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ASBMB TODAY

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

DEFYING STEREOTYPES

The scoop on **Ben & Jerry's** co-founder **Jerry Greenfield**

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Learn how Jerry Greenfield applied his scientific training when he and his friend built the ice cream empire that is Ben & Jerry's.

ASBMB TODAY
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Funding decisions: the HHMI method

By Steven McKnight

In this essay and in a subsequent essay, I will describe and compare how two organizations carry out the review processes dictating how they spend their funds. I first will cover the Howard Hughes Medical Institute, a science philanthropy that provides a bit under $1 billion annually in support of biomedical research and science education. Next month, I will turn to the National Institutes of Health, an agency of the U.S. federal government that distributes between $15 billion and $20 billion in annual funding of extramural biomedical research. My hope is that exploring how these two systems work — and studying their distinctive features — will inspire stakeholders to think seriously about how the NIH peer-review process might be improved.

The HHMI supports a variety of research and education programs, including work done at its own Janelia Research Campus in Ashburn, Va. Among its various programs, HHMI spends the vast majority of its funds in support of 324 individual investigators who perform research at more than 70 institutions in the U.S.

How are HHMI investigators first tapped? The organization periodically opens a competition for the appointment of new HHMI investigators. These competitions typically are restricted to emerging scientists with five to 15 years of independent research experience and are judged in two phases. The first phase involves reviewers from HHMI's scientific review board, its medical advisory board, ad hoc reviewers and existing HHMI investigators. Finalists emerging from the initial phase of review are then interviewed in person at the HHMI by scientific review board members, medical advisory board members and ad hoc reviewers.

HHMI investigators have terms of five years. Roughly one year prior to the end of an appointment term, each HHMI investigator must provide evidence of progress along with a brief plan for future research efforts. Reappointment candidates then present their science in person to the scientific review board, typically composed of 25 to 30 scientists. After reviewing the written materials and the oral presentation of a reappointment candidate, the scientific review board offers its recommendation as to whether or not the investigator should be reappointed. Based upon the review panel's recommendations, the administrative leadership of the HHMI then makes the final decision.

Having served on the HHMI scientific review board, I am familiar with the review process for both new appointments and reappointments. I highlight below three unique aspects of the review process.

First, more than anything, the HHMI endeavors to select and retain "individuals who have the potential to make significant contributions to science" (1). New investigators are chosen primarily on the basis of what they have accomplished early in their careers as independent scientists. For existing investigators, past performance during the four-year period preceding the review itself is the dominant criterion for reappointment.

Yes, the HHMI does consider the proposed research plans. But, more than anything, it weighs its appointment decisions upon what the scientists have accomplished during their initial period of independence and its reappointment decisions primarily upon discoveries made by the candidates during the appointment window immediately preceding the review.

The second distinctive feature that I have observed is that the HHMI review process obligatorily involves face-to-face interaction between candidates and reviewers. Although only three to four reviewers provide written assessments of each reappointment candidate, all of the 25 to 30 reviewers get to hear directly from the investigator.

The final distinctive feature concerns the qualifications of the individual reviewers. With respect to investigator reappointment, the HHMI uses its scientific review board to conduct the initial review. Its medical advisory board helps to ensure that the scientific review board's recommendations are fair and accurate.

The scientific review board consists of 37 biomedical researchers, and the medical advisory board has an additional 13 scientists. Among these 50 review participants, 37 are members of the National Academy of Sciences. It is no accident that 74 percent are academy members. Whether useful or appropriate or not, the HHMI clearly wants its most important decisions, investigator appointment or reappointment, to be guided by the input of accomplished scientists.

I readily admit that past scientific accomplishment does not directly equate to effective capacity to review. I do, however, believe that a reasonable correlation exists between the two. This belief is open for debate.

Why is it that the HHMI is able to induce accomplished scientists to participate in investigator reviews? I offer three explanations. First, the HHMI provides substantial compensation to its reviewers. Second, the review teams are composed of interesting and accomplished scientists, making it enjoyable for individual reviewers to participate. Third, the HHMI appointment or reappointment candidates are themselves of a relatively high level of accomplishment, so reviewers get to review exciting and inventive science.

I close by offering evidence that the HHMI supports unusually talented biomedical researchers. Seventeen active HHMI investigators, six HHMI alumni and one scientist from the Janelia Farm campus have won the Nobel prize. In addition, 23 current or former HHMI investigators have won the Lasker award in basic medical research or clinical medical research.

REFERENCE

1. www.hhmi.org/programs/biomedical-research/investigator-program

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Upcoming ASBMB events and deadlines

MARCH

Mar. 15: Accreditation deadline

Mar. 28 – Apr. 1: ASBMB annual meeting

Who should be funding biomedical research?

By Chris Pickett and Benjamin Corb

The federal government's investment in research through the National Institutes of Health, the National Science Foundation and other agencies is indispensible, but political maneuvering in Washington, D.C., has made for a challenging fiscal environment. The result has been a decade of nearly stagnant funding and decreased chances of successfully funding a research project.

Nonfederal funding mechanisms for research, such as philanthropic investments and crowdsourced funding, have increased in popularity, but are they right for you and your lab? Do they provide a reliable funding stream? A discussion prompted by those questions will be the basis of the Public Affairs Advisory Committee's session at the American Society for Biochemistry and Molecular Biology annual meeting later this month in Boston.

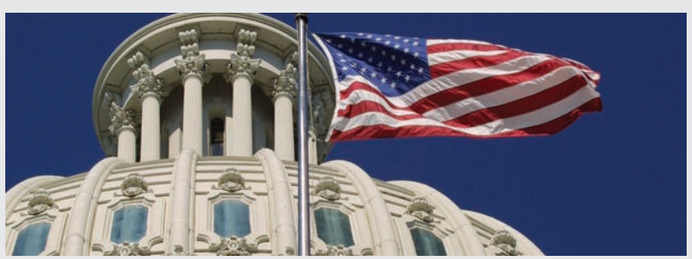
Venkatesh Narayanamurti of Harvard University will be one of the panelists. In addition to many other accolades, Narayanamurti is a member of the American Academy of Arts and Sciences, and he played a critical role in the academy's 2014 report "Restoring the foundation: the vital role of research in preserving the American dream." The report offers recommendations to establish long-term sustainability in the U.S. research enterprise and ensure the federal government remains the foundational investor in scientific research. An engineer by training, Narayanamurti has made many significant contributions to the fields of phonon optics and semiconductor nanostructures.

When federal funds aren't available, some scientists turn to the public for funding. Jai Ranganathan, another panelist, is executive director of #SciFund Challenge, which helps researchers crowdsource funding. Seeking to improve outreach, #SciFund Challenge trains scientists to communicate directly with the public about the value of the research they conduct. Furthermore, the group trains scientists to use these newfound outreach skills to carry out crowdfunding campaigns to fund their research. Ranganathan is a conservation biologist working at the National Center for Ecological Analysis and Synthesis.

Claire Pomeroy, president of the Albert and Mary Lasker Foundation, also will be a panelist. The Lasker Foundation supports biomedical research through recognition of excellent science as well as outstanding advocacy and public education efforts. In addition to her work at the Lasker Foundation, Pomeroy is a clinician with a lab researching infectious disease. She is also a staunch advocate for patients with HIV/AIDS and has been active in a variety of healthcare policy issues.

These panelists represent just some of the possible funding sources available to scientists today, and we hope you will join the conversation. The session — titled "Who should be funding biomedical research?" — will be held at 12:30 p.m. Sunday, March 29, in room 253A of the Boston Convention and Exhibition Center.


Chris Pickett (cpickett@asbmb.org) is a policy analyst at ASBMB. Benjamin Corb (bcorb@asbmb.org) is director of public affairs at ASBMB.



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Haltiwanger to join the University of Georgia

HALTIWANGER

Robert Haltiwanger, who leads the biochemistry and cell biology department at Stony Brook University, will join the faculty of the University of Georgia as its newest Georgia Research Alliance eminent scholar. Renowned for his work on glycobiology, Haltiwanger this fall will become a member of the Complex Carbohydrate Research Center at UGA, where he will direct various studies aimed at understanding complex human diseases, including cancer, congenital heart disease and developmental disorders. Haltiwanger and his team were the first to develop small-molecule inhibitors of O-GlcNAcase that subsequently led to the development of Alzheimer's drug candidates. Over the years, his research on glycoproteins has been supported by over $10 million in funding from the National Institutes of Health, the American Cancer Society and the Mizutani Foundation for Glycoscience. Haltiwanger is editor of the journal Gycobiology.

Matthews wins Carl Brändén award

MATTHEWS

The Protein Society named C. Robert Matthews the winner of its Carl Brändén award in recognition of his outstanding contributions to protein science. Matthews, chairman of the University of Massachusetts Medical School's biochemistry department, has spearheaded important advancements in the development of methods to determine protein folding, including the chevron plot, as well as site-directed mutagenesis. His research involving kinetics, energetics and biochemistry has provided seminal insights into the mechanisms of protein structure and function. Matthews is one of seven leaders of the international protein-science community who have been honored with the Carl Brändén award. He will receive his in July in Barcelona. Matthews served as president of the Protein Society between 2003 and 2005, co-founded the Protein Folding Consortium and has served on the editorial boards of numerous journals.

IN MEMORIAM: Jason Wolfe

WOLFE

Jason Wolfe, professor emeritus at Wesleyan University, died Dec. 23. He was 73. Wolfe earned his bachelor's from Rutgers University and his Ph.D. from the University of California, Berkeley. He then completed postdoctoral fellowships at Kings College in London and Johns Hopkins University in Baltimore. He then joined the faculty of Wesleyan, where he taught cell biology, human biology, biology of aging and the elderly, and structural biology for 39 years. Wolfe carried out research into the regulation of reproduction and aging. He is credited with leading the successful effort to win Wesleyan's first Howard Hughes Medical Institute Grant for Undergraduate Life Science Education, which supports undergraduate research.

IN MEMORIAM: Robert C. Nordlie

NORDLIE

Robert C. Nordlie, a scientist who was internationally renowned for his research on glucose-6-phosphatase and blood glucose homeostasis, died Jan. 8. Originally from New London, Minn., Nordlie earned his master's and doctoral degrees at the University of North Dakota's biochemistry department, which he ultimately chaired between 1983 and 2000. His scientific career, spanning almost 45 years, focused on gluconeogenic enzymology. Nordlie served on the editorial boards of Biochimica et Biophysica Acta and the Journal of Biological Chemistry, and he was the recipient of many prestigious awards, including the Thomas J. Clifford Award for Excellence in Research, the Burlington Northern Faculty Scholar Award and the Edgar Dale Award. Upon Nordlie's retirement, the university established the Robert C. Nordlie Endowment in Biochemistry and Molecular Biology, and the endowment continues to serve as an ongoing recognition of Nordlie's success and contributions to UND.

IN MEMORIAM: Lester J. Reed

Lester J. Reed, professor emeritus at the University of Texas at Austin, died Jan. 14. A native of New Orleans, Reed showed an early passion for chemistry as a child. His scientific inquiry led him to pursue a B.S from Tulane University and a Ph.D. in organic chemistry — which he earned at age 21 — at the University of Illinois, Urbana–Champaign. After completing a postdoctoral fellowship under Nobel laureate Vincent Du Vigneaud at Cornell University, Reed joined the UT–Austin chemistry department, where he conducted groundbreaking studies on the isolation of lipoic acids and the characterization of multienzyme complexes. Reed won the American Chemical Society Eli Lilly & Co. Award in Biological Chemistry in 1958 and the American Society for Biochemistry and Molecular Biology Merck Award in 1994.

Written by Aditi Iyengar

Breaking up the bone breakdown

By Maggie Kuo

Although no cure exists for osteoporosis, researchers are working to outline the pathways behind the bone-deterioration process. A study recently published in the **Journal of Biological Chemistry** describes a new pathway involved in bone breakdown, offering novel targets for pharmaceutical interventions against osteoporosis.

Bone remodeling involves two cell types: osteoclasts that break down existing bone and osteoblasts that form new bone. Too many osteoclasts result in bone breakdown exceeding bone formation, weakening the bone structure. Osteoclastogenesis, the development of osteoclasts from their precursor cells, hematopoietic stem cells, is regulated by receptor activator of nuclear factor κB ligand, or RANKL. RANKL binds to its corresponding receptor and begins the differentiation process. The signaling pathways initiated by RANKL, however, are not well understood.

This study adds more details to the signaling pathways that underlie osteoclastogenesis.

The research team lead by Byung-Soo Youn identified two novel proteins, progranulin, or PGRN, and PGRN-induced receptor-like protein during osteoclastogenesis, or PIRO, that are regulated by RANKL and are vital for osteoclast development. This study was a collaborative effort between Wonkwang University in Korea and OsteoNeuroGen, of which Youn is also the chief executive officer. Exposure of bone marrow cells to PGRN and RANKL resulted in dramatic formation of osteoclasts. Endogenous PGRN levels also increased with exposure time to RANKL. Furthermore, suppressing PGRN production reduced osteoclast formation. Together, these data support a role for PGRN in osteoclast differentiation and as a downstream target of RANKL.

The researchers next investigated the downstream targets of PGRN and discovered an uncharacterized gene whose expression increased 20-fold in the presence of PGRN. The researchers named the protein PGRN-induced receptor-like protein during osteoclastogenesis, or PIRO for short. Suppressing PGRN expression reduced PIRO expression. Moreover, when the bone-marrow cells were stimulated with RANKL, PGRN expression was highest at two days, and PIRO expression was highest at three days, suggesting sequential activation. These data reinforce the idea that PIRO is a downstream target of PGRN. Suppressing PIRO expression also markedly decreased the formation of osteoclasts, further supporting that PIRO is required for RANKL-induced osteoclast formation.

This study adds more details to the signaling pathways that underlie osteoclastogenesis. The findings support that after RANKL binds to its receptor, transcription of PGRN is initiated, and PGRN level increases. PGRN then triggers a second wave of signaling that leads to production of PIRO and ultimately results in the formation of osteoclasts. This study offers PGRN/PIRO as a potential therapeutic target for treating osteoporosis.

Maggie Kuo was an intern at ASBMB Today when she wrote this story. Today she is a writer at the American Physiological Society. She earned her Ph.D. in biomedical engineering at Johns Hopkins University.

Thematic minireview series on radical SAM enzymes

By David B. Iaea

S-adenosyl-L-methionine, or SAM, is one of the most common enzyme cofactors and serves as a ubiquitous methyl and sulfur donor for a variety of biological and chemical processes, including macromolecule methylation and biosynthesis of organic molecules. One enzyme group that uses SAM is the radical SAM enzyme family, which is only partially understood and characterized. While the radical SAM enzyme family originally was thought to be relatively small, it is now known to be quite large and highly prevalent. **The Journal of Biological Chemistry** recently published a thematic minireview series coordinated by associate editor Ruma Banerjee at the University of Michigan, Ann Arbor, featuring six short review articles that describe the diversity of chemical reactions catalyzed by these enzymes and demonstrate their shared structural and mechanistic themes.

Members of the radical SAM enzyme family use SAM and an iron-sulfur (4Fe-4S) cluster to catalyze a wide array of chemical reactions. These enzymes share structural and mechanistic motifs despite their functional diversity.

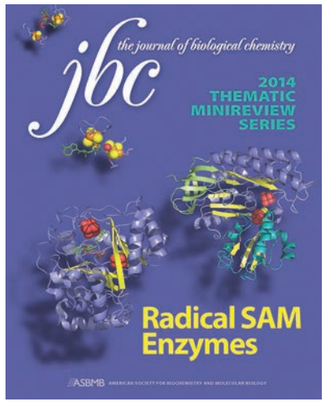
In the first minireview, Catherine L. Drenann and coworkers at the Massachusetts Institute of Technology describe the SPASM and Twitch domains in radical SAM enzymes. In addition to a core CX3CX2C motif required for interaction with a (4Fe-4S) cluster, the SPASM and Twitch domains in several radical SAM enzymes form extensions that can interact with an additional (4Fe-4S) cluster. These extensions provide a platform to facilitate functional and substrate diversification.

While the structures of the SPASM and Twitch domains could provide mechanistic insight into other radical SAM enzymes, several complex chemical mechanisms need to be elucidated. In the second minireview, Joseph Jarret of the University of Hawaii at Manoa discusses sulfur insertion chemistry required for a variety of biological cofactors and macromolecules. Mechanistically, radical SAM enzymes generate a highly reactive radical to introduce functional groups into normally unreactive positions containing carbon or phosphorus.

Continuing with elucidating the diverse and complex chemical reactions of radical SAM enzymes, Tadhg P. Begley of Texas A&M University and collaborators describe SAM enzymes' roles in the synthesis of several biologically active cofactors, including the iron cofactor heme involved in oxygen transport in red blood cells. The authors describe the active site of radical SAM enzymes as a unique, protected environment that allows the generated radical to undergo complex and unprecedented organic chemical reactions.

Not surprisingly, generation of unique metal-bearing cofactors requires a unique enzyme family. In the fourth minireview, Joan B. Broderick and colleagues at Montana State University describe the role of SAM enzymes in the generation of three unique metal cofactors. They are unusual in that they coordinate with unusual nonprotein ligands.

In the fifth minireview, Squire Booker and coworkers at the Pennsylvania State University cover methylation reactions mediated by radical SAM enzymes. While methylation of relatively unreactive carbon or phosphorus atoms in a variety of biomolecules is a common function of SAM enzymes, the mechanisms of methyl transfer for these reactions are diverse. The authors discuss the classification of radical SAM methyltransferase into four groups based on the components involved in the transfer reaction.



In the final minireview, Linlin Yang and Lei Li at Indiana University–Purdue University Indianapolis discuss the role of bacterial spore photoproduct lyase, a radical SAM enzyme, in ultraviolet-induced DNA damage repair. While the first several steps in DNA damage repair mediated by SPL have been elucidated, several questions remain as to the mechanism of the remainder of the catalytic cycle.

While the thematic minireviews provide multiple perspectives on our current knowledge of the enzyme superfamily, it is clear that we have only scratched the surface of these complex enzymes.

David B. Iaea (dai2004@med.cornell.edu) is a graduate student in the Tri-Institutional Program in Chemical Biology at Weill Cornell Medical College.

See algae run

New evidence support that, during coral bleaching, algae are not getting kicked out but leaving on their own

By Maggie Kuo

Corals do not handle change well: They turn ghostly white at a slight shift in water conditions because the algae residing in their cells, the source of their color, disappear. Although this phenomenon, coral bleaching, is well-documented and unfortunately occurring more often now, scientists are still not clear why the algae disappear. An international team of researchers recently reported in **Molecular & Cellular Proteomics** that the algae may run their own exit strategy when stressful conditions set in.

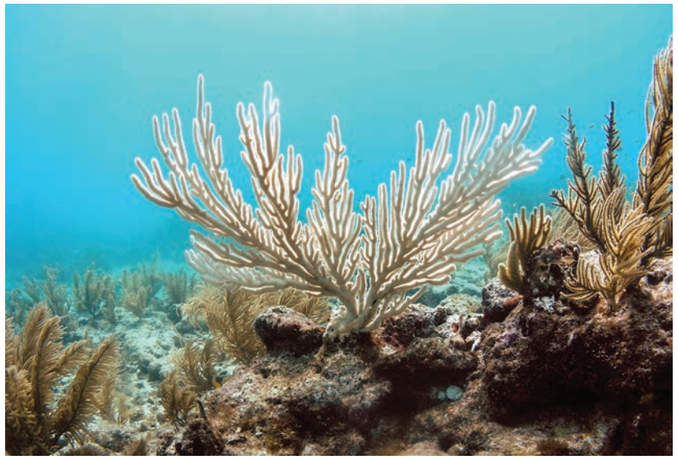


IMAGE COURTESY OF KELSEY ROBERTS, U.S. GEOLOGICAL SURVEY, A WIKIMEDIA COMMONS USER

A colony of the soft coral known as the "bent sea rod" stands bleached on a reef off of Islamorada.

