2013 second level national championships in both the adult amateur and open categories.

After considering becoming a veterinarian as an undergraduate, Martin did her Ph.D. in biochemistry and molecular biology at the University of Kentucky. "I figured out that I like healthy animals and not sick animals," she says.

When she first started graduate school, she studied nutrition and worked on the urological disease interstitial cystitis. Her Ph.D. research was in prostate cancer chemotherapy, specifically on taxanes, which have been used in the treatment of both prostate and breast cancers.

According to Martin, juggling the demands of dressage and graduate school was a huge challenge. "My horse was really primed. It was a really good time for him to be out on the circuit, and that means training five or six days a week."

Training involved a lot of early mornings. Martin went to the barn and had a lesson or did barn chores and then needed time to clean up and change clothes to ensure that she was lab ready after working with animals. "Graduate students look like a hot mess anyways, so I don't think anyone ever noticed," she laughs.

She made it through with the help of a "wonderful support system," including a trainer who rode Garth three to four days a week and a husband who was also willing to pitch in. Martin has now moved Garth to a farm that is near her office in Maryland, and she and Garth are gearing up to compete again in the fall.

When she accepted the policy fellowship, there was never a doubt that Garth would move with her. "My horse is my soul mate," she says.

Alexandra Pantos (apantos@asbmb.org) is an intern at the ASBMB and a senior biology student at the University of Maryland.

An online course on the art of science communication

By Geoff Hunt

Public speaking is a challenge. Comedian Jerry Seinfeld once observed that most funeral attendees "would rather be in the casket than giving the eulogy." Such discomfort extends to the scientific community, and research has found that scientists often shy away from participating in public outreach and engagement activities because of a lack — or perceived lack of ability to communicate with non-expert audiences (1).

For many scientists, presenting and communicating is a job requirement. But training scientists to perform these tasks receives very little attention. How many scientific talks have you been to that were ruined because the speaker spent the entire presentation reading his or her slides or talked exclusively in jargon?

To help make scientists more effective communicators, the members of the American Society for Biochemistry and Molecular Biology Public Outreach Committee, each of whom has extensive personal experience with communication and public engagement, have developed a course called "The Art of Science Communication." This online course trains you in the art of presenting science to a variety of audiences using nontechnical language. The course walks participants through the who, what, where, why, when and how of science communication.

The online format allows you to take part in class from wherever you are, whenever you are available. Consisting of a weekly set of virtual lectures, readings and other online resources, the course content covers the rationale for effective science communication and provides practical tips and insight into how to construct and then deliver a presentation. Expert mentors guide interactive, live discussions that help ensure you remain engaged and focused. The final product? Your very own polished presentation, ready to be delivered to an audience of your choosing, whether in a K – 12 classroom, in a science café, or at your family's Thanksgiving dinner.

Course presenter Susanna Greer, Director, Clinical Research and Immunology at the American Cancer Society.

That being said, there is no one right way to present. We are not trying to turn everyone who takes this course into a televised science communication superstar like Neil deGrasse Tyson. Our goal is to raise your ability level to the point that you are comfortable with and proficient in communicating science. Beyond that, it will be up to you to determine how you want to apply (and continue to improve) your communication skills.

Many of the concepts and techniques presented during the course, such as how to construct a presentation or the use of proper body language, are effective for settings within and beyond the scientific community. They work in poster presentations and formal seminar talks, in front of university classes and in the midst of public engagement activities that bring science beyond the lab.

If that isn't enough, participants who complete the course will receive free registration for the 2016 ASBMB Annual Meeting, to be held April 2 – 6 in San Diego. You also will receive a certificate from the ASBMB indicating that you have completed the course and demonstrated proficiency in science communication — something handy for the résumé.

Interested? The course will start early October and run through November. We expect that participants will spend three to four hours a week on the course going through the material, engaging in discussions with their peers and mentors, and working on final presentations. Note that there is a $25 charge to take the course, and participation is limited to 25 individuals.