A coral colony provides a protective environment for algae by allowing the algae to live in membrane-enclosed bubbles, or vesicles, inside its cells. In return for a home, the algae convert the coral's metabolic waste into oxygen and nutrients that the coral uses to sustain itself. Changes in the environmental conditions, like water temperature or light exposure, break this relationship and cause the algae to disappear. The coral is left bare, and if the algae are not re-established, the coral colony eventually dies.

Scientists have several theories on why the algae disappear. Some believe that the coral cells are breaking off or dying. Others argue that the effects are on the algae themselves, that the algae are being destroyed or getting thrown out by the coral cells. Paul F. Long, who led the team that authored the recent MCP paper, supports the idea that the algae are leaving the coral but that they are leaving on their own accord.

For the contents of a vesicle to be released out of the cell, the membrane of the vesicle has to merge with the cell's membrane. Membrane fusing involves soluble N-ethylmaleimide-sensitive factor activating protein receptor, or SNARE, proteins. SNARE proteins on the vesicle's membrane, v-SNAREs, latch onto SNARE proteins on the cell's membrane, t-SNAREs, bridging the two membranes together and allowing them to become one. During this exocytosis process, the vesicle's interior becomes exposed to the outside, and the vesicle's contents are flipped outwards.

An earlier study by Long's group found SNARE proteins in algae-harboring coral samples. Other studies had shown that intracellular microbes can mediate their own entry into and exit from host cells by encoding their own SNARE proteins. Long's team proposed that in a similar fashion, algae could have their own SNARE proteins so that they can enter and leave the coral at will. In this new study, Long and his team sought to determine if changes in temperature and light conditions altered the expression of the coral's and algae's exocytosis proteins.

The group collected corals from the Great Barrier Reef and, in tanks on a research ship, subjected their samples to temperature and light conditions that cause coral bleaching in nature: high light exposure in normal water temperature, high light exposure in high water temperature and low light exposure in high water temperature. The researchers then used proteomics analyses to measure the changes in protein expression under each condition. They took advantage of having both the coral's and algae's gene sequences, which only became available recently, to distinguish which proteins were the algae's and which were the coral's.

All three conditions resulted in bleaching of the coral samples and reduced photosynthetic activity of the algae, confirming that these treatments did stress the coral. The investigators observed a high level of t-SNARE and a low level of v-SNARE proteins in the coral, which suggests that the coral cells have the ability to exocytose their constituents. The investigators also saw no evidence of t-SNARE proteins in the algae, as they had expected, although they were surprised that no v-SNARE proteins were detected either.

Based on these data, the researchers propose that the algae express their own v-SNARE proteins when they first sense changes in their environment, initiating their mass flight out of the coral. Those algae that remain in the coral, the ones that ended up in the coral samples, would not express the v-SNARE proteins, because they are the ones that stayed.

The investigators write that the data support their notion that algae taking flight, not algae being destroyed or the coral breaking apart, causes coral bleaching. Moreover, they continue, the study provides more evidence that algae can control their comings and goings. The researchers intend to investigate next how this timing unfolds to, as they put it, better "predict the impact of environmental change on the future resilience of tropical coral reef ecosystems."

Maggie Kuo was an intern at ASBMB Today when she wrote this story. Today she is a writer at the American Physiological Society. She earned her Ph.D. in biomedical engineering at Johns Hopkins University.

ASBMB journals to request researcher ID numbers

By Karen Schools Colson

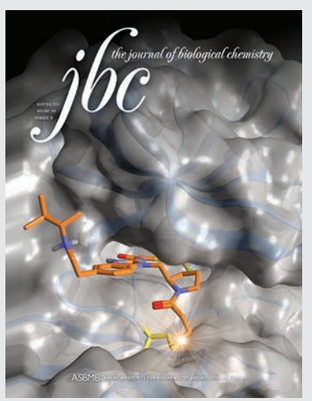
Do you have an ORCID? No, not the beautiful, expensive flower but a unique identification number that distinguishes you from fellow researchers with similar names.

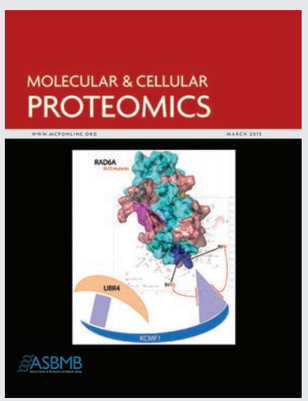
Known as ORCID for short, the Open Researcher and Contributor Identifier Registry's mission is to ensure that all of your professional contributions are fully credited to you. Publishers, funding agencies and repositories (such as PubMed) use the unique researcher identification numbers to credit properly individuals for their publications, datasets, patents and other contributions to the scientific enterprise.

The three journals published by the American Society for Biochemistry and Molecular Biology soon will begin collecting ORCIDs during the article-submission process. The journals also will publish ORCIDs in the full text and PDF versions of all articles. Several organizations and publishers already use ORCIDs, including the National Institutes of Health, the American Chemical Society, the American Association for the Advancement of Science and Elsevier.

It's easy to register for your ORCID — just three quick steps. Visit http://orcid.org/ to get started. You also can set up a profile page and search the registry for other investigators. Never get confused with someone who has a similar name again: Register for an ORCID today!

Karen Schools Colson (kcolson@asbmb.org) is the director of publications at ASBMB.





Two drugs are better than one

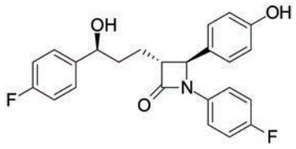
A two-pronged approach to increasing cholesterol elimination

By Mollie Rappe

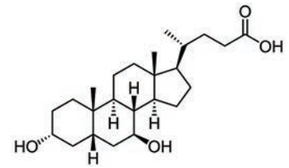
"Cholesterol: We can't live with it, can't live without it," quips Gregory Graf of the University of Kentucky, whose research team wrote in the **Journal of Lipid Research** about a potentially powerful two-drug combination that appears to be pretty good at removing the sometimes pesky molecule from the body.

The body regulates cholesterol in a complex manner. It makes cholesterol and absorbs it from food — achieving a balance that is not fully understood. The process of getting rid of excess cholesterol is even more complex. The liver is central to cholesterol synthesis and elimination. In addition to directly secreting cholesterol, the liver turns cholesterol into detergentlike bile acids. The gallbladder stores the bile — a mix of bile acids, unmodified cholesterol and many other waste products, such as bilirubin — before secreting it into the small intestine to help dissolve and absorb dietary fats. Much of the cholesterol secreted into the small intestine is then reabsorbed. The built-in redundancies of the cholesterol recycling process make designing drugs to target cholesterol elimination particularly difficult. The two-drug combination therapy developed by Graf's team stimulates cholesterol secretion from the liver and reduces cholesterol absorption in the intestine, leading to an increase in cholesterol elimination in a mouse model. Both of the drugs in the cocktail are already approved by the Food and Drug Administration.

One, ursodiol — originally found in bear bile — treats gallstones by making the bile a little bit more water-soluble to dissolve and flush excess cholesterol out of the gallbladder. The other, ezetimibe, blocks cholesterol absorption in the intestine and is modestly effective



Chemical structure of ezetimibe



Chemical structure of ursodiol

in the treatment of high cholesterol. Graf said he is hopeful "that these two agents may in fact be effective in working cooperatively to promote cholesterol elimination in human subjects" but cautions that there are differences between mice and humans.

Graf and co-workers tested ursodiol and determined that it increased the levels of a key cholesterol transport protein (the ABCG5-ABCG8 heterodimer, or G5G8). Ursodiol also increased the amount of cholesterol secreted into the gallbladder and eliminated in feces in a dose-dependent manner. Unfortunately, although cholesterol was flushed out of the body, the level of plasma cholesterol did not decrease, which is the clinical goal. Graf admits this puzzled them at first, but then they realized that the secreted cholesterol was being reabsorbed in the small intestine. So they added ezetimibe, a potent inhibitor of cholesterol absorption.

The combination led to no increase in G5G8 protein levels compared with the ursodiol-alone treatment, but mice treated with both drugs did excrete significantly more cholesterol in their feces. Compellingly, treatment with moderate amounts of ursodiol and high amounts of ezetimibe led to a modest but significant reduction in plasma cholesterol level. In addition, the researchers concluded that the marked decrease in the intestinal level of ABCA1 — a cholesterol transporter involved in making high-density lipoproteins — was the main cause for the lowered blood cholesterol level.

Graf and co-workers didn't stop there; they also wanted to see if the treatment was dependent upon the G5G8 transport pathway. They tested the ursodiol alone and the ursodiol-ezetimibe combination on mice lacking the G5G8 cholesterol transporter. The G5G8 knockout mice had significantly lower fecal cholesterol levels than the wild-type mice, but for both strains the ursodiol-alone treatment dramatically increased the amount of cholesterol eliminated in feces by the same proportion — 700 percent. On top of that, the combination therapy doubled the fecal cholesterol levels in both mice strains.

While the results from this work are promising, there are significant species differences, and it is unknown whether this combination will be effective in humans. Graf and co-workers are conducting a small clinical study in human subjects. Not only did Graf's team discover a promising one-two punch against cholesterol, but they also uncovered evidence for a cholesterol-elimination pathway not dependent upon the G5G8 transport protein. Characterization of this novel pathway could uncover new fundamental knowledge and innovative cholesterol-reduction therapeutics.

Mollie Rappe (mrappe@asbmb.org) is an intern at ASBMB Today and a Ph.D. candidate in biophysics at Johns Hopkins University.

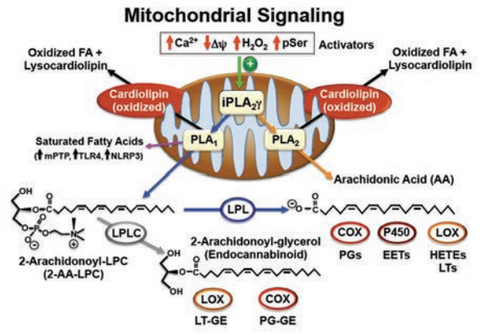
Mitochondrial phospholipases integrate cellular bioenergetics, signaling and cell fate

By Richard W. Gross

Phospholipases are enzymes that cleave ester linkages in phospholipids and often serve as the rate-determining step in the generation of a wide variety of lipid second messengers. Historically, endogenous phospholipid storage pools in the endoplasmic reticulum and the plasma membrane have been considered the major sources of polyunsaturated fatty acids that are hydrolyzed by intracellular phospholipases during cellular activation. The released polyunsaturated fatty acids serve as substrates for oxidation by a variety of cyclooxygenases, lipoxygenases and cytochrome P450s to generate a rich repertoire of lipid second messengers. However, recent studies using a wide variety of genetic, pharmacologic and mass-spectrometric approaches have demonstrated a prominent role for the activation of mitochondrial phospholipases and the hydrolysis of mitochondrial phospholipids in the production of a diverse array of signaling molecules by multiple distinct mechanisms.

Mitochondria fulfill multiple cellular functions regulating cellular metabolism, bioenergetics, signal transduction and cell fate. These pleiotropic roles of mitochondria are integrated precisely to promote metabolic efficiency and bioenergetic flexibility, which allows each cell to fulfill its physiologic functions and adapt to external perturbations.

Recent studies have demonstrated the prominent roles of lipid second-messengers and mitochondrial reactive oxygen species, or ROS, as physiologic signaling moieties. Conversely, the excessive and maladaptive production of ROS in disease states leads to the generation of toxic chemical species that promote mitochondrial dysfunction and cell death (e.g., necrosis through opening of the mitochondrial permeability transition pore, or mPTP, or apoptosis through the release of cytochrome c).



Generation of lipid second messengers by iPLA$_2\gamma$ and downstream enzymes

As such, strategies that modulate the activities of mitochondrial phospholipases and their production of downstream lipid second messengers offer a fertile area for pharmacologic intervention to attenuate the progression of disease processes.

Years ago, we identified the major measurable phospholipase in murine myocardial mitochondria, iPLA$_2\gamma$ (also known as PNPLA8) and by cloning the gene encoding the protein, identified a mitochondrial localization sequence at the N-terminus (1). To assess the roles of iPLA$_2\gamma$ in cellular function, we generated iPLA$_2\gamma$ knockout mice through ablation of the iPLA$_2\gamma$ active site, thereby eliminating iPLA$_2\gamma$ enzymatic activity as well as detectable protein (2). Moreover, genetic deletion of iPLA$_2\gamma$ altered cardiolipin content and molecular species distribution that was accompanied by defects in mitochondrial function.

Subsequent studies demonstrated a marked decrease in oxidized lipid second-messenger production in iPLA$_2\gamma$ knockout mice in multiple tissues in response to a variety of different stimuli (3, 4). Intriguingly, human recombinant iPLA$_2\gamma$ demonstrated a remarkable regiospecificity hydrolyzing phospholipids containing polyunsaturated fatty acids (e.g., arachidonic and docosahexaenoic acids) at the sn1 position to generate 2-arachidonoyl lysolipids with the concomitant release of potentially toxic saturated fatty acids in the inner

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mitochondrial membrane (5). We also demonstrated that iPLA$_2$γ readily catalyzed the hydrolysis of plasmalogens containing arachidonic acid at the sn2 position resulting in the direct release of arachidonic acid and the production of lysoplasmenylcholine.

Collectively, these results demonstrated that iPLA$_2$γ contributes to release of polyunsaturated fatty acids through both the traditional direct release of arachidonic acid (orange line in figure) as well as through a sequential two-step process initiated by sn1 hydrolysis generating 2-AA-LPC and the subsequent release of arachidonic acid by cellular lysophospholipases (blue lines in figure).

Although iPLA$_2$γ does not require divalent cations for catalytic activity, it is activated markedly by physiologic increments of calcium ion present in the mitochondrial matrix during metabolic stress (6). Accordingly, we compared the generation of calcium-stimulated eicosanoid lipid second messenger in mitochondria from wild-type mice to mitochondria isolated from iPLA$_2$γ knockout mice. The results demonstrated a dramatic decrease in calcium-stimulated eicosanoid production in mitochondria isolated from iPLA$_2$γ knockout mice (6).

In previous studies, Douglas R. Pfeiffer and co-workers demonstrated that a mitochondrial calcium-independent phospholipase modulated the opening of the mPTP and the release of cytochrome c (7). However, the molecular identity of the responsible enzyme was unknown. Accordingly, we used the iPLA$_2$γ knockout mouse to demonstrate that genetic ablation of iPLA$_2$γ markedly attenuated the calcium-induced opening of the mPTP (8). Collectively, these studies demonstrate the importance of mitochondrial iPLA$_2$γ in the generation of lipid second messengers, cellular signaling and cell-fate decisions.

The mechanisms underlying the activation of iPLA$_2$γ are an area of active investigation. Through genetic and pharmacologic approaches, we demonstrated that physiological increases in mitochondrial matrix calcium activate iPLA$_2$γ (6). Recently, studies by Pfeiffer and co-workers demonstrated that decreases in mitochondrial membrane potential activate iPLA$_2$γ activity (9). In addition, Petr Jezek and co-workers demonstrated that iPLA$_2$γ is activated by oxidative stress (10). Importantly, complement treatment of glomerular epithelial cells resulted in stimulation of iPLA$_2$γ by serine phosphorylation catalyzed by MAP/ERK kinase 1 (11). Based on these studies, it is apparent that iPLA$_2$γ serves as a prominent mediator of cellular bioenergetic and lipid signaling in multiple cell types in a spatial and context-dependent manner.

Valerian E. Kagan and co-workers, by identifying the iPLA$_2$γ-mediated release of oxidized polyunsaturated aliphatic chains in cardiolipin after cellular stress, elegantly demonstrated the importance of mitochondria in the production of signaling metabolites in response to cellular stress (12). When cardiolipin binds to cytochrome c, a conformational change in cytochrome c occurs, transforming cytochrome c from an electron carrier to a potent peroxidase with a remarkable specificity for oxidation of cardiolipin polyunsaturated aliphatic chains (13, 14). Using a powerful combination of mass-spectrometric technologies, genetic approaches and pharmacologic inhibition, they demonstrated that cytochrome c-oxidized cardiolipin aliphatic chains are released in response to cellular stress by an (R)-BEL inhibitable calcium-independent phospholipase (12). These results demonstrate a novel mechanism for lipid second-messenger generation where polyunsaturated chains on cardiolipin are first oxidized by cytochrome c and subsequently hydrolyzed by iPLA$_2$γ to serve as lipid second messengers, leading to the direct release of a panoply of known, and as yet incompletely characterized, signaling molecules.

Collectively, these studies identify the importance of mitochondrial phospholipases in serving critical roles in cellular signaling, bioenergetics and cell-fate decisions through the generation of a diverse array of lipid second messengers. Through these mechanistic insights, numerous therapeutic opportunities for the treatment of mitochondrial-mediated disease states have been identified.

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An invisible disease

By Indumathi Sridharan

How do you tackle an invisible disease? That is the challenge in diagnosing and treating endometriosis, a debilitating disease that affects at least 5 million American women of child-bearing age. March is endometriosis awareness month to highlight the lack of proper diagnosis and treatment options for patients. The nonprofit Worldwide Endo-March is organizing marches around the world, including in the U.S., to take place on March 28.

What is endometriosis?

The endometrium is the uterine lining that is shed and regenerated during a woman's monthly hormonal cycle. Endometriosis occurs when cells from the endometrial tissue spread beyond the uterus by a process called retrograde menstruation into other organs, such as the ovaries, Fallopian tubes, bowel and intestines (1). These extrauterine endometrial cysts respond to the monthly hormonal cycle, causing inflammation and scarring. Symptoms include painful cramps, heavy menstruation and digestive disorders. Endometriosis also causes infertility and can increase the risk of ovarian cancer or breast cancer.

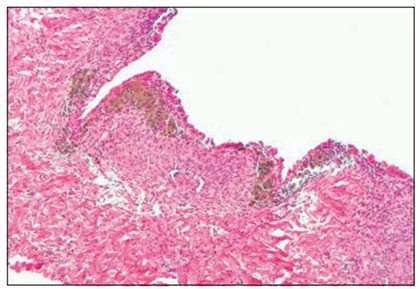

IMAGE COURTESY OF NEPHRON, A WIKIMEDIA COMMONS USER

Micrograph showing the features of endometriosis.

Why is endometriosis called "invisible"?

A study by the National Institutes of Health revealed that one in 10 women who present no symptoms of endometriosis actually have the disorder (2). Therefore, the actual number of women with endometriosis is higher than the currently estimated 5 million. Moreover, the painful symptoms often are misconstrued as just bad cramps. The lack of sensitive diagnostic methods impedes timely diagnosis (3).

What biochemical factors are involved?

In endometriotic tissues, upregulated aromatase activity increases the level of estrogen, which causes excessive cell proliferation. Estrogen induces cyclooxygenase-2, which is necessary for the synthesis of prostaglandin E2, or PGE2, a mediator of inflammation. PGE2 further stimulates aromatase activity (4). Also, the endometrial cells are resistant to changes in progesterone (an antagonist of estrogen), because chromatin methylation leads to the suppression of Homeobox genes.

What are recent advances in the diagnosis and treatment of endometriosis?

Aromatase inhibitors and estrogen-receptor blockers (e.g., chloroindazole and oxabicycloheptene sulfonate) prevent estrogen-dependent signaling and inflammation (5, 6). They could be effective alternatives to traditional synthetic progesterone treatments whose efficacy is highly variable.

The National Institute of Child Health and Human Development is preparing a multisite clinical trial to detect endometriosis based on a method developed by Linda Giudice and colleagues at the University of California, San Francisco. The researchers determined both the extent and severity of the disease by picking out unique expression pattern of genes involved in immune activation, steroid and thyroid hormone signaling and metabolism, and growth factor signaling (7).

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Five things to do before the annual meeting

By Angela Hopp

It's time to prepare to make the most out of the networking opportunities the American Society for Biochemistry and Molecular Biology annual meeting will offer.