To apply for a place in the course, please visit our website: *www.asbmb.org/outreach.*

See you online!

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1. Ecklund, E.H., *et al.* , *PLoS ONE*. **7**(5), e36240 (2012).

Geoff Hunt (ghunt@asbmb.org) is the ASBMB's outreach coordinator. Follow him on Twitter at twitter.com/thegeoffhunt.

Drawing added to Aspirnauts' toolkits

By Lauren Dockett

It's been 10 years since kidney-disease researcher Billy Hudson, who grew up in rural Arkansas and now directs the Center for Matrix Biology at Vanderbilt University Medical Center, and his wife, Julie Hudson, Vanderbilt's assistant vice chancellor for health affairs, dreamed up the Aspirnaut program.

Established to help rural K – 20 students achieve careers in the STEM fields, the program officially launched in 2007 with a wired school bus that provided middle- and high-school students with laptops and a broadband connection, allowing them to log into science, technology, engineering and math lessons during their long rides to and from school. Then came the weekly beaming of STEM labs into rural American elementary and middle-school classrooms and a summer STEM-related research program mentoring high-school and undergraduate interns from rural and underrepresented backgrounds on the Vanderbilt campus.

This year's summer Aspirnaut interns, who spent six weeks conducting research at Vanderbilt, were introduced to yet another new program called Drawing in Science. Emphasizing the ways in which art can inspire scientific creativity and is also an important tool for translating and summarizing complex scientific ideas, Hudson strongly encouraged his interns to develop drawing skills.

SUSAN URMY, VANDERBILT UNIVERSITY

Summer 2015 Aspirnauts

The Drawing in Science event launched with a visit from international portrait artist Igor Babailov. Forty Aspirnaut interns watched as Babailov — whose commissioned works include portraits of Popes Benedict, Francis, and John Paul, Vladimir Putin, Rudolph Giuliani and Canadian Prime Minister Brian Mulroney — sketched Jeff Balser, dean of Vanderbilt's medical school.

Many former mentees of the Apirnauts program have chosen to remain in the STEM fields and have also been involved with a string of discoveries at Hudson's lab. A mixed-age cohort of 83 Aspirnauts published a report in the Proceedings of the National Academy of Sciences on the evolutionary origin of a chemical bond, and other work by program participants has been featured in Cell and Nature Chemical Biology.

STEVE GREEN, VANDERBILT UNIVERSITY

Portrait artist Igor Babailov sketches Jeff Balser, the dean of Vanderbilt's medical school.

STEVE GREEN, VANDERBILT UNIVERSITY

Aspirnauts Lauren May and Sheila Johnson

Lauren Dockett (ldockett@asbmb.org) is the managing editor of ASBMB Today.

If you build it …

Accreditation, year 2

By Peter J. Kennelly

When the American Society for Biochemistry and Molecular Biology launched an accreditation program for bachelor's degrees in 2013, the underlying goal was to promote excellence in undergraduate education in biochemistry and molecular biology by providing students with the opportunity to earn a nationally recognized credential and faculty with informative, independent assessment data.

From its inception, the success or failure of accreditation has rested on the issue of community buy-in. Would the program be valued as something that served the needs of educators and students? While it had been conceived, designed and implemented by faculty volunteers, we had no way of being certain that our colleagues shared our vision. It is thus extremely gratifying to report that in year two of the program we have witnessed a dramatic growth in both interest and participation in accreditation and its assessment examination.

Growing numbers

In year two, the total number of accredited programs rose from six to 30, while applications from eight additional schools were approved on June 1. The list of accredited programs is diverse. It encompasses public, private, research-intensive, primarily undergraduate, and large and small colleges and universities located in 25 states scattered from Maine to California.