1. Make a schedule and commit to sticking to it.

Make a day-by-day plan for your conference experience. Visit the ASBMB meeting website to find the times, dates and locations of award lectures and symposia (1). Use the Experimental Biology itinerary builder, and download the conference app when it becomes available (2).

2. Identify people you want to meet.

Use the itinerary builder to create a list of leaders in your field and researchers whose work aligns with yours. Plan to attend their talks, and email them in advance to set up casual meetings in Boston.

3. Draft questions so you'll be prepared.

While you can't predict exactly what speakers will say, you can do your homework. Inevitably, you're going to have questions that won't be answered during their talks. Keep your questions handy so that you can pipe up when the time is right.

4. Don't just expect the unexpected — anticipate it.

A chance encounter might change your career trajectory. Your next boss or collaborator might show up at your poster. Think about how you will take advantage of those pivotal moments. Practice inserting into a conversation that you will be presenting a poster or giving a talk and welcome feedback. Order business cards — no matter your career status. Make letter-size copies of your poster for distribution. (For more poster presentation tips, see page 22.)

5. Get inspired so that your presentation will be, too.

While there are plenty of engaging science-related TED Talks and iBioSeminars (3, 4), branch out. You might find that a TED talk on a completely different subject — for instance, Brené Brown's lecture "The power of vulnerability" — inspires you to inspire others (5).

Author's note: Many thanks to ASBMB Today contributor Vivian Tang and ASBMB staffers Rajendrani Mukhopadhyay, Chris Pickett and Erica Siebrasse for their contributions to this list.

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PLENARY LECTURER

Something to talk about

Bonnie L. Bassler's career is based on figuring out how bacteria converse with each other

By Rajendrani Mukhopadhyay

Bonnie L. Bassler's exuberance and energy are hard to miss, even over the phone. "I like being the center of attention," says the quorum-sensing expert at Princeton University.

Bassler has been at the center of attention since 2002, when she received a MacArthur Foundation fellowship, also known as the "genius award." The recognition came for her work on the intricate communication systems used by bacteria, known as quorum sensing. Since then, Bassler has had a spotlight on her. She has been profiled by major news outlets and gave a TED talk in 2009, the video of which has accumulated almost 2 million views.

For all her gregariousness, it comes as a surprise to hear Bassler's postdoctoral adviser say his first impression of his protégé was "shy" and "quiet." Michael Silverman took on Bassler as one of his last postdoctoral fellows before he retired from science. Bassler says she owes her career to him.

IMAGES COURTESY OF BONNIE L. BASSLER

Luck and generosity

Bassler was lucky to meet Silverman 26 years ago. Silverman was an elusive figure among microbiologists. He was known for his work at the forefront of bacterial genetics — for example, as a graduate student, he made the seminal discovery that bacterial flagella have rotary motors. But Silverman hated public speaking, so not many people got to meet him at meetings and conferences.

However, in 1989, Silverman made an exception. He accepted an invitation to speak at a symposium in Baltimore. At that time, Silverman was studying an obscure marine bacterium called Vibrio fischeri, which glows in the dark. The bioluminescent bacterium relies on quorum sensing to produce its light-emitting molecules.

During his lecture, he described the genetic components he was untangling to figure out how the bacterium chatted with its brethren to determine when they should turn on their glow-in-the-dark molecules. Bassler was in the audience during this lecture. At this time, she was a graduate student at The Johns Hopkins University in Baltimore working under Saul Roseman on the biochemistry of bacterial chemotaxis toward a food source of carbohydrates.

Bassler didn't know much about genetics, so she had trouble following the details of Silverman's talk. But she grasped the big-picture concept — bacteria communicate and do something as a group. They aren't solitary or silent. The idea of bacterial chitchat gripped Bassler's imagination so much that she approached Silverman for a postdoctoral stint, to which he agreed.

Once she completed her Ph.D., Bassler packed her bags and her cat and headed to Silverman's laboratory at the Agouron Institute in La Jolla, Calif., in 1990. Silverman's team was small. At the time Bassler joined, it was just Silverman, a postdoctoral fellow and two technicians. "One of our most powerful tools was a sterile toothpick," says Silverman with amusement. They used the sterile toothpicks to pluck off bacterial colonies from the plates of agar to create large arrays of mutant bacteria to manipulate and test under different conditions.

Into this world entered Bassler. "I was this card-carrying biochemist. I went to his lab, and the pH meter barely functioned. It was a lab filled with toothpicks. That was it. I didn't

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know what the heck I was doing. I had never cloned a gene. I didn't know what a promoter was. I didn't know what a transposon was, and he'd be like, 'Let's do transposon mutagenesis,'" recalls Bassler. "I was so scared of him thinking I was stupid."

She was so terrified of him that when a coyote killed her cat a few weeks after she moved to California, she refused to let the loss stop her. "I didn't want to take days off, because I wanted to show him I was a hard worker," she recalls. "I would just come and cry into my Petri plates."

Bassler's doggedness soon paid off. Silverman clearly remembers the day when, in his eyes, she came into her own as an independent researcher with her distinctive assertiveness. "She came into my office and wanted to talk to me," says Silverman. "She said she thought she had learned a lot and she wanted to take over the project she was working on. I guess it surprised me how confident she was."

Silverman, who believes in giving people room to test their wings, agreed. Bassler points to moments like this with Silverman as examples of his generosity. He gave his trainees the freedom to explore and take complete ownership of their work, which in Bassler's case was another marine bioluminescent bacterium called Vibrio harveyi.

V. harveyi caused Bassler a lot of grief during her postdoctoral training: She couldn't make mutants of the bacterium that were deficient in quorum sensing. Silverman already had made mutants of V. fischeri by knocking out the enzyme LuxI, which makes autoinducer 1, a quorum-sensing molecule, and LuxR, its receptor.

But first sets of V. harveyi mutants that Bassler made kept up with their quorum sensing. After a lot of frustration at being outwitted by a single-cell organism, Bassler realized that the V. harveyi must have two communication systems, not one. The mutants she was making were defective only in one communication system so they kept on talking to each other with the other system. This led her to propose that V. harveyi had an autoinducer-1 and an autoinducer-2, two different molecules that allow bacterial species to chat with each other.

During Bassler's postdoctoral stay with Silverman, she also learned the business of running a laboratory. Because it was a small lab, Bassler says, she learned what it was like to be an independent investigator even before she got a faculty position. "It was the best practice for being a young professor. I ordered everything, I racked all the tips, I thought of all the experiments, I wrote my papers with him," she explains. "But also, because he hated traveling, I gave every talk that he was ever invited to give." Bassler says she remembers people asking her at these talks if Silverman even really existed.

Bonnie L. Bassler and Michael Silverman, her Ph.D. adviser, hike in Wyoming.

When it came time for her to be an independent investigator at Princeton University, Bassler was the recipient of Silverman's generosity again. "I had an unusual policy for science, which is I let the postdocs take their projects with them," he says. "How are they going to make a living if they have to go out and start anew and compete with their old colleagues?"

In 1994, Bassler headed back to the East Coast to set up her laboratory with a research focus on V. harveyi (which she now unabashedly calls her favorite bug). A year later, Silverman retired from science and moved with his wife to Wyoming.

Mind-opening moments

Back in the 1990s, scientists didn't view Bassler's V. harveyi as a treasure trove of biological discoveries. Bacterial communication was seen as a quirk limited to V. fischeri and V. harveyi. Funding agencies weren't clamoring to support work on cute but obscure glowing marine bacteria.

Bassler has told the tale of how her laboratory survived without much federal research funding, relying heavily on Princeton's support. In 2006, she told The Scientist magazine, "This lab was held together with chewing gum and rubber bands for the first 10 years."

Then the MacArthur award happened in 2002. The awards are five-year fellowships given out annually to 20 to 30 individuals by the MacArthur Foundation. According to the foundation's website, "There are three criteria for selection of Fellows: exceptional creativity, promise for important future advances based on a track record of significant accomplishment, and potential for the fellowship to facilitate subsequent creative work."

For Bassler, the award changed how everyone viewed her offbeat research. "It was a validation of my lab's work as well as that of the entire field," says Bassler, who is also a Howard Hughes Medical Institution investigator and a member of the National Academy of Sciences. Quorum sensing was no longer quirky.

By 2002, Bassler's group isolated autoinducer 2, a molecule that allows bacterial species to chat with each other. Her group went on to show that bacteria related to V. harveyi (including Vibrio cholera, which causes cholera) also relied on the autoinducer 1 and 2 systems to communicate.

To find the enzyme that made autoinducer 2, Bassler's group embarked on a gene hunt. They found one called luxS. LuxS, when they looked closer, was broadly conserved in the bacterial world. Bassler's team went on to show that LuxS' ubiquity was because the autoinducer-2 system was the way bacteria chatted across different species, almost like a universal language. Bassler has described it as Esperanto for bacteria.

Bassler's group doesn't stop at the genes. They delve into the structural biology of the proteins made by the genes. They figure out how these communication molecules bind to their receptors and then, using molecular and biochemical tools, work out how the binding triggers signaling cascades. These signaling cascades tell the bacteria to glow, make toxins, or do whatever it is they need to do to survive and flourish as communities.

Based on what they discover about the quorum-sensing molecules, Bassler's team also is developing inhibitors of the quorum-sensing system. The inhibitors are useful on two fronts: They can be used to discover more about the cogs and wheels of the quorum-sensing machinery and have the potential to be used as antibacterial agents.

This type of "follow that molecule" research has led the Bassler group into the RNA arena, because they discovered that small RNAs, rather like eukaryotic microRNAs, work as switches to control the bacteria's entry and exit into quorum-sensing mode. "We always knew there was a missing component" that made sure that hundreds of genes "turn on and off in the right order at the right time," says Bassler, adding that these RNAs "allow more versatility than proteins: lower noise, higher robustness, more rapid quorum-sensing transition rates."

Figuring out that small RNAs are a critical component in quorum sensing was "a mind-opening moment," notes Bassler. "We're so biased about thinking that proteins run the show."

Communication as a part of scholarship

Mind-opening moments drive Bassler as a scientist. "At your core, the reason why you're in this business is because you're curious," she states. "That's the main reason." This type of curiosity — the deep, probing and relentless kind — is what Silverman says sets Bassler apart from other people as a scientist.

Figuring out what bacteria have developed for their evolution and survival is the quest, says Bassler, who is the current chair of the molecular biology department at Princeton. "It's you against the bacterium. That's the competition … Can you trick this bacterium into giving up its secrets?" Then, within a beat, she adds with a hoot of laughter, "Guess who's not winning?"

With her passion to discover the unknown, Bassler can't fathom how some people don't find science to be awe-inspiring. "I can't understand when people think it's boring, hard or not relevant," she says and doesn't hold back on her views of science phobia and science illiteracy. "We have a huge problem in this country where people don't like science, don't think it helps their lives be better, and don't believe in data as a way of making decisions," she says. "This is unfortunate."

But Bassler isn't the kind to walk away from the problem. She sees science communication as central to her scholarship and puts a lot of time and effort into her lectures by rehearsing them, making sure her slides make concise and clear points, and weaving the points together to make a good story.

"I believe you don't have to be boring to deliver content," says Bassler, who also teaches aerobics and has done so for 32 years. "You can be funny, you can be excited, and you can be easy to understand."

Bassler, who will be a plenary lecturer at the American Society for Biochemistry and Molecular Biology's annual meeting next month, knows firsthand how a lecture can change someone's worldview. After all, her career got its jumpstart by the fateful talk Silverman gave in 1989 when she says "I was mesmerized and awestruck."

Bonnie L. Bassler will give a plenary lecture at the American Society for Biochemistry and Molecular Biology annual meeting in Boston. She will present her lecture, titled "Manipulating quorum sensing to control bacterial pathogenicity," at 8 a.m. Sunday, March 29, in Ballroom West, on the third level of the Boston Convention & Exhibition Center.

Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the senior science writer for ASBMB. Follow her on Twitter at twitter.com/rajmukhop.

PLENARY LECTURER

‘Choose a problem that you’re passionately interested in’

By Rajendrani Mukhopadhyay

Ian A. Wilson is a structural biologist at The Scripps Research Institute. His laboratory focuses on how the immune system recognizes and neutralizes foreign antigens, such as the ones found on pathogens. The laboratory uses high-resolution X-ray crystallography to study various components of the immune system, such as antibodies and T-cell receptors, and their complexes with antigenic proteins.

Rajendrani Mukhopadhyay, the science writer for the American Society for Biochemistry and Molecular Biology, spoke with Wilson to learn more about his laboratory’s work and to find out what Wilson views as the big challenges in structural biology. The interview has been edited for length and clarity.

What does your lab work on?

We’re working on the structural biology of influenza virus, HIV and hepatitis C virus. We are trying to understand how these viruses are recognized by the immune system and, in particular, how broadly neutralizing antibodies recognize the viruses they target. We are thinking about how we can use that information for structure-based vaccine design.

What are your favorite structures?

Oh, that’s difficult. Most recently, one of the major successes that we’ve had is something we’ve worked on for many, many years. It was the HIV trimer, the structure of which appeared in (the journal) Science last year. We started working on that in the early 2000s through a collaboration with John Moore and Rogier Sanders at Cornell (University) in New York City. People had been waiting for that particular structure for a long time. My colleague Andrew Ward solved a similar structure with a different antibody by electron microscopy. We solved it by X-ray crystallography. That is my most recent favorite structure.

From the past, one of my favorite structures was the T-cell receptor structure. That was also something that was very, very challenging. We solved that in 1996. That was also quite a significant breakthrough at the time.

My all-time favorite structure, stemming from my postdoctoral work, is influenza virus hemagglutinin, and we continue to work on that to this day! It doesn’t go away. We solved a structure of hemagglutinin from the H3 subtype when I was at Harvard (University) in 1981. Since then, we’ve continued to solve lots of different subtypes — H1, H2, H5, H6, H7, H10 — for all of the emerging influenza viruses, complexed with neutralizing antibodies.

(Author’s note: The influenza type A virus is a class, which causes seasonal flu epidemics, can be categorized into subtypes based on two proteins on its surface: hemagglutinin, designated by “H,” and neuraminidase. There are 18 different hemagglutinin subtypes.)

You understand it’s a hard question to answer with one favorite structure. Several structures have been quite revealing once they were solved.

What have been the major advances in X-ray crystallography in the past 10 to 15 years?

We’ve been developing higher throughput methods for X-ray crystallography. The technological breakthroughs in X-ray took place a number of years ago with synchrotrons and with better detectors. The question became “Can you actually solve structures a lot faster?” By developing tools like crystallization robots and better expression systems — basically better ways of screening constructs to be able to actually get them to crystallize and to get crystals that diffract — the field has been able to accelerate the progress on X-ray crystallography. Larger and larger structures are being done. We’ve seen that with the ribosome. The technology just continues to improve, so the bottleneck goes back to the expression of proteins you are interested in.

What are the big challenges in structural biology?

Clearly one would like to look at the entire cell. Can we reconstruct the whole cell from a structural point of view? It can be done by integrative approaches, by using all of the biophysical technologies, such as X-ray crystallography, electron microscopy, and (nuclear magnetic resonance), and combining the results using computation. We want to be able to reconstruct large organelles and eventually reconstruct a whole cell. I think that’s where the field is going — toward more challenging systems, such as multiprotein complexes. You want to reconstruct how a cell operates at a structural level and obviously relate that to function.

What made you decide to become a scientist?

I was interested in chemistry. We’re going back a long ways now, back to the ’60s. I really hadn’t done much biology, and biochemistry was an emerging field then. I thought that seemed like a very interesting thing to do. I grew up in Scotland. There was a lot of pressure to become a medical doctor. But I became really interested in biochemistry. I became more fascinated as structures started to appear when I was in high school and as an undergraduate. I wanted to understand how proteins evolved. That took off, and I’ve been doing that ever since.

Who have been your scientific mentors and inspirations?

When I was in Oxford (for my Ph.D.), the professor I worked with was David Philips, who had solved the lysozyme structure. He inspired me to work on enzyme structures and try to use the structural information to understand function. I think that’s important — it’s not just doing structure for structure’s sake but to understand what that structure is telling you.

Then I went to Harvard, where I worked with Don Wiley. It was a fantastic project that I heard about when I was at Oxford. Don was working with John Skehel on influenza virus hemagglutinin. It was a very exciting challenge to understand what the structure of a viral antigen was and how that structure informed how influenza worked — how receptor binding and fusion worked and how the immune response was generated against influenza virus. It was very inspirational to work in Don’s lab.

Outside of your expertise, what area of research do you find fascinating?

What’s really driving a lot of the excitement at the moment … is the ability to sequence very quickly. To be able to sequence whole organisms has driven the field and opened up all sorts of exciting new possibilities. For example, microbiomes. We can now sequence the collection of organisms that are present in our guts and in other parts of our bodies.

The same thing is true in virology now. You’ve got the ability to pull out single B cells, sequence the antibodies and look at the evolution of an immune response upon infection. Not only can you look at the antibodies that are produced, but you can see how the virus is mutating to escape the recognition. Again, that’s opened up huge possibilities for understanding how the virus evolves to escape when the immune system starts to mount a response.

Do you have any hobbies?

I like to play golf. As I said, I grew up in Scotland, so golf is the game. I like to do things I can still get better at, and I can still get better at golf. In Southern California, you can play year-round, which is also nice and not true for Scotland. I like skiing. Again, it’s something I can improve at. I also like to go to the opera. I have season tickets at the L.A. Opera and the San Diego Opera. I also like cooking.

What advice do you have for young scientists?

Choose a problem that you’re passionately interested in but that is also challenging. If you find a good problem, you can pursue it for the rest of your life. I’ve been working on influenza hemagglutinin since 1977, and it’s still very exciting and topical!

Ian A. Wilson will give a plenary lecture at the American Society for Biochemistry and Molecular Biology annual meeting in Boston. He will present his lecture, titled “Structural basis of broad neutralization of viral pathogens,” at 8 a.m. Wednesday, April 1, in Room 253 A/B/C of the Boston Convention & Exhibition Center.

Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the senior science writer for ASBMB. Follow her on Twitter at twitter.com/rajmukhop.

PLENARY LECTURER

On histones and glamour

By Rajendrani Mukhopadhyay

C. David Allis at Rockefeller University is an expert in chromatin, the complex formed between DNA and histones. His laboratory is interested in the post-translational modifications that occur on histones to remodel regions of chromatin into active and quiescent forms. Mutations in histones have been linked to several diseases, including a lethal form of pediatric cancer.

For his work on chromatin, Allis won the 2015 Breakthrough Prize, which is funded by Silicon Valley heavyweights including Sergey Brin of Google and Facebook's Mark Zuckerberg. Rajendrani Mukhopadhyay, the science writer for the American Society for Biochemistry and Molecular Biology, spoke with Allis. The interview has been edited for length and clarity.

What is your group working on right now?

One area is centered around what I nickname "oncohistones." It is the pursuit of mechanisms that underlie some absolutely groundbreaking discoveries made at the end of 2012 and throughout 2013 by other groups that identified histone mutations in a pediatric cancer.

Histones are encoded by many copies of their genes. These researchers identified high-frequency point mutations in only one copy of only one allele of the genes that encode a particular histone.

In a (pediatric) brain-stem cancer, there is a point mutation in a histone. The mutation is most often a lysine-to-methionine (mutation). We can speculate all day — how can that one mutation be a problem when there are so many wild-type copies of the perfectly fine histones around? That's been a puzzle. The point mutation acts like a poison that seems completely to inactivate the enzyme system that's responsible for adding methyl groups (to histones).

Basic researchers like myself have been connecting with physicians who treat these devastating tumors. The goal is to learn more mechanistically about what's going wrong with the hope that a therapeutic option might surface. These kids who get these brain-stem tumors often are in the age group of 5 to 10. They are often dead in six months to a year. Most all of them. It just can't get more tragic in my book.