This year, 465 students from 27 accredited programs took the ASBMB's 2015 certification examination. The exam contained 13 questions, plus one pilot question being validated for use in future exams. The questions were arranged by Bloom's taxonomy of learning domains (1). Students who earned scores of "proficient" or "highly proficient" on six of the nine higher Bloom's-level questions and three of the four lower Bloom's-level questions were recognized as ASBMB certified. Those certified students who were proficient or highly proficient on eight or more of the higher Bloom's-level questions were recognized as being certified with distinction.

Of the 465, 194 students — 42 percent in all — exhibited the breadth of knowledge and the depth of critical thinking necessary to qualify for ASBMB certification of their degrees. Of those 194, a total of 62 were recognized as certified with distinction.

Grassroots involvement

One of the distinguishing characteristics of the ASBMB's accreditation program is its grassroots nature. At its heart, this is a community-owned-and-operated program. Every aspect of accreditation — from conception and design to application screening and question development, answer key construction and scoring — is reliant on the time, effort, ideas and community spirit of our volunteers, who are ably assisted by a handful of ASBMB staff members.

The ASBMB is extremely grateful for the support of our many volunteers, and it is with pride and pleasure that we acknowledge the contributions of these ASBMB education fellows by listing their names on the following page.

Looking ahead

Accreditation is an evolving program that we are working actively to improve. The last two years have taught us much. Additional volunteers have enriched the program with new ideas and perspectives. As we look ahead to 2016, we have set our sights on the following goals:

- Reviewing and improving the program-accreditation criteria.
- Enhancing the clarity of the program application process.
- Constructing and validating new questions and rubrics for future assessment examinations.
- Developing means for online delivery of future assessment examinations.
- Streamlining the scoring process.

Join us

The volunteers who participate in the ASBMB's accreditation program not only are vital to its success but also are stakeholders who help shape the program as we move forward. To get involved in constructing future questions, scoring student responses and so forth, contact Andrew Mcintyre at amacintyre@asbmb.org.

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1. Bloom, B.S. Ed. Engelhart, M.D., Furst, E.J., Hill, W.H., Krathwohl, D.R., *Taxonomy of Educational Objectives, Handbook I: The Cognitive Domain.* New York: David McKay Co Inc. (1956).

Peter J. Kennelly (pjkennel@vt.edu) is a professor of biochemistry at Virginia Tech.

American Society for Biochemistry and Molecular Biology education fellows

Benjamin Alper
Sacred Heart University

Ellen Anderson
University of St. Joseph

Cindy Arrigo
New Jersey City University

Cheryl Bailey
Mount Mary University

Suzanne Barbour
National Science Foundation

Ana Maria Barral
Wabash College

J. Ellis Bell
University of Richmond

Jessica Bell
Hardin-Simmons University

Michael Borland
Bloomsburg University of Pennsylvania

Cory Brooks
California State University, Fresno

Benjamin Caldwell
Missouri Western State University

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Michael Carastro., Jr.
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University of Kentucky

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Edward Ferroni
Benedictine University

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Northeastern University

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Scott Gabriel
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Veronica Godoy-Carter
Northeastern University

Allison Goldberg
Yale University School of Medicine

Joy Goto
California State University, Fresno

David Gross
University of Massachusetts Amherst

Ephraim Gwebu
Elizabeth City State University

Jennifer Hennigan
Holland School of Sciences & Mathematics

Weiping Jiang
Biolegend

Sara Johnson
Purdue University

Carol Jones
Central Connecticut State University

Kelley Keenan
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Peter Kennelly
Virginia Tech

Anne Kruchten
Linfield College

Jim Lawrence
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Western Kentucky University

John Richardson
Austin *College*

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Wellesley College

Ann Wright
Canisius College

Janet Xiao
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Meet Cecilia Martinez

By Andrew Macintyre

Tell us about your current career position.

I am an assistant professor at Michigan State University in the Department of Microbiology and Molecular Genetics. My lab group focuses on studying how one-carbon compounds, such as methane and methanol, are used by bacteria as a sole source of carbon and energy (methylotrophy). We are very excited because by studying the biochemistry of this specialized but fundamental type of metabolism, we are identifying the role of uncharacterized cofactors such as lanthanides, commonly known as rare-earth elements. Our long-term goal is to solve fundamental questions of how carbon distribution is regulated, enabling us to engineer bacteria for the production of value-added compounds, such as plastics and biofuels.

What are the key experiences and decisions you made that have helped you reach your current position?

I think the most fundamental decision for my current position was to come to the USA to get my Ph.D. in microbiology. I was an undergraduate student at the National University of Mexico majoring in chemistry, and I already had an offer to work in a lab in the biochemistry department for my graduate studies. Even though I loved my undergraduate project and the program in Mexico, I always wondered how research was done in developed countries such as the United States. I decided to leave my

family and friends and joined the microbiology program at the University of Wisconsin–Madison. It was a decision that allowed me to expand my training and learn from the very best. This is a place where working hard is highly rewarded, and that is refreshing and highly motivating.

How did you first become interested in science?

I liked science since I was a child. My mom and I would talk about immunology while cooking dinner together when I was young, and I remember thinking that the human body was the most amazing and enigmatic thing to study. I decided that I wanted to become a principal investigator when, in junior high school, I spent a summer doing research with Edelmira Linares in the biology department at the National Autonomous University of Mexico. I was involved in a project studying the medicinal plant Arnica. Linares' passion for research was so inspiring. Her mentoring style made her so approachable, and it was an experience that allowed me to be engaged in the project and feel part of a team. After this experience, I knew that I wanted to be like her – that I wanted to motivate young students to do research while encouraging them to work as a team.

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

Yes, for sure. One major project I had when I was a graduate student was to characterize an S-adenosylmethionine (known as SAM for short) radical enzyme named ThiH, and I was scooped by a competing lab. I felt defeated. There was always the question, "Did I not work hard enough? Am I not skilled enough? Am I not smart enough?" My mentor, Diana Downs, motivated me to continue to work hard and not to get discouraged. In the end, she said, I was getting amazing training and the skills necessary to succeed. She was right. Her lab does such elegant genetic work for microbial metabolic studies. By analyzing the genetic data of several graduate students of her lab, we hypothesized that ThiC, then a poorly understood enzyme in thiamine biosynthesis, could be a SAM radical enzyme even when no canonical motif was evident. I used the same knowledge and training I had acquired with ThiH and was able to purify the enzyme in an active form, something that researchers had tried to do for

more than 50 years. We were able to expand this family of enzymes and provide the framework to characterize one of the most enigmatic reactions in biology.

What advice would you give to young people from under-represented backgrounds who want to pursue a career in science similar to yours?

Never to get discouraged and to work hard. Sadly, it is inevitable that a peer will eventually make comments that will devalue your work, insinuating that an award, fellowship or job was granted because you are a minority. Those comments are so destructive. In the past, they made me doubt myself, and they affected my self-esteem. However, that is not the case anymore. If anybody says something like that now, I choose not to waste my time on such a comment, and instead I move on. I keep working hard and pay attention to what I love to do: research.

What are your hobbies?

Ha! Unfortunately, I do not have hobbies at this time. I have two little kids (ages 2 and 6) at home, so I try to spend as much of my free time as possible with them and my husband. We play so much together. It is so refreshing to act like a kid in my free time. When they become more independent, I would love to go back to training for triathlons, which was my hobby when I did not have kids. Hopefully very soon.

What was the last book you read?

The last book I read was by Mario Benedetti titled "La Tregua" or, in English, "The Truce." It was a reminder of how life should not be monotonous and meaningless.

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

Yes, Frida Kahlo is one of them, and it is not only her art that inspires me. It is her path. I think she is a Mexican woman who broke so many barriers, socially and professionally, and she did so even when she was very sick. She inspires me to work for my goals and not to find excuses. Everything is possible when you work for it.

What is it that keeps you working hard and studying science every day?