The other area we continue to be excited about is nonconventional post-translational modifications. We don't discover them, necessarily; top-notch mass-spectrometry labs do that. We get excited about the enzymes that put on the modifications and ones that take them off. We like to nickname those kinds of enzymes "writers" and "erasers." Post-translational modifications are read, so we like to call the proteins that do that "readers." Then the $64,000-question is what does a post-translation modification do? Does it open chromatin? Does it close chromatin?

We've been putting a lot of energy into a modification that's almost an acetyl lookalike. It happens to be two carbons longer, and it has one extra double bond. It's called a crotonyl group. We can perturb cells with various genetic or environmental changes that cause the crotonyl-CoA ratio relative to acetyl-CoA to change. It seems you can reprogram the chromatin to switch from predominantly acetyl to predominantly crotonyl. Then you can jerry-rig the cells so it goes back to different acetyl marks.

How did you become interested in studying histones?

In my graduate program (at Indiana University), we had some strict requirements for seminars. I was pretty scared of them, so I put it off, put it off, put it off, because the professor who was in charge was known to be a real bulldog. Then (for my seminar), I picked this new topic on chromatin. It was one of those days when all of the stars aligned, and everything I said in my talk came out right. Feeling I had a really successful seminar, I got interested in the topic of chromatin.

It came time for me to graduate and pick a postdoc. I was going to stick with Drosophila, which was the organism that I chose for my Ph.D. work, but a postdoc in my Ph.D. lab got me to consider using Tetrahymena. It's a ciliated protozoan. After doing some reading, what was cool about it to me was that it has two nuclei.

One nucleus is always silent. It doesn't transcribe anything. In fact, you can suck that nucleus out with a micropipette, and the cell is just fine. What's it doing? It turns out it's the nucleus that plays a role in the next generation. The other nucleus is responsible for all the gene expression. It occurred to me that was nature's gift for having essentially a pot of silent chromatin and a pot of active chromatin. *(Author's note: The actively transcribing nucleus in Tetrahymena is the macronucleus. The silent and smaller nucleus that goes into the germline is known as the micronucleus.)*

There was the laboratory of Martin Gorovsky in Rochester, N.Y. He had worked out methods to separate the two nuclei. I made a commitment to leave Drosophila, go to his group and learn how to do this separation of nuclei. I decided to look at the histone proteins. There were big differences. The macronucleus had hyperacetylated histones.

When I started my own group as an assistant professor, I went after the enzyme system (that puts on the acetyl groups). A graduate student named Jim Brownell used the Tetrahymena macronucleus in 1996 as a starting point to purify this enzyme system. We published the study in Cell, and it was picked as a Cell Classic last summer.

What inspired you to become a scientist?

I don't come from a science family at all. It was 100 percent decided for me that I would go to medical school. I gave it a crack for a couple of years. I had to do some moonlighting to pay bills. I was able to work for the Cincinnati coroner. He said to me, "You might want to rethink this whole thing about med school and consider science. Have you ever been in a real lab?"

I said, "I did chemistry."

He said, "No, no, have you ever been in a real lab?" When he said it, it caused my heart to pause. He said, "I think you're going to make a crummy physician. I think you'd be an amazing researcher. If you get interested, let me know. I have a friend in the med school who's young and cool."

I went to this person and interviewed. His name was Michael Bharier. He was at the Cincinnati medical school in the microbiology department. I took a leave of absence. (Bharier) took me under his wing and cut me loose on an enzyme.

I loved it. I brought all my medical school friends to show them the lab. My wife was like, "Oh, you're kidding me. You're going to do this?" Her family was especially crushed that I took this leave of absence. I just got hooked and never looked back. I enrolled in the Ph.D. program (at Indiana University) eventually. The rest is history.

What was it like to win the Breakthrough Prize in the life-sciences category?

They took us out to Silicon Valley. The star of the movie "The Imitation Game," Benedict Cumberbatch, was at this ceremony. The main actor from "The Theory of Everything" was there as well. *(Author's note: It's Eddie Redmayne.)* At our table was Christina Aguilera. Talk about being a kid from Cincinnati who works on chromatin and histones … It was unbelievable.

The ceremony was done like the Academy Awards. The coolest thing for me was meeting Jon Hamm. He played Don Draper in "Mad Men." My wife and I had become hooked on "Mad Men." We didn't know when we were out there who was going to be our introducer. You know you've won a prize, but you certainly don't know who's going to introduce you. Out comes Jon Hamm and Lauren Powell Jobs, Steve Jobs' widow. They were the ones who did the whole spiel on me. It was ultracool. I also got to talk remotely with Stephen Hawking.

It was a hoot to meet all these stars. The fact that Jon Hamm and Lauren Powell Jobs were there, taking pictures with me, was a crack-up. And oh, the emcee for the whole gala was Seth McFarlane.

With this prize, they are trying to show that science and mathematics are cool. They treat us as they would movie stars and sports people. I give these people a lot of credit.

What advice would you give younger scientists?

Everybody is hooked in their bubble. Everybody is on a device of some sort. I hope that young researchers get the thrill of science through direct one-on-one communication. Nothing is a bigger turn-on for me than meeting face to face with scientists. I think the scientists who have good people skills, the ones who are willing to communicate openly and frequently, are the ones who do the best.

C. David Allis will give a plenary lecture at the American Society for Biochemistry and Molecular Biology annual meeting in Boston. He will present his lecture, titled "Beyond the double helix: varying the terrain of epigenetic landscapes in development and disease," at 2:45 p.m. Tuesday, March 31, in Room 253 A/B/C of the Boston Convention & Exhibition Center.

Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the senior science writer for ASBMB. Follow her on Twitter at twitter.com/rajmukhop.

10 reasons your poster will impress and amaze at the annual meeting

By Quinn Vega

After months or years of working on your research project, you now have an opportunity to present your project to the scientific community. Although you may be nervous about sharing your results with a larger audience, once you have completed the experiments, there are only a few extra steps needed to make your presentation a success.

1. You thought about your audience

Although you may have been working on your project for some time, the audience for your poster presentation may not be as familiar with the subject matter or your scientific question. Therefore, when preparing your poster and your presentation, it is important that you think about your research from an outsider's perspective. Will somebody who doesn't know your research be able to follow the logic of your experiments and your conclusions?

2. You thought about your project as a connected set of experiments

All posters should tell a story, and your goal is for the audience to follow your story from beginning to end. In this story, the audience needs to understand your scientific question, your experimental results and how your results contribute to our understanding of your scientific field. This means that your introduction should set up the question, your results should help answer the question through a logical set of experiments, and your conclusion should tie in to both the original hypothesis and the experimental results.

3. Your figures were easy to see and understand

Given that a poster presentation is largely a visual medium, your figures should be a major focus in the presentation. While you might be tempted to include as much information as possible in the figure, the results should be clear and easily visible. Each figure should be properly labeled (each axis in a graph, for example), and the figures should be sufficiently large to be seen from three to five feet away. Appropriate controls and the reason for these controls should also be clear to the audience.

4. You made good use of white space

Although you want your poster to be comprehensive, some basic use of blank space will help make your poster clearer, and therefore more informative, to the audience. Looking at a poster from three to five feet away, can the audience easily follow the project? By providing some space between figures and text, you can highlight certain aspects of the poster instead of having everything blend together.

5. You kept text to a minimum

A little goes a long way. A picture is worth a thousand words. Less is more. You can pick your saying, but the conclusion is the same. Use words sparingly. Most individuals who view your poster will do so for seconds or minutes. Clear visuals (useful images and clear headings) will help people follow your poster and give them an opportunity to analyze the results and think about the significance of your experiments. Adding text only as necessary will help the audience follow the poster more easily, resulting in more useful feedback.

6. The text you did use was easily visible

Although you will be working on your poster up close, the audience likely will be three to five feet away. At this distance, the title and the headings should be legible. Also, remember to stay away from fonts that may seem stylish but that are difficult to read from a distance.

7. Your presentation was clear and concise

You may have 10 minutes or less to present your entire poster to your audience (usually an individual). This means that you will need to explain all of your information in a relatively short amount of time, and you need to decide which aspects of the project are the most critical for the audience member to hear to understand your project. I usually ask my students to be able to summarize their projects in 30 seconds, five minutes and 10 minutes. In this way, they can gauge the interest and knowledge of the individual listening to the poster and then provide the appropriate level of information.

8. You used your poster strategically during your presentation

While giving your presentation, remember to speak calmly and refer frequently to your poster. While the audience should be able to follow your poster without your assistance, your presentation can walk people through the key aspects of the project and explain the reasoning behind the experiments you performed and your view of the results.

9. You were ready for questions

Students often fear a question that they cannot answer. There are three things that will help you through this section. First, you probably know more than you think. Remember, you have been working on this project for some time, and you have been studying this material more than most. Second, it is OK to say that you don't know. While you may feel that you should know everything about your project, part of the reason you are presenting is to get feedback. Any questions that you cannot answer will help you better understand your project and may help direct your research in the future. Finally, remember that scientists like to ask questions almost as much as they like to answer them. Therefore, think of these questions not so much as a test but as a discussion between two scientists interested in the same question. What is cooler than that?

10. You enjoyed yourself

You spent a great deal of time getting these results, and while you may be nervous about presenting your research to other scientists, you should let your enthusiasm for your project and the experience show. Although most of my students have been nervous before presenting, all were excited about getting the opportunity to discuss their projects, and they all had great experiences.

Quinn Vega (vegaq@mail.montclair.edu) is a professor of biology and molecular biology at Montclair State University.

HERBERT TABOR RESEARCH AWARD

Steitz recognized for her significant contributions to the field of RNA biology

By Kathleen McCann

Joan Steitz of Yale University has won the American Society for Biochemistry and Molecular Biology's Herbert Tabor Research Award for her outstanding and numerous contributions to the field of RNA biology. This award honors scientists who have impacted significantly the field and the scientific community through their excellent research. Steitz is the first woman to receive this award since its inception in 2004.

Steitz is a pioneer in the field of gene expression. "Steitz's work throughout her career has touched all aspects of the central dogma," said Karla Neugebauer, a colleague of Steitz at Yale University. The central dogma states that DNA is transcribed into RNA, which is then translated into protein. Indeed, Steitz has made many seminal discoveries that illuminate the many functions of RNA in gene expression.

Joseph Gall, a longtime mentor and colleague of Steitz, remarked that Steitz "almost single-handedly established several of the most important features of RNA transcription, splicing and translation."

Just five years after joining the Yale faculty, Steitz made the fundamental discovery that a short, seven-nucleotide sequence in mRNA base-pairs with the ribosomal RNA to initiate protein synthesis in E. coli. Susan Baserga, a professor at Yale and former postdoctoral fellow in Steitz's lab, explained that this finding is important "because it meant that RNA uses the chemistry of its bases to carry out its function in gene expression."

Steitz's most influential breakthrough was the discovery with her M.D./Ph.D. student Michael Lerner that small nuclear ribonucleoproteins, now known as snRNPs, are involved in pre-mRNA splicing. In a landmark paper, Steitz's group was the first to propose that the small nuclear RNAs of the snRNPs base-pair with the splice sites of the pre-mRNA to facilitate removal of introns. This hypothesis "galvanized the mRNA processing field for decades to come" said Christine Guthrie of the University of California, San Francisco. Steitz's lab subsequently has elucidated the function of the snRNPs in pre-mRNA splicing and was one of the discoverers of the minor spliceosome, which excises a distinct class of rare introns.

Steitz has explored other fundamental aspects of RNA structure and function in gene expression. Her lab discovered new metazoan small ribonucleoprotein complexes in the nucleolus, or snoRNPs, and demonstrated that some function in ribosomal RNA biosynthesis.

Most recently, her research has focused on how mammalian viruses use small RNAs and RNA elements to regulate expression of both viral and host genes. Included is the exciting and unprecedented observation that a viral RNA element stabilizes RNA levels by forming a triple helix with the poly(A) tail of the RNA. This pivotal finding has "challenged the field to consider a novel regulatory mechanism relevant to both normal cellular function and disease," Neugebauer said.

Steitz also contributed to the field of RNA biology through her dedicated mentorship of scientists at all stages in their careers. She is a founding member of the RNA Society and serves as an editor for several eminent journals, including RNA and the Journal of Cell Biology. She is hailed as an exemplary role model for young female scientists and is devoted to the training and advancement of women in science. She has mentored a remarkable number of students who have gone on to become independent scientists and to make their own significant contributions to the field.

Steitz graduated with a bachelor's degree in chemistry from Antioch College and went on to earn her Ph.D. in biochemistry and molecular biology at Harvard Medical School, where she was the first female graduate student in the laboratory of James Watson. Steitz completed a postdoctoral fellowship at the Medical Research Council Laboratory of Molecular Biology at the University of Cambridge before joining the faculty of Yale. She has received many awards and honors, including election to the National Academy of Sciences, the National Medal of Science, the RNA Society Lifetime Achievement Award and the Rosalind Franklin Award for Women in Science.

Steitz will receive her award during the Experimental Biology 2015 conference in Boston, where she will deliver the opening lecture of the ASBMB meeting. Her presentation, "Noncoding RNAs: small, large and viral," will take place at 6 p.m. Saturday, March 28, in Ballroom West on the third level of the Boston Convention and Exhibition Center.

What ties together the important discoveries of my entire career is no more than looking for base pairing between RNA molecules and how that simple interaction contributes to gene expression. I am enormously indebted to the many talented students and postdocs who have joined me in this somewhat esoteric quest.

– JOAN STEITZ

Kathleen McCann (Kathleen.mccann@yale.edu) is a graduate student in the genetics department at Yale University.

EARL AND THRESSA STADTMAN DISTINGUISHED SCIENTIST

Dixon recognized for outstanding contributions to scientific research and leadership

By Aditi Dubey

Jack E. Dixon at the University of California, San Diego, won the Earl and Thressa Stadtman Distinguished Scientist award from the American Society for Biochemistry and Molecular Biology in recognition of his work on eukaryotic signal transduction and, in particular, reversible phosphorylation.

Dixon has made several seminal contributions toward understanding enzymes that remove phosphate from proteins (phosphatases) through his work characterizing several members of the protein-tyrosine phosphatases, or PTPases, superfamily.

"His scientific achievements are outstanding, and he continues to be a powerful advocate for excellence in biochemical and biomedical research," Minor J. Coon, professor emeritus at the University of Michigan Medical School, wrote in his nomination letter.

Dixon was born in Nashville and received his B.A. in zoology from University of California, Los Angeles, in 1966. He went on to earn his

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Ph.D. in chemistry from University of California, Santa Barbara, in 1971. He completed his postdoctoral training in biochemistry as a National Science Foundation postdoctoral fellow in the laboratory of Nathan O. Kaplan at UCSD. He then began his career as a faculty member at Purdue University, where he discovered the first dual-specificity phosphatase VH1, encoded by Vaccinia virus. He also showed that the virulence plasmid of Yersinia pestis produces the most active PTPase ever described, in that it drastically affects the host's immune defenses and results in the pathogenicity of these bacteria.

With these key discoveries, Dixon quickly established himself as an expert in the field. He went on to define several members of this new family of phosphatases and discovered a novel mechanism of their catalytic action. His work is considered to have, as Coon said, "radically advanced the molecular basis of pathogenesis."

Among Dixon's recent notable discoveries are the identification of PTEN tumor suppressor as a phosphoinositide phosphate and myotubularin — a protein mutated in muscle myopathies. He also has identified novel covalent post-translational modifications, such as hydroxylation, and O-linked glycosylation of peptide hormones. His laboratory continues to pursue key questions on cell growth and differentiation through a comprehensive study of PTPases.

Scientists mentored by Dixon describe him as a supportive, approachable and encouraging adviser who allows his trainees to develop their projects with freedom while still giving them the requisite guidance and advice. They speak of his investment in their careers and his honest, enthusiastic and collaborative attitude toward scientific discovery.

"I am indebted to Jack for so much of my professional development," wrote David Pagliarini, assistant professor at the University of Wisconsin, Madison. "The guidance and mentorship I received from him have truly shaped me as a scientist."

During his tenure as vice-president and chief scientific officer at the Howard Hughes Medical Institute, Dixon was instrumental in developing programs that support young scientists and establishing the open-access policy that allows the work of HHMI researchers to be shared with the scientific community. The HHMI Early Career Scientist Program, the Hughes Collaborative Innovation Awards and a collaboration with the Gordon and Betty Moore Foundation for plant science research are examples of innovative programs developed under Dixon's leadership to support scientists and their career paths.

In addition to his role at HHMI, Dixon has served as the president of the ASBMB and is a member of the National Academy of Sciences, the American Association for the Advancement of Science and the Institute of Medicine. He is a foreign member of the Royal Society. He has received several awards and fellowships in recognition of his contributions to the research enterprise, including two previous awards from the ASBMB, the William C. Rose Award in 2003 and the ASBMB-Merck Award in 2005.

Earl and Thressa Stadtman, after whom Dixon's latest ASBMB award is named, were outstanding biochemists and mentors. According to a historical exhibit dedicated to the two scientists at the National Institutes of Health, their laboratories conducted research held to the highest standard of scientific rigor while also fostering a congenial environment for training and mentoring future scientists. The Stadtmans were known to credit junior scientists generously for their ideas and results on publications. Colleagues came to refer to this model of scientific research as "the Stadtman way." The ASBMB established the award in their names to preserve their legacy and honor basic research scientists who exemplify those qualities.

I am extremely pleased about this honor. Earl and Thressa were role models for me when I was a young scientist. I had the pleasure of knowing them and interacting with them over a number of years. They also trained so many outstanding people. It is just great to be a small part of their legacy.

– JACK E. DIXON

Earl Stadtman once said: "Productive laboratories are not merely the reflection of good scientific discipline and expert direction but depend almost as much on the establishment of a congenial atmosphere in which science can flourish as a consequence of free thought, unguarded exchange of ideas, critical discussion and a respectful interaction among all of its personnel."

Dixon will give his award lecture, titled "Novel kinases that phosphorylate proteins and proteoglycans in the secretory pathway," at the ASBMB annual meeting in Boston. It will be at 8:45 a.m. Sunday, March 29, in the Ballroom West on the third level of the Boston Convention & Exhibition Center.

Aditi Dubey (dubeyad@scarletmail.rutgers.edu) is a graduate student studying the mechanism of selenocysteine incorporation at Rutgers University Robert Wood Johnson Medical School.

PLENARY LECTURER, FRITZ LIPMANN LECTURESHIP

Klevit, pushing 'physical techniques to their limits to solve truly important biological problems'

By Maggie Kuo

Rachel E. Klevit, professor of biochemistry at University of Washington, will give the Fritz Lipmann Lecture at the 2015 American Society for Biochemistry and Molecular Biology annual meeting. The society issues the award every two years to recognize researchers who've contributed conceptual advances in biochemistry, bioenergetics or molecular biology.

Klevit's "research contributions have made a profound impact on the way we understand many very important aspects of biological chemistry," writes Trisha N. Davis of University of Washington in her nomination letter. "Her research has been instrumental in understanding the mechanism of disease of two scourges, breast cancer and Parkinson's. Moreover, she has changed the way research in this area is done."

Klevit is recognized for innovatively using physical methods to determine the structure and function of proteins. Her most lauded contributions are using nuclear magnetic resonance spectroscopy to solve the structure of the Cys2-His2 zinc finger fold, a common motif present in many DNA-binding proteins, and defining the BRCA1-mediated ubiquitination system that is fundamental to the pathogenesis of breast cancer.

Klevit is considered a pioneer in using NMR to study ubiquitination enzymes. "Indeed, she is the unmatched leader in the analysis of ubiquitination by NMR," writes Michael Rape of the University of California, Berkeley, in his letter of support. Along with her investigations of the BRCA1 enzyme, she recently discovered a new class of ubiquitination enzymes that has implications in understanding the development of Parkinson's disease.

A defining characteristic of her approach is "a willingness to boldly push the biophysical methods to extract the most important biological insights from the system under study," writes Lila M. Gierasch at the University of Massachusetts.

Besides her many significant scientific contributions, Klevit is known for her commitment to the scientific community and training young scientists. "Her graduate students are enthusiastic about science – they love working for her," writes Rape. "Rachel is also most welcoming to young colleagues that have just entered her field, and she supports them heavily during their first hard years as principal investigators," he continues. "These characteristics make Rachel one of the most cherished and important members of the ubiquitin community."

Klevit has served on numerous study sections for the National Institutes of Health and the California Breast Cancer Program and was a member of the editorial board for the Journal of Biological Chemistry.

Klevit received her D. Phil. in chemistry from Oxford University in England. She did her postdoctoral training at Duke University Medical Center and University of Washington. She then joined the research faculty of the department of chemistry at University of Washington and later became professor of biochemistry there.

Klevit will give her lecture, "Structural, functional and mechanistic diversity in protein ubiquitination," on Tuesday, March 31, at 8 a.m. in Room 253 A/B/C in the Boston Convention and Exhibition Center.

It's a special honor to be recognized by ASBMB with a Fritz Lipmann Award. One of my guiding principles is to apply chemical concepts and intuitions to understand biology, and this practice led Lipmann to his groundbreaking and seminal contributions. When teaching undergraduate students, I encourage them to think conceptually rather than learn by rote. The many talented students, postdoctoral fellows, collaborators and colleagues with whom I have had the pleasure to associate over the years have provided a fertile and fun environment in which to try to better understand how molecules make biology work.

– RACHEL E. KLEVIT

Maggie Kuo was an intern at ASBMB Today when she wrote this story. Today she is a writer at the American Physiological Society. She earned her Ph.D. in biomedical engineering at Johns Hopkins University.

ASBMB AWARD FOR EXEMPLARY CONTRIBUTIONS TO EDUCATION

Colleagues recognize Bell for his role in numerous education and society initiatives

By Joseph P. Tiano

The American Society for Biochemistry and Molecular Biology named J. Ellis Bell of the University of Richmond the winner of its Award for Exemplary Contributions to Education.

Bell, a professor of chemistry, has mentored several graduate students and dozens of undergraduates who have gone on to graduate school. He has spent his entire career making huge contributions to student education, especially in the field of biochemistry and molecular biology, where his research interests lie.

He has had such an impact on many of these students that they credit him for a large part of their success. Stacy Horner, one of Bell's students while he was at Gustavus Adolphus College, remarked in support of Bell's nomination for the award, "From mentoring to teaching me in class and challenging me to think at a higher level, Dr. Bell played a critical role in my development as a young scientist. I am incredibly thankful to Dr. Bell for his guidance and support during my early years in college."

Bell began his career at the University of Rochester before moving to Gustavus Adolphus College, where he taught biochemistry for 10 years. He joined the University of Richmond in 2001. At each institution, he created biochemistry and molecular biology degree programs that integrate research into learning experiences.

Bell also served as a program director at the National Science Foundation's Division of Molecular and Cellular Biosciences, where he awarded and managed cutting-edge research programs that provided exceptional training opportunities for undergraduates. He was one of the original members of the NSF's highly influential Vision and Change working group, which has catalyzed the modernization and incorporation of research into biology education.

Lisa Gentile, a dean at Westminster College, said, "One of the many things I appreciate about working with Ellis is his willingness to brainstorm and then roll up his sleeves to help implement good ideas."

Bell is the longest-serving member of the ASBMB Educational and Professional Development committee. He founded the society's Undergraduate Affiliate Network and its newsletter, Enzymatic. The UAN serves undergraduates as a biochemistry club and provides resources for those interested in teaching, outreach and research. Bell also is editor-in-chief of the "Mentoring in Academia and Industry" series published by Springer Science+Business Media.

Along with all his work toward improving biochemistry education, Bell also maintains an active research program focused on understanding protein structure-function relationships. More specifically, he is interested in how dynamic aspects of protein structure, such as changes caused by post-translational modifications or ligand binding, are involved in both catalysis and allosteric regulation of multisubunit proteins.

"(What) stands out most about Ellis," Gentile said, "is his commitment to research with a diverse group of undergraduates as well as his commitment to outreach – high-school, middle-school, elementary-school teachers and students. He has always been a willing partner in ventures that touch on any of these areas."

It's an honor to receive this award, and I would like to thank the amazing undergraduates with whom I have had the privilege of working over the years — they have been a true inspiration to everything I have tried to do — and my faculty friends and colleagues around the nation who have contributed much to any successes I have had.

– J. ELLIS BELL

In just the past five years, Bell's NSF grants have supported the training of 37 undergraduates, four high-school and middle-school students, and two K – 12 teachers.

Bell will receive his award during the ASBMB annual meeting, which will be held in conjunction with the Experimental Biology 2015 research conference. His award lecture will be titled "Don't teach biochemistry, teach students!" It will take place at 12:15 p.m. Sunday, March 29, in Room 253 B/C of the Boston Convention & Exhibition Center.

Joseph P. Tiano (tiano233@hotmail.com) is a postdoctoral fellow at the National Institute of Diabetes and Digestive and Kidney Diseases in Bethesda, Md.

ASBMB YOUNG INVESTIGATOR AWARD

Saphire, a 'leading light in molecular biology and human health'

By Maggie Kuo

Erica Ollmann Saphire, professor of immunology and microbial science at The Scripps Research Institute, is the recipient of the American Society for Biochemistry and Molecular Biology Young Investigator Award. Her success solving the structures of complex viruses has pushed forward the effort to develop treatments to fight Ebola and other deadly viruses. Saphire's work has deepened researchers' understanding of fundamental principles of biochemistry and molecular biology.

This award recognizes outstanding contributions to biochemistry and molecular biology by early-career scientists. "In the 10 years of her independent career, Dr. Saphire has ingeniously applied structural biology and protein biochemistry to the problems of global health, making fundamental new discoveries along the way in how proteins behave," George N. Phillips Jr. of Rice University said. "I don't know of any other young structural biologist with such insight and who has made so many textbook discoveries this early in her career."

As a Ph.D. student, Saphire solved the crystal structure of a broadly neutralizing antibody against HIV-1. Her "findings immediately guided vaccine design," Robert V. Stahelin of the Indiana University School of Medicine at South Bend said, "but, for the wider field of immunology, it was and still remains the only structure of the entire human antibody."

Saphire's first discovery as an independent investigator was the structure of the Ebola virus surface glycoprotein. That "revolutionized thought in the field of Filovirus cell entry," Michael G. Rossmann of Purdue University said. It predicted that the Ebola receptor was in the endosome and not on the cell surface, where the rest of the field was looking. Saphire then solved the structures of the Sudan virus glycoprotein and Marburg virus glycoprotein. These structures, Stahelin wrote, "have become a critical roadmap for development of lifesaving antibody therapies against Ebola and related viruses."

Saphire's recent work is considered widely as the most fantastic of her already impressive accomplishments. Saphire demonstrated that the Ebola virus matrix protein VP40 folded into multiple, distinct, 3-D structures, each form having a different function in the virus life cycle. "This is remarkable," Stahelin said, "because, as molecular biologists, we learned a central dogma that a protein sequence defines its single and particular structure, which, in turn, defines its function." Her findings are "a thought-provoking expansion of the central dogma of molecular biology," said Phillips, "revealing new ways information is encoded in the genome and compelling the field of structural biology and biochemistry to re-evaluate when we think 'the' structure is solved rather than 'a' structure is solved."

Saphire also is "an extraordinary citizen of the community, not just by doing science in her laboratory at Scripps but also by going into the field," Rossmann praised. "She travels to Africa (for a collaboration) to develop her proteins into diagnostics, to understand the ecology of these diseases and see the interaction between pathogen and host," wrote Stahelin. "Her proteins not only solve structures and provide biochemical sights, they are being used right now in clinic to diagnose disease and save lives."

This is an award to be shared with many others. I am fortunate to work alongside gifted collaborators and the talented postdocs, students and technicians in their labs and my own. Credit also goes to my field. The community of Ebola virus researchers pulled together this year to advance basic research, diagnostics and treatments in order to alleviate what suffering we could during this outbreak and prepare for any re-emergence.

– ERICA OLLMANN SAPHIRE

Saphire earned her bachelor's from Rice University, where she worked under Kathleen Matthews, winner of ASBMB's William C. Rose Award. "I am thrilled to join Kathy at ASBMB this year," Saphire said. "She turned me on to research in biochemistry and has always been my model for how to be a scientist and a scientific citizen." Saphire went on to earn her Ph.D. from The Scripps Research Institute. She continued onto a postdoctoral fellowship at Scripps and

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later joined the faculty there.

Saphire will receive her award at the Experimental Biology 2015 conference in Boston, where she will deliver her award lecture, "The molecular toolkit of viral hemorrhagic fevers." The presentation will take place 3:55 p.m. March 29 in Room 257A/B in the Boston Convention and Exhibition Center.

Maggie Kuo was an intern at ASBMB Today when she wrote this story. Today she is a writer at the American Physiological Society. She earned her Ph.D. in biomedical engineering at Johns Hopkins University.

HOWARD K. SCHACHMAN PUBLIC SERVICE AWARD

U.S. Rep. DeLauro and U.S. Sen. Moran recognized for their support of science

By Erica Siebrasse

The American Society for Biochemistry and Molecular Biology Public Affairs Advisory Committee awarded the Howard K. Schachman Public Service Award to U.S. Rep. Rosa DeLauro, D-Conn., and U.S. Sen. Jerry Moran, R-Kan.

Howard K. Schachman served as the PAAC chair for more than 10 years. Shortly thereafter, in 2001, the committee instituted the Schachman Award, which recognizes up to two individuals each year for their dedication to public service in support of biomedical science.

DeLauro has spent 25 years representing the people of Connecticut's 4th District in the U.S. House of Representatives. During that time, she has been a champion of biomedical research and has introduced numerous bills in support of the enterprise. Most recently, DeLauro co-sponsored the Accelerating Biomedical Research Act, which would restore the National Institutes of Health's purchasing power.

Thomas D. Pollard at Yale University, a constituent of DeLauro, said, "I am blessed to be represented in Congress by Rosa DeLauro, a fellow cancer survivor, who is more enthusiastic about the value of basic biomedical research than anyone else at the national level. She appreciates that fundamental knowledge about biological systems is required to understand human disease well enough to develop rational strategies for prevention and cures. She also appreciates that getting this information depends on hard work and a long-term investment by the federal government working with our educational and research institutions."

Dr. Schachman has dedicated his professional life to educating generations of scientists, and I am honored to receive this award named after him. As a cancer survivor, I know the importance of biomedical research, and I am in awe of what our scientists do. The scientific and medical breakthroughs supported by NIH have allowed millions of Americans to live happier, healthier and longer lives. This award is inspiration to keep fighting for funding so we can ensure those breakthroughs keep happening for years to come.

– U.S. REP. ROSA DELAURO, D-CONN.

It is an honor to receive the Howard K. Schachman Public Service Award. By supporting biomedical research, we are saving lives today and investing in our future. Given the vast amount of progress made over the last century and the great potential current research holds, now is not the time for our nation to waiver on its commitment to advancing medical research. This dedication will benefit our children and our country for generations to come by saving lives, improving health, growing the economy, reducing health care costs and strengthening America's role as a global leader in innovation.

– U.S. SEN. JERRY MORAN, R-KAN

Moran represented Kansas' 1st Congressional District for 14 years before his election to the U.S. Senate in 2010. He has championed legislation to prioritize research at the NIH and spoken about the importance of biomedical research on the Senate floor and in multiple news publications.

"During his time in the Senate, Sen. Moran has been a consistent and vocal booster not only of the NIH but of education in the sciences. Whether speaking to the citizens of Kansas or his colleagues in the Senate, Sen. Moran has argued repeatedly that tax dollars spent on the NIH are a wisely spent investment in the future of America," said Gerald M. Carlson at the University of Kansas Medical Center and a member of the PAAC. "He realizes that support of scientific research must be nonpartisan, that other countries are spending proportionately more than we are on such research, and that our recent spending on science has been at a standstill."

Both DeLauro and Moran have been invited to give remarks and receive their awards at a reception after the ASBMB spring Hill Day.

Erica Siebrasse (esiebrasse@asbmb.org) is the education and professional development manager for ASBMB. Follow her on Twitter at twitter.com/ericasieb.

AVANTI AWARD IN LIPIDS

Reue recognized as a 'leader in the field of lipid and energy metabolism'

By Mark Stewart

Karen Reue, professor and interim chair of human genetics and professor of medicine at the University of California, Los Angeles, won the Avanti Award in Lipids from the American Society for Biochemistry and Molecular Biology. The award recognizes Reue's novel contributions to our understanding of lipid metabolism and homeostasis.

Reue's scientific success is, in part, due to "her expertise in both mouse genetics, especially as applied to lipid metabolism, and molecular biology," said Peter Edwards at the University of California, Los Angeles, who nominated Reue for the award.

Using naturally occurring mutations in mice and positional cloning, Reue identified the lipin gene family (lipin-1, lipin-2 and lipin-3). The three lipin proteins are phosphatidate phosphatases required for the conversion of phosphatidic acid to diacylglycerol. Reue's work has demonstrated that lipin proteins play critical roles in adipogenesis and triacylglycerol storage, energy metabolism and insulin sensitivity in skeletal muscle, and lipid homeostasis in the aging brain. Recently, Reue's laboratory identified a role for lipin-1 in autophagy, which may relate to the disease symptoms of lipin-1-deficient individuals.

"The lipin proteins are now studied in numerous laboratories in several countries, an indicator of the important biological role of the lipin proteins," says Rudolf Zechner of the Institute of Molecular Biosciences in Graz, Austria.

Reue's lab also identified an additional novel gene, Diet1, isolated from a mouse strain resistant to high blood-cholesterol levels. Inactivating mutations in Diet1 impair signaling from the intestine to the liver, resulting in excess cholesterol being converted to bile acids. These bile acids are secreted into the intestine and subsequently are excreted from the body. These metabolic changes prevent the accumulation of excess cholesterol in the blood.

Future work will explore the role of Diet1 genetic variants in human cholesterol homeostasis. It is hoped that such studies may explain why certain people are resistant to hypercholesterolemia. "The significance of Diet1 in physiology and its potential as a therapeutic target have been

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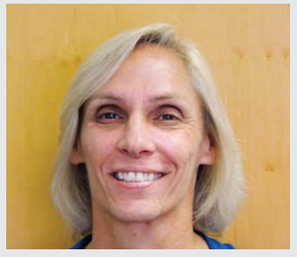

I am truly honored and excited to receive the Avanti award, which previously has been presented to some of my personal heroes in the field of lipid research. I acknowledge the many wonderful mentors, colleagues and trainees who have influenced my work over the years.

– KAREN REUE

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widely recognized," says Stephen Young at the University of California, Los Angeles.

Alan Attie from the University of Wisconsin-Madison said Reue "thinks deeply about important questions in biology and finds elegant ways to study them." Zechner added that "a hallmark of her research is the comprehensive nature of the studies."

Reue earned her Ph.D. from the University of California, Los Angeles, after which she began her postdoctoral training at The Rockefeller University in New York. Reue returned to UCLA and rose through the ranks to professor. Reue's work has been funded continuously by the National Institutes of Health.

Reue will receive her award during the ASBMB annual meeting, held in conjunction with the Experimental Biology 2015 conference in Boston. She will deliver an award lecture, "The lipin protein family, cellular lipid storage and disease," at 3:05 p.m. Monday, March 30, in the Ballroom West, on the third level of the Boston Convention & Exhibition Center.

Mark Stewart (mstewa10@gmail.com) earned a Ph.D. from the University of Alabama at Birmingham. He now works at the Institute of Medicine of the National Academies, in Washington, D.C., as a research associate.

PLENARY LECTURER, ASBMB-MERCK AWARD

Chen recognized for his contributions to understanding protein ubiquitination and innate immune signaling

By Umesh D. Wankhade

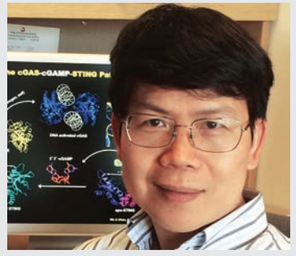
Zhijian "James" Chen, professor of molecular biology and a Howard Hughes Medical Institute investigator at the University of Texas Southwestern Medical Center at Dallas, won the 2015 American Society for Biochemistry and Molecular Biology-Merck Award, which recognizes outstanding contributions to research in biochemistry and molecular biology.

Chen received this award for his work on the mechanisms of cell signaling, inflammation and innate immunity. In the mid-1990s, his group unraveled an unanticipated function of ubiquitin as an activator of protein kinases in cytokine signaling. Until that point, conventional thinking dictated that ubiquitin only had one molecular function – to tag other proteins for destruction by the cell's proteasome.

Chen also found that mitochondria contribute to the body's immune response. For example, his group identified MAVS, a mitochondrial protein critical for immune defense against many RNA viruses, including influenza, West Nile and hepatitis C. Chen and colleagues recently discovered a new pathway, called the cGAS pathway, that activates the immune system in response to microbial and host DNA.

"By establishing in vitro assays to purify, clone and characterize new components of the NF-kB signaling pathway, Chen was the first to demonstrate that protein ubiquitination could have a regulatory role in signal transduction through protein kinase activation, distinct from the traditional role of ubiquitin in targeting protein degradation by the proteasome," said Eric Olson of UT-Southwestern in his nomination letter about Chen. Olson added, "Chen's most recent discovery of the cGAS pathway is especially thrilling and has important implications for numerous diseases."

Steven McKnight, a professor at UT–Southwestern and the ASBMB's president, said: "The Merck Award from the American Society for Biochemistry and Molecular Biology is one of its most coveted prizes. Past winners constitute a 'who's who' in the field of biomedical research."



I am thrilled and humbled to see my name next to my scientific idols who received the ASBMB–Merck award before me. It is a great honor to receive this award on behalf of a wonderful team of dedicated and talented students and postdoctoral fellows at UT–Southwestern who made the discoveries that are recognized by the award.

– ZHIJIAN "JAMES" CHEN

Chen earned his undergraduate degree in biology from Fujian Normal University in China. He earned a Ph.D. from the State University of New York at Buffalo. After spending the early years of his career in industry, he joined UT-Southwestern in 1997.

Chen previously won the Robert A. Welch Foundation Norman Hackerman Award in Chemical Research in 2005, the National Academy of Sciences Award in Molecular Biology in 2012 and election to the National Academy of Sciences in 2014.

Chen will receive his ASBMB award at the Experimental Biology 2015 conference in Boston. He will present his award lecture, "Enemy within — immune and autoimmune responses to cytosolic DNA and RNA," at 8 a.m. Monday, March 30, in Ballroom West on the third level of the Boston Convention and Exhibition Center.

Umesh D. Wankhade (udvets@gmail.com) is a postdoctoral fellow at the National Institute of Health's diabetes, endocrinology and obesity branch.

BERT AND NATALIE VALLEE AWARD IN BIOMEDICAL SCIENCE

Eisenberg lauded for contributions to understanding of amyloid fiber structure and its role in neurodegenerative diseases

By Umesh D. Wankhade

David Eisenberg, a professor at the University of California, Los Angeles, is the second winner of the American Society for Biochemistry and Molecular Biology's Bert and Natalie Vallee Award in Biomedical Science.

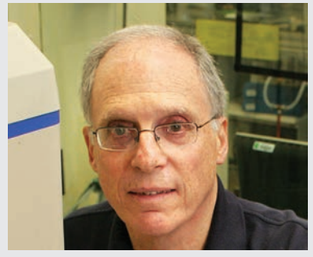
The award was established by the Bert and N. Kuggie Vallee Foundation in 2012 to recognize established scientists with outstanding accomplishments in basic biomedical research. Eisenberg's research focuses primarily on protein interactions as well as the structural underpinnings for the conversion of normal proteins to the amyloid state and the conversion of prions to the infectious state.