The excitement for potential discovery and service. It is a privilege to be paid to test ideas. It is also a privilege and great responsibility to have the opportunity to teach young minds what others have discovered and how they have discovered it. Finally, this is the best time of my life. I finally get to run my own team, and they are young and motivated to expand our understanding of methylotrophy. This is the fun part!

Andrew Macintyre (amacintyre@asbmb.org) is an education and professional development manager at the ASBMB.

STUDENT CHAPTERS | A PROGRAM DESIGNED FOR UNDERGRADUATE BMB STUDENTS AND FACULTY

MEMBER BENEFITS

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- Members eligible for the National Biochemistry and Molecular Biology Honor Society
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- Networking opportunities for students and faculty from other institutions

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To learn more, visit: www.asbmb.org/studentchapters

New ASBMB scholarship recognizes students' commitment to diversity

Meet the 2015 recipients of the Distinguished Undergraduate Scholarship

By Andrew Macintyre

The rich variety of perspectives and experiences that make up a diverse scientific community tend to enhance innovation. Indeed, we can all learn from those with different skill sets and different cultural, educational and social backgrounds. In recognition of the importance of diversity to the scientific and biomedical workforce, the American Society for Biochemistry and Molecular Biology's Minority Affairs Committee recently launched a new diversity-in-science scholarship. The Distinguished Undergraduate Scholarship was first announced at the 2015 annual meeting in Boston and provides financial support to students who actively promote diversity in biochemistry or molecular biology.

All ASBMB undergraduate members are eligible to apply for the scholarship. Applicants have to explain how they help to build diversity on campus or in the wider scientific community, describe challenges they have overcome in pursuit of their education and outline how the scholarship could help them achieve their career goals.

A panel drawn from both the MAC and the Student Chapters' steering committee reviewed applications for the 2015 scholarship. The panel was led by MAC members Lana Saleh and Stacey Slijepcevic, who together spearheaded the development of the award.

The enthusiasm and caliber of the scholarship applicants were impressive, but most striking was the range of activities undertaken to promote diversity. Applicants organized a science-exposure program for inner-city children, tutored first-generation college students in science, technology, engineering and math, supported lesbian, gay, bisexual, and transgender and disabled students on campus, organized women-in-science networking events, ran a Hispanic scholarship fund, mentored biochemistry students from underrepresented minorities, and volunteered at head start programs for economically disadvantaged children. The applicants' commitments to fostering diversity were even more notable given the challenges many of them faced pursuing their own educations.

Five Distinguished Undergraduate Scholarships were awarded for the academic year 2015 – 2016, with each recipient receiving $2,000 toward the cost of tuition.

The 2015 scholarship recipients

NEWSAD

Shelby Newsad (Ohio State University)

Newsad and a fellow student from Ohio State developed Beginner's Access to Science Education to engage elementary-age children in science. "BASE will start to decrease the education disparities in inner-city Columbus schools and ignite in the students a natural curiosity and passion for the sciences," says Newsad. BASE was piloted in two schools this summer by a diverse group of Ohio State students and reached more than 100 children. The program will expand to additional schools in the fall. After graduation, Newsad plans to pursue a master's in bioinformatics and a Ph.D. in biochemistry. Describing her long-term goal, she says: "I hope to eventually create my own research-and-development company focusing on the synthesis of new antibiotics."

MCLEAN

Craig McLean (University of Arkansas)

In the spring of 2012, McLean worked with faculty members at the University of Arkansas to found a Hispanic Scholarship Fund scholar chapter. Outlining his work with HSF, Mclean says, "I was responsible for the creation of over 40 on-campus and off-campus workshops designed to promote the education development of students in the area and demystify college to parents who never had the opportunity to attend." After he graduates, McLean intends to pursue a Ph.D. while developing new techniques to measure accurately

metabolites in marine environments and eventually run his own research group.