Sabeeha Merchant and James Bowie at UCLA, who nominated Eisenberg for the award, said in their nomination letter, "David's achievements are truly remarkable, not only because of their enormous fundamental impact on the fields of medicine, but also because success was so improbable. He has transformed the field of amyloid diseases and is exceedingly deserving of this recognition."

In 2005, Eisenberg's group published the first atomic-resolution structure of an amyloid fiber. His work led to other researchers determining the atomic-level structures of more than 100 other fibers. These structure determinations have revolutionized the field.

Eisenberg's work enabled the development of algorithms to predict segments of proteins with high propensity to form amyloid fibers and provide useful hypotheses for amyloid-forming mechanisms in many disease-related proteins. His research also opened up the possibility of true atomic-level drug-design approaches to prevent fiber formation. Eisenberg's group has worked on drug design too, and several candidates are in development.

Although Eisenberg started his career looking at protein structure and binding affinity, he developed an interest in the role of aberrant proteins in neurodegenerative diseases. Eventually, his combined passion for medicine and basic research led him to consider fundamental scientific questions about neurodegenerative diseases.



How nice it is to receive an award named for a scientist whose lectures I heard when I was an undergraduate. But my name as the sole recipient masks the fact that the recognized work is the product of more than a dozen scientists in our group. Perhaps more than most laboratories, we work as a group, with diverse backgrounds and skills combining to produce each finding. We tackle hard problems, gaining confidence from each other that we can overcome the obstacles that we invariably encounter along the path. Much of my pleasure in science comes from our cooperative mode of scientific discovery.

– DAVID EISENBERG

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Eisenberg began his career as an undergraduate at Harvard University under the tutelage of protein scientist John Edsall. He became interested in the computational and physical sciences as well as the biochemical sciences. Eisenberg went on to get a D. Phil. at Oxford University in the U.K. In 1989, he was elected to the National Academy of Sciences. He has received numerous awards, such as the Amgen Award of the Protein Society in 2000 and the Harvey International Prize in Human Health in 2009.

Eisenberg will receive his award at the ASBMB annual meeting, held in conjunction with the the Experimental Biology 2015 conference in Boston. He will deliver an award lecture, "The amyloid state of proteins," at 8:45 a.m. Monday, March 30, in Ballroom West on the third level of the Boston Convention and Exhibition Center.

Umesh D. Wankhade (udvets@gmail.com) is a postdoctoral fellow at the National Institute of Health's diabetes, endocrinology and obesity branch.

WILLIAM C. ROSE AWARD

Matthews recognized for 'total lack of selfishness, her openness and frankness'

By Elizabeth Meier

The American Society for Biochemistry and Molecular Biology has chosen Kathleen S. Matthews at Rice University as the recipient of the William C. Rose Award for her groundbreaking biophysical and biochemical research on DNA-binding proteins, particularly Escherichia coli repressor proteins and the Hox protein Ultrabithorax from Drosophila melanogaster.

The Rose award recognizes exceptional contributions to biochemical and molecular biological research as well as an investment in the training and education of young scientists.

"I feel strongly that (Matthews') work over the past 40 years has established in textbook detail the molecular mechanisms for allosteric induction of the E. coli lac operon by sugar and DNA binding to LacI," said John S. Olson of Rice University, who nominated Matthews for the award.

Matthews graduated from the University of Texas at Austin with a B.S. in chemistry in 1966 and earned her Ph.D. in biochemistry from the University of California, Berkeley, in 1970. She joined Rice University as a faculty member in 1972 and today is the Stewart Memorial professor there.

"Along the way, Kathy became interested in other bacterial repressors, eukaryotic transcription factors, Ubx and p53, and even proteins as materials, the studies of which … have provided reference points for her continuing understanding of lac repressor," explained Catherine Royer of Rensselaer Polytechnic Institute, who collaborated with Matthews as a graduate student at the University of Illinois.

In addition to her significant scientific contributions, the award recognizes Matthews' outstanding mentorship to emerging scientists. She has supervised 33 Ph.D. students, 21 of whom were women or minorities, three female M.A. students, and more than 130 undergraduate students, more than half of whom were women or minorities. She has also won numerous universitywide teaching awards, including three esteemed George R. Brown awards for superior teaching.

Furthermore, Matthews helped found the National Science Foundation-sponsored ADVANCE program to increase the number of women and minorities at Rice University's Schools of Natural Science and Engineering and to provide support and mentoring for new faculty members.

This honor is especially meaningful because it encompasses so many former students and colleagues, whose passion and diligence have shaped the direction of work in my laboratory. This recognition also reminds me of my gratitude for the special guides who nurtured my own scientific growth. Mentoring has been a constant joy and a deep source of energy and passion for the research endeavor in my life, and more has been learned from this process than was given!

– KATHLEEN S. MATTHEWS

"I can attest to her total lack of selfishness, her openness and frankness, and the very strong example she sets for scientific quality and ethics," Royer said.

Matthews has been a fellow of the American Association for the Advancement of Science since 1996 and served on the editorial board of the ASBMB's Journal of Biological Chemistry from 1989 to 1994 and as an associate editor from 1994 to 1999. She led Rice University's biochemistry and cell biology department from 1987 to 1995 and served as dean of its Wiess School of Natural Sciences from 1998 to 2009. Simultaneously, she helped found the Keck Center for Computational Biology and the Gulf Coast Consortia, which support many successful graduate-student and postdoctoral training and research programs in the larger Houston area.

Matthews will give her award lecture at the ASBMB annual meeting in conjunction with the Experimental Biology conference in Boston. Her lecture, "A tale of two proteins," will be at 2:30 p.m. Monday, March 30, in the Ballroom West on the third level of the Boston Convention & Exhibition Center.

Elizabeth Meier (meier.lizzie@gmail.com) is a third-year Ph.D. student at Johns Hopkins School of Medicine, where she studies bacterial cell division in Erin Goley's lab.

ALICE AND C.C. WANG AWARD IN MOLECULAR PARASITOLOGY

Cowman 'a world leader in malaria research'

By Maggie Kuo

Alan F. Cowman, professor and head of the Division of Infection and Immunity at the Walter and Eliza Hall Institute of Medical Research in Melbourne, Australia, is the recipient of the 2015 American Society for Biochemistry and Molecular Biology's Alice and C.C. Wang Award in Molecular Parasitology.

The award is given to researchers who have made significant contributions to the field of molecular parasitology. Recipients of this award are internationally recognized scientific leaders who have made important discoveries in the field and continue to lead the forefront of research in the area. Cowman was awarded for his work on understanding Plasmodium falciparum, the protozoan parasite that causes the most severe form of malaria in humans.

"Professor Alan Cowman has made a number of profoundly important discoveries over the past 25 years of his research career in malaria that see him recognized as one of the very top, possibly the actual top, in the field internationally," Brendan Crabb of the Burnet Institute wrote in his letter of support for Cowman's nomination.

Malaria is a mosquito-borne infectious disease that is a major cause of illness in approximately 100 countries. More than 300 million people are infected by the parasite, and up to 800,000, mostly children, die every year.

From the start of his career, the findings and technologies produced from Cowman's laboratory have been revolutionary for the field of malaria biology. His early work identified mutations in P. falciparum genes that conferred resistance to anti-malarial drug compounds. "The work provided an understanding of the evolution of resistance to those compounds and, as a direct result, provided the information to allow the study of the geographical spread and emergence of drug resistant P. falciparum in endemic areas, giving rise to a new field of molecular epidemiology," Doug Hilton of the Walter and Eliza Hall Institute of Medical Research wrote in his nomination letter.

Cowman's laboratory was the first to create a genetic knockout in P. falciparum by genetically manipulating its genome. The feat was followed by

It is a great honor to receive the Alice and C.C. Wang award, and I thank Alice and C.C. for their continued support of parasitology research. This award recognizes the many talented graduate students and postdocs who have been so pivotal to the work done by the lab over the years. I would like to thank them and the many collaborators with whom I have worked.

– ALAN F. COWMAN

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the first large-scale knockout screen in malaria biology. The screen identified proteins key to the parasite's survival in the host. "This was a significant leap in the field, and the genetic technology he created is now used in every malaria research laboratory in the world," Hilton continued.

The impact of Cowman's work expands beyond the scientific community into the realm of public health. The tools developed during his early work to monitor molecular markers of drug resistance have been used to determine which drugs would be most effective in patients in specific endemic areas. Using the genetic technology he had developed, Cowman and his laboratory collaborated with Stefan Kappe at the Seattle Biomedical Research Institute to create the first genetically engineered live attenuated malaria vaccine. The vaccine has completed Phase 1 clinical trials, which were funded by the Bill and Melinda Gates Foundation and the Grand Challenges Foundation.

The quality of his work is reflected in his extensive publication record, with many in the "world's most prestigious scientific journals, where they belong," B. Brett Finlay of the University of British Columbia wrote in his letter of support. This award will add to a long list of honors already bestowed upon Cowman, including induction as a Howard Hughes Medical Institute International Scholar, a fellow of the Australian Academy of Science and a fellow of the Royal Society.

"Working in a highly competitive field, on an organism that is notoriously difficult to manipulate, his laboratory relentlessly makes significant leaps in our understanding of malaria pathogenesis," Finlay wrote. "These breakthroughs have changed people's lives and health outcomes – something very few researchers can ever hope to claim in their lifetime."

Cowman received his Ph.D. from the Walter and Eliza Hall Institute of Medical Research. After a postdoctoral fellowship at the University of California, Berkeley, Cowman returned to the institute and has been there since.

Cowman will receive his award during the 2015 Experimental Biology conference in Boston, where he will deliver his award lecture. The presentation, titled "Moving in and renovating: invasion and remodeling of the human erythrocyte by the malaria parasite," will take place at 9:45 a.m. March 30 in the Boston Convention and Exhibition Center, Room 253 A.

Maggie Kuo was an intern at ASBMB Today when she wrote this story. Today she is a writer at the American Physiological Society. She earned her Ph.D. in biomedical engineering at Johns Hopkins University.

MILDRED COHN AWARD IN BIOLOGICAL CHEMISTRY

Klinman touted for 'her willingness to set aside old theories and embrace new theories'

By Elizabeth Meier

Judith Klinman of the University of California, Berkeley, won the American Society for Biochemistry and Molecular Biology's Mildred Cohn Award in Biological Chemistry for her far-reaching contributions to the field of mechanistic enzymology.

The Cohn award honors the scientific accomplishments and character of the late Cohn, the first president of the ASBMB. The award recognizes scientists who have advanced significantly the understanding of biological chemistry using innovative physical approaches.

"Judith Klinman's accomplishments truly parallel those of Mildred Cohn, with respect to outstanding scientific achievement and advancing the cause of women in science," affirmed Natalie G. Ahn of the University of Colorado Boulder, who nominated Klinman for the award. "As the first woman professor in any of the physical sciences at UC Berkeley, the first tenured female professor in the UC Berkeley chemistry department and later as the first woman chair of the chemistry department, she has been instrumental in changing attitudes toward women in science."

Klinman earned her Ph.D. in organic chemistry from the University of Pennsylvania in 1966. Thereafter, she pursued postdoctoral studies at the Weizmann Institute of Science in Israel in physical organic chemistry and at the Fox Chase Cancer Center in biochemistry. In 1978, she began her professorship at UC Berkeley, where she remains to this day.

In his letter of support of Klinman's nomination, Amnon Kohen of the University of Iowa emphasized "her discoveries of new biological cofactors that result from auto-catalyzed post-translational modification of natural amino acids; the elucidation of quantum mechanical effects in biological catalysis, and the identification of protein motions as the next critically under-understood area in enzymology."

JoAnne Stubbe of the Massachusetts Institute of Technology added, "Judith's contributions have received international recognition and have established her as arguably the best chemist studying detailed enzymatic mechanisms, in the world."

Klinman's pioneering discoveries have positioned her both at the forefront and interface of chemistry, biochemistry and biophysics.

"One of the most admirable characteristics of Judith is her willingness to set aside old theories and embrace new theories in an effort to explain the experimental data and understand the underlying fundamental principles," said Sharon Hammes-Schiffer from the University of Illinois at Urbana-Champaign.

A member of both the American Academy of Arts and Sciences and the National Academy of Sciences, Klinman served as the president of the ASBMB from 1998 to 1999. She has received many awards, including the Merck Award from the ASBMB in 2007 and the National Medal of Science in 2014.

Previous Cohn award recipients include Lila M. Gierasch (2014) and Jennifer A. Doudna (2013).

Klinman will give an award lecture at the ASBMB annual meeting held in conjunction with the Experimental Biology conference in Boston. Her lecture, "Moving through barriers: unlocking the mysteries of how enzymes really work," will be at 2:30 p.m. Sunday, March 29, in Ballroom West on the third level of the Boston Convention & Exhibition Center.

Elizabeth Meier (meier.lizzie@gmail.com) is a third-year Ph.D. student at Johns Hopkins School of Medicine, where she studies bacterial cell division in Erin Goley's lab.

I am deeply honored to be this year's recipient of the Cohn award. Mildred prevailed in the absence of opportunities for women in science, was a model for how women can successfully combine family with career, worked alongside many giants in biochemistry and pioneered the use of NMR to understand enzyme mechanism. She was a remarkable scientist and mentor whose deep understanding of science and the world were an inspiration to me and all who were privileged to know her!

– JUDITH KLINMAN

WALTER A. SHAW YOUNG INVESTIGATOR IN LIPID RESEARCH AWARD

Brügger lauded for 'execution of quality science and outstanding productivity'

By Samarpita Sengupta

Britta Brügger of Heidelberg University is the winner of the American Society for Biochemistry and Molecular Biology's Walter A. Shaw Young Investigator in Lipid Research Award for her work on lipid-protein interactions and lipid sorting.

"Britta Brügger is simply a winner," declared Vytas A. Bankaitis of the Texas A&M Health Science Center, who nominated Brügger for the award. Brügger's work, which showed that the binding of the transmembrane domain of the p24 cargo receptor proteins to a specific molecular species of sphingomyelin is of functional significance, is "a real tour-de-force," Bankaitis said, "that has broad implications for protein-lipid interactions in integral membrane proteins."

Using quantitative lipidomic strategies, Brügger's group has achieved several exciting new discoveries. It found that HIV-1 morphogenesis requires a specific lipid microenvironment, that p24 cargo receptors need specific lipid-protein interactions, and that sphingomyelin nanodomains exist and are defined by the interactions of specific sphingomyelin species with cholesterol. Bankaitis described Brügger's studies as original and impactful and the result of longstanding collaborations. Not only has Brügger demonstrated excellent scholarship in her career, he said, but she also has "amply demonstrated execution of quality science and outstanding productivity."

Brügger earned her undergraduate degree in Germany at Frankfurt University. She earned her Ph.D. in the laboratory of Felix Wieland at the Ruprecht Karls University in Heidelberg. After a two-year postdoctoral

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fellowship at the Sloan Kettering Institute in the laboratory of James E. Rothman, Brügger returned to Germany and the lab of her graduate mentor. In 2002, she took a staff-scientist position at the Heidelberg University Biochemistry Center. In 2014, she accepted a faculty position at Heidelberg University, and she is now a dean there.

With several publications in top-tier journals, memberships in academic societies and now awards, Brügger has left her mark in the field of lipid research already. Despite being so successful, Bankaitis said, Brügger is modest and humble. She is careful in her analysis and does not overstate her science, he added.

Bankaitis also said that, given the opportunity, he would value Brügger's contributions to his students' thesis committees. "I always counsel my students in the importance of choosing the right faculty for their committees, that they should choose faculty whose scientific insight they respect, that their committee members be well respected by the broader scientific community, that their committee members be available to them for scientific interaction, that their committee members be easy to interact with, and that their committee members exhibit the scientific honesty of providing the critical input needed," he explained. "Frankly, I find faculty who fit all of these criteria to be in short supply. My opinion is that Britta Brügger is one such faculty member. As a matter of principle, is there any higher compliment one can offer a colleague than seeking his/her counsel in the training of one's graduate students?"

Instituted in 2010, the Walter A. Shaw Young Investigator in Lipid Research Award, named after the founder of Avanti Polar Lipids, recognizes scientists with 10 or fewer years of experience who have made significant contributions to lipid research. The winner each year is invited to give a talk at the society's annual meeting and receives a plaque and a cash prize of $2,000. Mary L. Kraft won the award last year.

Brügger will give her award lecture, titled "From lipidomics to cellular functions: lipids as modulators of protein activity," at the ASBMB annual meeting in Boston. She will give her talk during the "Lipid magic: How do they do it?" symposium at 1:15 p.m. Wednesday, April 1, in Room 252A/B of the Boston Convention & Exhibition Center.

I am thrilled and very honored to be this year's recipient of the Walter Shaw Young Investigator Award. I share this award with my co-workers in the laboratory and am grateful to my collaborators for their important contributions, helping us to study protein-lipid interactions in a truly interdisciplinary way. Many thanks also to the German Research Foundation. Without its support, this work wouldn't have been possible.

– BRITTA BRÜGGER

Samarpita Sengupta (samarpita.sengupta@utsouthwestern.edu) is a postdoctoral fellow in the pediatrics department at the University of Texas-Southwestern Medical Center at Dallas.

DELANO AWARD FOR COMPUTATIONAL BIOSCIENCES

Folding@home founder Pande 'a creative leader in molecular dynamics'

By Preethi Chander

Vijay Pande, the mastermind behind the Folding@home project, is the 2015 DeLano Award for Computational Biosciences recipient. This award recognizes Pande, a professor of chemistry at Stanford University, for his innovative development of computational technologies that enable life-science research at the molecular level.

The Folding@home project pushes the frontiers of scientific crowdsourcing. Molecular dynamics techniques used to explore questions in protein folding and computational drug design require large amounts of computational power. The Folding@home project uses the idle processing power of thousands of volunteered computers around the world; each solves subtasks within the greater problem. These simulations are of great interest in disease research, such as that into Alzheimer's, Huntington's and cancer.

"He built a novel vision and an important enterprise in computational biology," said Ken Dill of Stony Brook University, who nominated Pande for the award. He "has gotten thousands of people involved in caring about protein structures and pharmaceutical discovery and wanting to help."

Born in Trinidad to Indian parents, Pande trained as a physicist. He earned his bachelor's degree in physics from Princeton University and his Ph.D. in physics from the Massachusetts Institute of Technology. At MIT, where he also completed a postdoctoral fellowship, he worked under Toyoichi Tanaka and Alexander Yu Grosberg.

Along with exploring questions in theoretical and biophysical chemistry, Pande pushes the limits of supercomputing paradigms. Folding@home has become the most powerful supercomputer cluster in the scientific world. Recently, Pande teamed up with Google to use its cloud-based computer systems to simulate the receptor-site transformations in G-protein-coupled receptors. Also, in collaboration with Pande's lab, Sony just released its Folding@home app for smartphones, which can be downloaded from Google Play.

John Kuriyan at the University of California, Berkeley, who wrote in support of Pande's nomination for the award, described Pande as "one of the most prominent of the current generation of leaders in the field and certainly one of the most creative."

Pande will receive the award at the ASBMB annual meeting, held in conjunction with the Experimental Biology conference, in March in Boston. His award lecture, titled "Understanding protein folding yields important insights into protein conformational changes," will be at 8:45 a.m. Tuesday, March 31, in Room 253 A/B/C of the Boston Convention & Exhibition Center.

I'm truly honored to receive the 2015 DeLano award. I got to know Warren DeLano and greatly appreciated his vision for scientific software. That vision has made an impact in my own work and in countless others throughout the world.

– VIJAY PANDE

Preethi Chander (chander.preethi@gmail.com) earned a Ph.D. in structural biology from Purdue University and completed a postdoctoral fellowship at the National Institutes of Health. She works at the National Institutes of Health, Bethesda, Md., as a health science program administrator.

RUTH KIRSCHSTEIN DIVERSITY IN SCIENCE AWARD

JoAnn Trejo recognized for her support of underrepresented minorities

By Joseph P. Tiano

The American Society for Biochemistry and Molecular Biology named JoAnn Trejo at the University of California, San Diego, the winner of the Ruth Kirschstein Diversity in Science Award. The award recognizes outstanding scientists who show a strong commitment to mentoring and encouraging underrepresented individuals to enter the sciences.