BRACEY

Syrena Bracey (University of Maryland, Baltimore County)

Through her participation in the Meyerhoff Scholars Program, Bracey performs science outreach with school children in Baltimore County. "We work to create programs for these students, show them everything cool about science to keep them interested and help them excel academically," she says. Bracey wants to pursue "an M.D. /Ph.D. degree in an area between chemical biology and clinical pharmacology, which will later be applied to a career in research."


CHEUNG

Matthew Cheung (St. Louis University)

Over the past two years, Cheung has acted as a peer mentor to more than 100 students as part of the Health Sciences Learning Community at St. Louis University, and shortly he will be returning to the program as a resident adviser. After graduation, Cheung plans to pursue an M.D. /Ph.D. and become a physician-scientist. This was not the path that he initially envisioned for himself. "I originally wanted to become a physician and only began working in a lab as a way of ruling out the idea of research," says Cheung. "Little did I know that this is where I would find my interest: in basic science and clinical research."

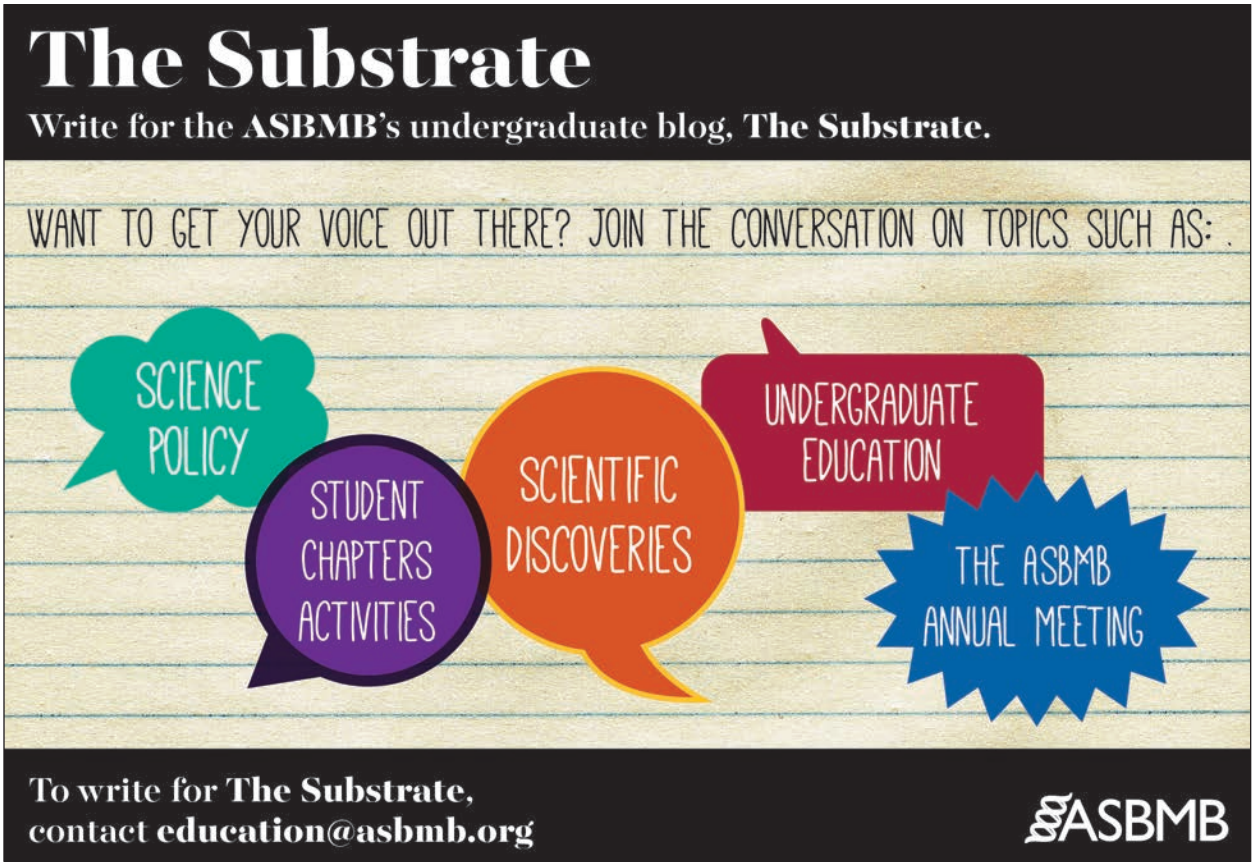

REYES

Jose Reyes (Texas State University)