Trejo was the youngest of five children in a family of migrant farm workers led by a single mother with little education. She credits her mother's strong work ethic along with her teachers' support for helping her become a leading educator and world-class researcher in the field of molecular pharmacology. "These principles served her well and have guided all aspects of her life," said Susan S. Taylor, who nominated Trejo for the ASBMB award. "(She) has continued to be remarkable not only for her creative research that is pioneering new frontiers at the interface between lipids, proteins and membranes but also by her dedication to academics and to underrepresented students and fellows in particular."

Trejo earned her bachelor's degree in toxicology and biochemistry at the University of California, Davis. She then earned her Ph.D. in the lab of Joan Heller Brown at UCSD. When Trejo was challenged in those early years, Brown said, "she really showed her colors, responding in ways that truly proved her capabilities." Trejo then completed a postdoc in the lab

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of Shaun Coughlin at the University of California, San Francisco, where she focused on vascular cell biology.

She took her first faculty position at the University of North Carolina, Chapel Hill, in 2000 and then moved to UCSD, where she was promoted to professor a few years ago.

Throughout her academic career, Trejo has been a champion for diversity. She has trained 25 students and fellows and 23 undergraduates, many of whom were women and from groups underrepresented in science. "Her own experiences have transformed her into a passionate advocate for (underrepresented minorities), and she has used this passion creatively to mentor at all levels and to build new programs and new awareness in her colleagues," Taylor said.

Trejo is a member and served as the diversity coordinator of UCSD's umbrella Biomedical Sciences Graduate Program and the Medical Scientist Training Program. In addition, she is active on many national advocacy committees, including the American Society for Cell Biology's Women in Cell Biology and Minority Affairs committees, the Society for the Advancement of Chicanos and Native Americans in Science, and the Keystone Symposia Diversity Advisory Committee.

In 2013, Trejo became director of the Institutional Research and Academic Career Development Award, or IRACDA, Postdoctoral Training Program at UCSD. IRACDA is a unique National Institutes of Health-sponsored program designed to develop a diverse group of highly trained scientists to address the nation's biomedical research needs, and this position represents a tremendous honor for Trejo and reflects her commitment to diversity in science. Trejo received the 2014 UCSD Chancellor's Award for Excellence in Postdoctoral Scholar Mentoring.

Trejo's research focuses on understanding the regulation of G protein-coupled receptor signaling, specifically the mechanisms responsible for regulating signaling by protease-activated receptor-1. PAR1 is a GPCR for the coagulant and anticoagulant proteases. Trejo has made numerous novel discoveries related to the regulation of GPCR signaling and has published more than 60 papers on this topic.

Trejo has led two Gordon Conferences; has received many honors, including the American Heart Association's Established Investigator Award; and has given many keynote addresses.

Trejo will receive her award during the Experimental Biology 2015 conference in Boston. Her award lecture, "Exploring GPCR-biased signaling from inside and outside the cell," will take place at 3:05 p.m. Sunday, March 29, in the Ballroom West on the third level of the Boston Convention and Exhibition Center.

I am truly honored to receive the Ruth Kirchstein Diversity in Science Award. Diversity is imperative for the advancement of science and we must cultivate talent with inclusion of individuals from across the social spectrum. Ruth Kirchstein was a champion for individuals underrepresented in science and receiving this award is a real inspiration.

– JOANN TREJO

Joseph P. Tiano (tiano233@hotmail.com) is a postdoctoral fellow at the National Institute of Diabetes and Digestive and Kidney Diseases in Bethesda, Md.

DEFYING STEREOTYPES

The scoop on Ben & Jerry's co-founder Jerry Greenfield

By Rajendrani Mukhopadhyay and Geoffrey Hunt

Stacks of Ben & Jerry's ice-cream pints fill grocery-store freezers around the world, the sky-blue containers embellished with fluffy white clouds and flavor name puns hinting at the brand's quirky irreverence. So it might come as a surprise that a critical part of the brand's global success is rooted in the staid world of science. "My biochemistry background allowed me to come up with the world-famous Ben & Jerry's ice-cream formula," asserts Jerry Greenfield.

With his friend and business partner Ben Cohen, Greenfield parlayed the scientific knowledge he gained as a lab technician and medical school hopeful into the development of the internationally renowned ice cream. There now are more than 600 Ben & Jerry's scoop shops in 35 countries, and annual sales of the ice cream reach $500 million.

Rejection

Greenfield and Cohen met in junior high school in the 1960s in upstate New York, where they were, according to Cohen, the "two slowest, fattest kids in gym class." While Cohen didn't have much interest in school (and eventually dropped out of college to become a potter), Greenfield had an aptitude for math and science. Because he "wasn't driven to do something else," Greenfield decided to become a doctor.

The first step in the process was to get a bachelor's degree in biology from Oberlin College in Ohio. To bolster his medical-school applications, Greenfield then did stints as a technician in biochemistry labs at the Public Health Institute of the City of New York and the University of North Carolina.

But his lack of passion and drive for medicine was apparent. Greenfield freely admits he was "a middle-of-the-pack kind of person" and was rejected from medical schools twice. "I give the admissions people from all these medical schools a lot of credit for seeing that my future was going to be much better served somewhere else," says Greenfield, his amusement apparent.

Meanwhile, Cohen was unsuccessful at trying to sell his pottery. "We probably had no choice but to start our own business," he recalls. The friends contemplated opening a restaurant because, as Cohen wryly notes, "the only thing we were really interested in doing was eating." But a friend informed them that breaking into the restaurant business was tough and suggested instead that they focus on making a single food item.

So Cohen and Greenfield turned their attention to bringing a big-city food trend to the rural college-town setting in which they both hoped to live. In the 1970s, the trendy choices were either bagels or home-made ice cream. The machinery for bagels was too expensive. That left ice cream.

Jerry Greenfield IMAGES COURTESY OF BEN & JERRY'S

Informal ice-cream education

In 1977, Greenfield and Cohen each plopped down $2.50 to pay for a correspondence course from Pennsylvania State University on how to make ice cream. They next splurged on the textbook "Ice Cream," the so-called bible of ice-cream making written by Wendell S. Arbuckle, a professor of dairy science at the University of Maryland. Arbuckle and his wife, Ruth, were so famous for their knowledge of ice cream that they were known as "Mr. and Mrs. Ice Cream."

Their studying complete, Greenfield and Cohen set out to establish the now-iconic Ben & Jerry's ice cream. Greenfield applied his scientist scrutiny to the tiniest details of the process, focusing in particular on the workings of the single five-gallon ice-cream maker he and Cohen had at their disposal. "Jerry's knowledge

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In the early days of Ben & Jerry's, the duo made their ice cream in old-fashioned machines like this one.

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of science and math really came in handy," Cohen acknowledges.

During the late 1970s, other ice-cream makers were pooh-poohing the old-fashioned freezing method, in which the outside of an ice cream maker barrel is packed with ice and rock salt while the internal dasher churns and whips the ingredients. Convinced that the ice-and-rock-salt mix was still workable, Greenfield pressed ahead with a method that commercial ice-cream makers thought would work only in people's homes.

Additional tinkering with the freezing process, again informed by Greenfield's knowledge of scientific processes, helped the duo with another aspect of the signature ice cream. "Part of what makes ice cream smooth and creamy is that there is air whipped into ice cream," points out Greenfield. The balance of air, water and solid must be just right to make the ice cream rich and dense. "The larger the ice crystals are, the more icy and granular the ice cream tastes. That's something you don't want," cautions Greenfield.

Just as important was the flavor. Cohen and Greenfield experimented extensively to come up with the perfect recipe, incorporating various mixtures of milk fat, egg yolks, sugar and water along with chunks of cookies and candy (Cohen's preferred childhood additive).

The Americone Dream

The perseverance and hard work paid off in 1978 when Ben & Jerry's opened its first ice-cream parlor in a repurposed gas station in Burlington, Vt. "We were doing everything in this very small machine and doing everything by hand," Greenfield recalls. As the scoops became more popular and demand began to rise, Greenfield says that the company had to pay attention to ensure that they got the same quality of ice cream from the higher-volume manufacturing processes.

The first franchised Ben & Jerry's scoop shop opened in 1981 in Shelburne, Vt., and the company continued to expand. Ten years after they opened their first parlor, Greenfield and Cohen were named the "U.S. Small-Business Persons of the Year" by President Ronald Reagan in a White House Rose Garden ceremony. Ben & Jerry's now offers more than 70 unique flavors, including Cherry Garcia, Karamel Sutra and, Greenfield's own favorite, Americone Dream.

Greenfield and Cohen sold their company to the consumer goods conglomerate Unilever in 2000, but Greenfield says Ben & Jerry's retains its reputation of being "a little offbeat, unconventional, irreverent and antiauthoritarian." He acknowledges that such impudence would not have flown in his original chosen field of medicine. "I think Ben & Jerry's has gotten a lot of freedom to create the kind of business we want to create and do it with our own rules that people in science, and certainly doctors, don't have."

Nonetheless, Greenfield proudly states, his training "was put to incredibly good use." Millions of satisfied customers agree.

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Teaching old (and new) dogs new tricks

The benefits from attending an ASBMB student-centered education symposium

By James T. Hazzard

The American Society for Biochemistry and Molecular Biology will host its fourth undergraduate education meeting July 30 through Aug. 2 at Missouri Western State University. Society members might reasonably ask, "How does the ASBMB benefit from sponsoring these meetings?" That is best answered by the title to the 1964 Bob Dylan song "The Times They Are A-Changin'," which perfectly describes the attitude driving transformations in the field of science education, for which many in the ASBMB have been strong advocates.

Beginning with the publication of "BIO 2010" and more recently with the release of "Vision and Change," sponsored by the American Association for the Advancement of Science, calls have gone out urging educators to transform the way we disseminate information to undergraduates in our lecture and laboratory courses (1, 2).

A recent Science magazine report entitled "Lectures aren't just boring, they are ineffective, too" (3) indicated that the era of the talking-head, 50-minute lecture format, which originated in the Middle Ages, is drawing to a close, replaced by a more student-centered and peer-learning approach to science education.

For our laboratory courses, science-education experts have been urging us to do away with the traditional methods-and-techniques programs and replace them with guided-inquiry, researchlike laboratory experiences, especially at institutions where these lab courses offer the closest thing students may have to a research project.

Not being an expert in the education field, I often find pedagogically focused publications filled with bewildering terminology and methods of statistical analysis that are quite foreign to my more physical-biochemistry-oriented mind. Often these same articles provide ample justification for changing your pedagogical approach without the nuts-and-bolts, how-to information.

Finally, being rather conservative, I initially viewed these calls for transformation at the annual ASBMB education-focused symposia with a great deal of skepticism. After all, I had designed from scratch a biochemistry laboratory course that received rave reviews from students, who often stated it was the best course they had ever taken at our university. How dare anyone suggest that we could design a better course? And several faculty members in my department told me bluntly, "If it ain't broke, don't fix it!"

The problem was that I began to have a nagging feeling that maybe, if it was not exactly broken, our lab course could perhaps be improved dramatically.

Finally, in 2009, I attended the first ASBMB-sponsored small education conference at Colorado College. The primary benefit of this education-focused meeting was that we were able to have meaningful dialogues (which have continued in the ensuing years) with people who actually had carried out such transformations in lecture or laboratory courses, resulting in much greater engagement of their students in the curriculum. It often is difficult to have these kinds of conversations at national meetings due to time constraints.

Another great aspect of attending this small meeting came about when, as part of a workshop headed by a National Science Foundation program director, we wrote proposals describing how we would use funding from that agency to alter one of our courses. This thought-provoking exercise was, for me, the beginning of a major overhaul of our biochemistry laboratory course, which has since gone from a traditional method-and-technique-based course to one in which 60 percent of the semester is devoted to a guided-inquiry, researchlike experience.

Now when students join our class at the beginning of the semester, rather than saying, "You will learn how to do this and that," we tell them they are joining a long-term research project for which the ultimate objective is to produce site-specific mutations of E. coli alkaline phosphatase. In a similar manner, my whole approach to the biochemistry lecture course that I teach to nonmajors two semesters a year has gone from a traditional 50-minute talking-head model to one in which students interact much more in peer groups solving problems and discussing key concepts.

These changes have not all occurred overnight; rather they have evolved (and continue to evolve) through small, discrete modifications. As in any long journey, you have to take the first step, and a very good step for any new faculty members, postdoctoral students or graduate students who envision themselves teaching undergraduates is to attend the upcoming Transforming Undergraduate Education in the Molecular Life Sciences meeting in July.

I would suggest that established faculty members who are wondering what the pedagogical-transformation ruckus is all about attend as well. Your eyes certainly will be opened to some fantastic new educational concepts. And if you are willing to open your minds to the fact that there just may be a better way to disseminate your course material, you too will get to experience classes that a lot more fun to teach.

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Practicing best practices

IMAGE COURTESY OF MICHAEL CARASTRO, UNIVERSITY OF TAMPA

An-Phong Le of Florida Southern College (left), Sergiy Borysov of the University of South Florida (center) and Jewels Morgan of Georgia State University (right) participate in the Designing Scientific Teaching Tools for BMB Education workshop in Tampa, Fla., in January. The 20 attendees broke into groups. Each developed a broad learning goal, specific learning objectives, expected outcomes and assessment questions, and tools. Later, each presented its work. For a detailed report on the event and its outcomes, visit www.asbmb.org/education/enzymatic.

Inspiring students with disabilities to earn STEM doctoral degrees

'Simple accommodations can create a dramatic difference'

By Sharon Rozovsky

My colleague Karl Booksh and I are the organizers of an undergraduate research experience program that offers students with disabilities scientific internships, advice and connections with other students who face similar life circumstances. Last year, we advertised the program nationally and ran it for the first time in its full scope with eight students.

The program's long-term goal is to increase the participation of students with disabilities in science, engineering, technology and math professions. It combines conventional aspects of undergraduate research programs with the added layer of forming a community willing to discuss specific themes shared by this particular group.

Each participating student worked for eight weeks with a research group and presented his or her work at the end of the summer. The student I mentored came with a large and very lovable service dog. The dog quickly became bored with the lab work, but the student and I had a lot of fun.

Despite my concerns, the group seemed to bond almost instantly. Participants were amazingly encouraging and treated each other much like brothers and sisters. Over time, they chose to disclose many personal experiences.

Getting the program off the ground

Karl and I started collaborating when I joined the department of chemistry in 2008, and we became good friends. We'd regularly chat after meetings to mend our discouragement over grant writing. During these conversations, Karl often described his mentoring activities with the community of scientists with disabilities and pondered out loud about what type of programs would be most effective to increase the participation of this community in STEM professions. I thought Karl's ideas were genuinely creative, and I asked if I could participate.

In the next few months, Karl and I wrote several grant applications to fund this program and also a separate program focusing on graduate training. The next year, we initiated the undergraduate program on a small scale, with only a few participants, using funds from our respective National Science Foundation grants. Subsequently, we won a dedicated grant from the NSF that helped us launch the full program this past summer.

'Learning the ropes'

Part of the NSF grant supported special accommodations, most of which were easy to anticipate ahead of time, such as the use of an American Sign Language interpreter and the construction of a small platform to wheel our friendly service dog, who stayed in a cage, in and out of the lab. However, some accommodations we hadn't initially thought about, like using an interpreter to describe the surroundings for the visually impaired during visits to museums and reducing environmental noise and dimming lights for students on the neurobiological spectrum. Luckily, the students had much patience for us as we were learning the ropes.

Simple accommodations can create a dramatic difference: meeting a student ahead of the program to familiarize him or her with the lab, covering travel expenses for a parent to help a student settle in, asking the student what information to share with group members. Some of the most frequent requests we had

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'An accumulation of societal and structural impediments'

By Karl S. Booksh

Two years ago, Sharon Rozovsky and I started an undergraduate research program at the University of Delaware for chemistry and biochemistry students with disabilities. This unique program offers research, mentoring and community-building opportunities to outstanding scholars who happen to have a recognized disability that impacts one or more aspects of their lives.

The core of the program is an eight-week residency laboratory experience culminating with a presentation at the university undergraduate research poster day. During the two months, we discuss the intersection between disability and career. Topics include navigating graduate school, research expectancies, and strategies for disclosure of disabilities and requesting accommodations.

I was impressed with how quickly the students integrated into their respective laboratories and formed a mutual support network. For most of the students, this was their first experience in a real research laboratory and their first experience being encouraged to consider graduate school. Furthermore, it was their initial first-hand encounter with the notion that people with disabilities can easily surpass societal expectations that limit their accomplishments.

'Far from typical'

Many view my path to the professoriate as typical, potentially ideal. Yet it was very different from the early career trajectories of most science, technology, engineering and math students with disabilities.

I did not grow up identifying as having a disability: I broke my neck the day after my 19th birthday while playing flag football during organized "reading day" activities before spring semester finals of my freshman year. I remember lying on the field, unable to feel my arms or legs, thinking, "Never let anybody see that you are hurt."

Such an attitude prompted me to spend the first part of my career denying that I had a disability and led me to approach challenges as if they were personal attacks rather than impersonal societal constructs. I spent the next summer in rehab at Craig Hospital in Denver learning how to navigate the world from a wheelchair with only minimal use of my hands.

I returned to classes at the University of Alaska, Fairbanks, the next academic year and graduated with a bachelor's — cum laude — in chemistry. My undergraduate research experience at UAF, with two published papers, led me to graduate school and a career as a university professor. I earned a doctorate from the University of Washington and completed a postdoctoral fellowship at the University of South Carolina before joining the faculty at Arizona State University.

Along the way, I was fortunate to find mentors who did not see my disability as a source of limitations. Instead, the faculty advisers saw my past successes as evidence of hard work, creativity and the ability to overcome obstacles. Consequently, honors and awards followed: National Science Foundation Graduate Research Fellowship Honorable Mention, American Chemical Society Graduate Fellowship, NSF Postdoctoral Fellowship, and Camille and Henry Dreyfus New Faculty Fellowship.

After I received tenure, I realized that my experience was far from typical for students with disabilities in STEM. While I saw many undergraduates identifying as having disabilities, I seldom noticed graduate students at national conferences or other institutions with visible disabilities. I did not hear tales of encouraging participation and inclusion.

Instead, their experience was of marginalization and the need to fight for access to a level playing field in each class. Some schools were worse than others, but nobody seemed to have had as ideal an experience as I did.

The few faculty members I knew who had progressed through school while identifying as having disabilities were all at smaller, less research-intensive institutions. To this day, I know of no other chemistry or biochemistry professor at an institution classified by the Carnegie Foundation as "very high research activity" who identified as having a disability as an undergraduate or graduate student.

'There is no single cause'

National demographics bear out these observations.

People with disabilities comprise 13 percent of the U.S. noninstitutionalized population between 18 and 49 years old. Students with disabilities are interested in STEM at the same proportion as students without disabilities (21.7 percent to 23.1 percent for matriculating freshmen and 20.3 percent to 21.3 percent for those entering graduate school). Yet less than 2 percent of STEM doctoral degrees from U.S. institutions are earned by students with disabilities. This statistic has not changed since the passage of the Americans with Disabilities Act in 1991. There are so few STEM postdocs with disabilities that the NSF does not present these demographics.

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I have come to believe that there is no single cause for the disproportionately low advanced-degree attainment in STEM for students with disabilities. Instead, there is an accumulation of societal and structural impediments that hinder progress for these students as a class.

Expectations for students with disabilities are lower; there is a relative lack of encouragement, mentoring and role models at all levels. Our belief in a meritocracy stigmatizes and prevents people from requesting needed accommodations, even when the accommodations are unrelated to the essential tasks at hand. Many institutions are still unprepared or unwilling to provide needed accommodations in a timely manner; students must anticipate, identify and negotiate accommodations anew each semester.