In his time at Texas State, Reyes has volunteered with several programs to promote science careers to the Hispanic community. He has visited schools in predominantly Hispanic neighborhoods to explain how research works and community colleges to talk to underrepresented students about continuing their education. Outlining his future ambitions, Reyes says, "I plan to attend a United States medical school and continue taking part in research while pursuing a Doctor of Medicine degree. After receiving this degree and completing my residency with a focus in internal medicine, I hope to practice medicine while simultaneously performing research."

Congratulations to all the 2015 scholarship recipients! The MAC will invite applications for academic year 2016 – 2017 scholarships in the spring of 2016. For more information, visit www.asbmb.org/minorityaffairs/undergraduatescholarship/.

Andrew Macintyre (amacintyre@asbmb.org) is an education and professional development manager at the ASBMB.



2017 ASBMB Special Symposia

Call for Proposals

Partner with the American Society for Biochemistry and Molecular Biology to bring your community together! The ASBMB Special Symposia Series provides you, as a specialized researcher, a unique opportunity to present cutting-edge science in an intimate setting.

Proposals due: Dec. 1, 2015

How We're Different

Format: Majority of talks selected from abstracts, invited speakers, 2–4 days in length

Attendees: 75–200 attendees, including investigators, industry professionals, graduate students and postdoctoral fellows

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Funding: ASBMB provides initial funding as well as complete meeting management

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Learn more about the Special Symposia Series and proposal submission guidelines at
www.asbmb.org/specialsymposia

Attention
department chairs & program directors

The ASBMB is conducting its annual survey to learn about YOUR biochemistry and molecular biology graduates. If you did not receive an e-mail about this survey but would like to participate, please contact education@asbmb.org

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Upcoming ASBMB events and deadlines

SEPT

Sept. 10: Oral abstract deadline for ASBMB Special Symposium Kinases and Pseudokinases: Spines, Scaffolds and Molecular Switches, San Diego
Sept. 17 – 20: ASBMB Special Symposium: Membrane-Anchored Serine Proteases, Potomac, Md.
Sept. 18 – 19: ASBMB Science Communication and Outreach Career Symposium, San Antonio, Texas
Sept. 22: Early registration deadline for ASBMB Special Symposium Kinases and Pseudokinases: Spines, Scaffolds and Molecular Switches, San Diego
Sept. 27 – 30: 14th Human Proteome Organization World Congress (HUPO 2015), Vancouver, Canada, Molecular & Cellular Proteomics booth #413

OCT

Oct. 14: Poster abstract deadline for ASBMB Special Symposium Kinases and Pseudokinases: Spines, Scaffolds and Molecular Switches, San Diego
Oct. 27: Registration deadline for ASBMB Special Symposium Kinases and Pseudokinases: Spines, Scaffolds and Molecular Switches, San Diego
Oct. 29 – 31: Society for Advancement of Hispanics/Chicanos and Native Americans in Science (SACNAS) National Conference, Washington, D.C.

NOV

Nov. 5: Abstract submission deadline for ASBMB 2016 Annual Meeting, San Diego
Nov. 12: Travel award application deadline for the 2016 Annual Meeting, San Diego
Nov. 11 – 14: Annual Biomedical Research Conference for Minority Students (ABRCMS), Booth #900, Seattle

DEC

Dec. 1: Deadline for 2017 Special Symposia proposals
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