The availability of federal support for inclusion in STEM fields sends a strong message regarding the importance of broadening participation to institutions. The 2010 Federal Inventory of Funding shows a 20-fold difference between federal support targeted to underrepresented minorities in postsecondary STEM and that targeted to students with disabilities. (Perhaps not coincidentally, STEM doctoral attainment has been steadily increasing for blacks and Hispanics across the past 25-years while it has remained stagnant for students with disabilities.)

The Matthew Effect

Common assumptions by faculty members about the appropriate path to (and through) graduate school are biased against students with disabilities: students with disabilities are more likely to attend small undergraduate institutions, more likely to pursue their degrees part time, less likely to engage in undergraduate research, and less likely to be supported on a research assistantship awards in graduate school.

Furthermore, studies have shown that "solo status" (a feeling of isolation or being in a fishbowl when a person is the only member of an underrepresented group) and "stereotype threat" (feeling at risk of confirming the negative stereotypes of your underrepresented group) suppress the performance of underrepresented minorities. While people with disabilities in academia have not been explicitly studied, it is reasonable to assume such effects are in play.

The cumulative effect of such small societal and structural biases has been termed the Matthew Effect, inspired by the biblical passage regarding the rich getting richer and poor getting poorer. Research opportunities lead to local awards, which lead to more opportunities, which lead to larger awards and so forth. On the other hand, students who are impeded in their first few steps quickly fall behind and never regain an advantage in the race for recognition.

It is now en vogue to focus on just the negative side of the Matthew Effect and to contemplate how so-called microaggressions harm groups. But it is clear that the constant negotiating for accommodations, being split away from your peer group to receive accommodations and having to repeatedly defend your capabilities all take a toll on your ability to succeed and excel.

In a system where awards and honors are required to succeed, and given that these awards go to only the top 2 percent, it does not take much unintended bias to derail an exceptional candidate. However, I contend that the positive aspects of the Matthew Effect are personally empowering — each of us can reach out to one or two students a year and make a profound difference in career trajectories. Perhaps you will encourage a future colleague.

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were uncomplicated: securing single-occupancy rooms to allow for down time or providing direct contact with housing services.

Ultimately, the main challenge was no different than that encountered with any student we mentor: how to make research an educational and enjoyable experience given the student's personality and interests.

Group sessions

Unique to our program were discussions held in group meetings that concentrated on preparation for graduate school and how physical and learning disabilities may influence this choice.

Personally, my main apprehension involved group dynamics. Why would a group of strangers discuss personal questions of identity? Would discussions about disclosure and the definition of students with disabilities as a community be considered an intrusion? Would our students wish to share their experiences with us all? Would our group sessions feel contrived?

Despite my concerns, the group seemed to bond almost instantly. Participants were amazingly encouraging and treated each other much like brothers and sisters. Over time, they chose to disclose many personal experiences.

One group discussion that stood out was about disclosure: How and when should a disability be disclosed when applying to graduate school? How does disclosure factor into selecting a mentor or socializing with peer students?

Karl was instrumental in sharing insights from his many years of mentoring students with disabilities as well as his own personal experiences. Most students started out thinking they did not want their disabilities to define them or influence whether they were admitted into a graduate program. But many of us left thinking that the decision was more nuanced and complex than we originally perceived and tightly coupled with identity.

Should we not seek to be accepted for who we are? We are all part of a minority group, of a hierarchical power structure, and we all are concurrently insiders and outsiders. I am the outsider in our cohort, because I do not have a neurobiological or physical disability. Yet questions of inclusiveness, exclusiveness and self-identification lie at the heart of our program and are common to all of us. Being a part of this discussion still resonates with me.

Sharon Rozovsky (rozovsky@udel.edu) is an assistant professor in the chemistry and biochemistry department at the University of Delaware.

Advocating for equity in STEM

By Shaila Kotadia and Sabriya N. Rosemond

Nearly 200 women and a few men arrived at the University of California, Berkeley, last fall for an event called Expanding Potential: A Workshop on Navigating the Hurdles Faced by Women in STEM Fields. The all-day workshop, co-organized by the Synthetic Biology Engineering Research Center and the California Institute for Quantitative Biosciences at Berkeley, offered informational sessions, panels and a speed-networking session, all with the intent of opening the discussion about systemic issues that women face and promoting career development. Here we've collected some of the best pieces of advice and most compelling insights from speakers and attendees.

Implicit bias

Anne MacLachlan, a senior researcher with UC Berkeley's Center for Studies in Higher Education, defined implicit bias as a combination of unconscious beliefs that govern our attitudes and behavior toward others. If someone says something discriminatory, she said, you should ask him or her to repeat it. This allows that person to reflect on his or her language, thereby focusing on how the comment may come across with an unintended negative connotation. This removes the blame and turns the focus away from the person who received the statement and instead makes the assailant take responsibility for his or her poor choice of words.

Imposter syndrome

Maria Padilla from UC Berkeley's Office of Harassment and Discrimination said most people with impostor syndrome are successful, but they feel like frauds or that they don't belong. The climate of the workplace and the fear that you are in a program or lab only to meet a demographic quota are two factors. This presentation sparked discussion between undergraduates and higher-level STEM attendees on how to employ effective approaches to cope with impostor syndrome, confirming the age-old advice that peer support is key to retention.

Beyond teachable moments

Julia Chang, a Ph.D. candidate at UC Berkeley, bristled at the idea that victims of discrimination should turn those incidents into teachable moments. "(I) felt like individuals were being evaluated on how well they are able to turn these micro- and macro-aggressions into teachable moments, rather than strategize about policies that would hold the people in positions of power — the ones likely to hold and state discriminating views — accountable to do better." This criticism highlights a topic brought up several times during the workshop about the age difference between some of the speakers and attendees. Younger women are less accepting of the norms for dealing with micro- and macro-aggressions, which suggests that a positive shift is taking place in the STEM landscape toward standing up for one's right to fair treatment.

Handling harassment

Both MacLachlan and Padilla recommended seeking out institutional offices that handle harassment and becoming familiar with harassment policies. For example, Title IX is not exclusive to sports and can be used as a basis to fight harassment that occurs in the workplace. Seek out individuals at your host institution who specialize in enforcing these laws to fight against unlawful behavior.

Negotiation is expected

Alan Sachs of Life Technologies insisted that "it is expected that you negotiate" when you're up for a new job. "What's not expected is that you will take the first offer and say nothing." Remember, he added, that a counteroffer can extend beyond your salary to include various "intangibles," including stock options, moving costs, vacation time, bonuses and so forth. Sachs insisted that people not be afraid to negotiate, because once a company makes an offer it is unlikely to retract it. After all, he said, the worst that it will do is say no.

Learn more about the inaugural Expanding Potential workshop and watch videos of the speakers at synberc.org/expanding-potential.

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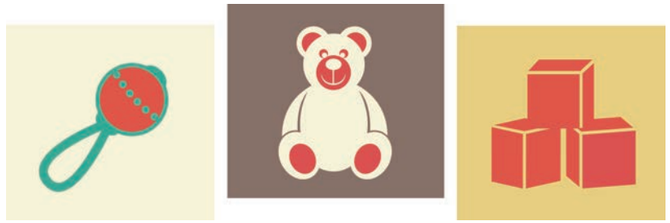
Shaila Kotadia (skotadia@berkeley.edu) is the education and outreach manager, and Sabriya N. Rosemond (sabriya.rosemond@gmail.com) is the diversity fellow for the Synthetic Biology Engineering Research Center. Both co-organized the Expanding Potential workshop.

From diapers to dissertation

Having a baby in graduate school

By Jen McGlaughon



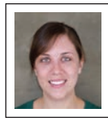
Just like most fifth-year graduate students, I have a number of things on my mind: writing my thesis, finishing projects and figuring out what to do after graduation. However, in the past several months, you might say my mind has become occupied with a few other things as well: baby names, nursery themes, daycare facilities, and the list goes on.

After much consideration, my husband and I made the decision to have a baby while I was still in school. This was not a choice that came easily or quickly. In fact, I can remember many sleepless nights wondering if we knew what we would be getting ourselves into. Before coming to this decision, I had to reevaluate the timeline that 10 years ago I had somehow established in my mind: go to graduate school, get married, find a job, buy a house and then start a family, in that order. As I approached my fifth year of graduate school and a 30th birthday, I wondered: Who says it has to be done in a certain order? There are plenty of graduate students, including several in my own program, who have become mothers while working on a Ph.D. Why not me? While it might not be the right decision for everyone, we felt that it was the right time for us for several reasons.

One of the reasons that came to mind was stability with flexibility. Between my stipend as a graduate student (I am lucky to have a fairly generous one) and my husband's job as a research technician, we felt that we had the stability to start a family. When I expressed concern to my mother once that I was not making as much money as I had envisioned myself making before starting a family, she was quick to remind me that while she was pregnant, she and my father both unexpectedly lost their jobs. She told me that even the best-laid plans do not always work out how you imagined, but you work with what you have. While we may not have the money to buy a top-of-the-line $1,100 stroller (yes, this stroller exists), we certainly have the means to provide for a baby. As for the flexibility, being a graduate student allows my schedule to have a little more versatility than a 9-to-5 job. There is no way to know that wherever I end up next, whether in a postdoc position, a job or a fellowship program, I will have the same benefit.

Secondly, and maybe most importantly, is support. A supportive spouse, a supportive family, a supportive adviser, a supportive graduate program: You get the idea. I remember being very nervous to tell my adviser that I was pregnant, which in hindsight I realize was ridiculous. I am fortunate to have a very understanding adviser. I am also fortunate that the graduate school has some great resources for graduate students with families, including the option of a six-week parental accommodation period and grant programs to help cover the cost of daycare. Also, I know that I can turn to any number of graduate students in my program who have recently had children whenever I need advice.

Someone once told me that if you wait for everything to be perfect before starting a family, you might be waiting forever. With this line of thinking, there will always be something holding you back. The important thing is that you are ready. The closer I get to my due date in May, the more anxious I become, yet I am eager to start this new chapter, even if 20-year-old me thinks the chapters are a little out of order. But then I ask myself, what does she know anyway?



Jen McGlaughon (jla254@cornell.edu) is a graduate student in the molecular biology and genetics department at Cornell University.

Taking stock

By Preston Hensley

Recently Bruce Alberts and co-authors concluded that biomedical research in the U.S. has become an "unsustainable hypercompetitive system that is discouraging even the most outstanding prospective students from entering our profession" (1). They noted that we are producing about 8,000 Ph.D.s per year and only about 20 percent of recent Ph.D.s obtain academic positions. As they and others (2) point out, this is a complex problem affecting the long-term competitiveness of the U.S. biomedical research enterprise, and they make a number of specific recommendations.

For those who are graduate students or postdoctoral fellows, these observations are sobering. So the question is where one goes from here. The answer is personal and not easy to come to, as the pressure to continue on is great and few graduate or postdoctoral programs are set up to help young scientists explore alternatives.

What I describe here is my odyssey through graduate school. It's a product of the times, the 1960s and '70s, and not unlike many others from that period. It's certainly not meant as a model except in one respect: From time to time, during the early phases of your training (or life), it's good to take a break.

It's one thing to have an opinion. It's another to act on it.

Measured in fish

After undergrad, I took off the summer and did commercial salmon fishing in Alaska. I moved from a world where everything was measured in grades and papers (the University of California, Santa Barbara) to one where everything was measured in fish (Egegik, Alaska).

The coolest guy in town caught the most fish, the second coolest guy caught the second most fish, and so forth. (There was a scale factor for the size of the engine in your boat, but that just made the math more complicated.) At the end of the summer, I hitchhiked from Fairbanks, Alaska, to San Francisco. That took about a week and provided stories upon stories. That was my first break from my trajectory since childhood. And it set an internal precedent, though I didn't appreciate that at the time.

In the middle of my graduate career at Cornell University, I woke up and realized that I was there by choice as much as by lack of choice. I had just kept taking the next step. I was pretty unhappy but couldn't tell anyone why, especially me. So I just stopped going into the lab.

Those were relaxed times, and my boss, Stuart Edelstein, was forgiving. Not sure that would work now. I went to live with my friends on a farm (hippies – you know the story) and milked cows and cut hay. Then I hitched from New York to California and back and all through eastern Canada (maybe 20,000 miles). The best of times. Great for recharging your humanity batteries.

Then one day I woke up again and doing calculations seemed like lots of fun, so back I went (and, importantly, I was allowed to). So that was a mini (but now slightly more conscious) internal sabbatical.

The tools of democracy

But the break wasn't quite as clean as that, really. We were in the middle of the Vietnam War, and my draft number was 34. In 1969, we had a conscripted (drafted) military, in contrast with the volunteer military of today. These numbers were determined by lottery. If you had a low number, you were off to Vietnam; if you had a high number, you were not. Mine was not high, and I was classified 1A, or fit for service. My conscientious objector petition had been turned down, so Canada was on my horizon. Remember the line from Samuel Johnson about facing the gallows in the morning focusing the mind? It does.

At that point, I was pretty involved in the anti-war movement, and then an interesting opportunity came up. The 1971 May Day protests were being organized, and the goal was for people from all around the country to go to Washington, D.C., to block all the roads into town, to stop the government and stop the war — civil disobedience. With 200,000 others, I was off. I was arrested twice in the next four days, along with 14,000 of my brothers and sisters (the most arrests for any event in U.S. history).

It's one thing to have an opinion.

IMAGE COURTESY OF BETTMANN/CORBIS/AP IMAGES

Philip Berrigan (left) and his brother, Daniel Berrigan, both Roman Catholic priests, watch two baskets of draft board records burn on May 17, 1968, after the records were removed from the Cantonsville, Md., draft board office. The Berrigans were arrested along with the seven other participants, including three other priests. Dan Berrigan was a mentor to the author: "He spoke in poetry and of the moral alternative to war."

IMAGE COURTESY OF THE WASHINGTON STAR

The author participates in a demonstration on May 5, 1971, in Washington, D.C. He recalls: "This photo was taken at about noon on the first day of the demonstration on M Street. This was a show of force by then-President Nixon. These were National Guard troops. I was reminding them that this was just a demonstration and to keep their guns in their pockets. Remember that this was just a little over a year since the student war protestor killings by National Guard troops at Kent State University. Memories were still vivid."

It's another to act on it. For me, there were a few years of demonstrations. Demonstrations change you. Before I went to my first (protesting the firing of Clark Kerr, the University of California president, by the university regents upon the election of Ronald Reagan as governor), Steven Goodspeed, then dean of students at UCSB, made the following observation: The most affected people in a demonstration are the demonstrators. That is exactly true. And when you take the next step and go to jail, you cross another line. Now life is serious, and you get a sense of what is reasonable to do when push comes to shove. It's a significant investment in your understanding of what citizenship means. I didn't fully get that for a while (maybe a decade or so).

A role model for me back then was Dan Berrigan. He was the Jesuit chaplain at Cornell University when I was there for grad school. He spoke in poetry and of the moral alternative to war. He later served two years in federal prison for an exercise of conscience: using homemade napalm to burn draft files in the parking lot of a Maryland draft board.

A note here — during all these demonstrations, I had little hope of really changing anything. The mood of the country was not supportive of the counterculture and the anti-war movement. I was there because my schoolmates (and former football teammates) were getting killed. Sitting around listening to the Rolling Stones was just not on.

However, with the release of the Watergate tapes in 1974, it became clear that those demonstrations did have an effect on the occupants of the Oval Office. That was satisfying. It took another four years for the war to stop, but the point remains that really big, really bad things can change when we use the tools available in our democracy. Remember also the civil rights movement.

Also in those days, I saw many who dropped out of school. The ones who didn't come back (that I know of) did interesting things. Most of my friends then were high-energy physicists.

One became an electrician, one a carpenter, one an investment banker, one a professor at Maharishi University and one a teacher. Many never came back. But the ones who did had new focus and much more realistic attitudes about school and career.

This leaves me with the following advice. At some break in your career — after high school, undergrad, grad — stop and get out of town. Do something really orthogonal with your life — Peace Corps or something in that line. Something where you have to leave the country and, importantly, do things for other people. Going to the developing world is a good choice. The point here is to find out who you are, what your natural gifts are. That's

CONTINUED ON PAGE 56

IMAGE COURTESY OF HENSLEY

The author went to Haiti in 2012 with his daughter. He recalls: "My part in this exercise was to do a basic dental inspection of 300 beautiful children over the period of a week at an open-air church. There's nothing I can tell you about what I saw that you haven't heard many times on the news. But when you're there and you've been a parent, it doesn't take long before you begin to relate to those kids as your own. Parent genes are strong."

CONTINUED FROM PAGE 55

a lifelong process, but this will be a big step in that direction, and at a critical time.

It's also interesting who you meet when you're on these journeys — other people doing just what you are (broadly) doing. It's invigorating and supportive, and many will be friends for life. Some you may marry.

With your own eyes

In 2012, I accompanied my daughter on a trip to Haiti as part of a high-school project she and a friend had organized. My father had helped me similarly when I was 16. So I guess this was passing it forward.

My part in this exercise was to do a basic dental inspection of 300 beautiful children over the period of a week at an open-air church. There's nothing I can tell you about what I saw that you haven't heard many times on the news. But when you're there and you've been a parent, it doesn't take long before you begin to relate to those kids as your own. Parent genes are strong.

The majority had health issues. For a few, it was quite serious, but for most, $10 in medicine would take care of it. A Haitian doctor with us wrote the prescriptions, but it's hard to imagine how any were filled.

I felt like, if I were 20 again, I would go to medical school so that I would have a practical skill to use in the world. We have enough scientists in the U.S. to handle all our biochemical needs. We don't have enough physicians (and resources) to handle our world health needs. Seeing it with your own eyes changes everything. And that's really the point of this whole discussion.

We have enough scientists in the U.S. to handle all our biochemical needs. We don't have enough physicians (and resources) to handle our world health needs.

Courage

So, to students, I say maybe it's time to stop and think a bit. Maybe it's time for an internal sabbatical, and the more radical the course change the better. This advice may seem to be imprudent and impractical and to make little (or no) financial sense. But it works, and the only way to find that new trajectory is to step out of your comfort zone and, importantly, to get in touch with others doing the same thing.

After this journey, you may return to academics or a related effort as I did, refreshed and revitalized, or you may continue in a newly discovered passion as many of my friends have. Both are equally great.

It's sort of the advice given in the last few paragraphs of a recent advertisement promising to make you a "Confident and Successful Industry Professional" (3). But realize that industry in many ways is not much of a change. There are lots of alternatives to consider. In contrast with the same advertisement, I would advise you not to overthink it. Go with your instincts. Or (if your instincts are not yet informed — which is likely) meet some interesting person and go with him or her.

Take action

These are very difficult times in the world. We need revolutionaries. So be one.

Forty percent of the world's population doesn't have potable water. From 2000 to 2003, 769,000 children under 5 years old in sub-Saharan Africa died each year from diarrheal diseases. Help change that.

A country's access to medicines and treatments depends on a number of factors: efficient regulation, provision and use of products; and policies on selection, pricing and supply. It also depends on a qualified health workforce, information systems, functioning health infrastructure and good governance. There are a lot of opportunities here. Work with the World Health Organization and governments of relevant countries in one of those capacities to improve those conditions.

We have lived a very privileged life — handfed for all these years. We have an obligation to our fellows — who, by accident of birth, did not have this opportunity — not to waste this (our) opportunity.

We have lived a very privileged life — handfed for all these years. We have an obligation to our fellows — who, by accident of birth, did not have this opportunity — not to waste this (our) opportunity. Again, a moral alternative to injustice and inequality.

This isn't meant as national policy, of course, but personal suggestion. It may or may not work for you, but I'll bet it does. Listen to about 10 TED talks and ask yourself, "Where did those people come from?" Very few come from career-development programs. One you might especially enjoy is by Zack Kopplin. As a high-school student, he organized 78 Nobel laureate scientists in a campaign against the Louisiana Science Education Act, a creationism law. It's an example of what you can do even if the odds against you are great. (Kopplin won the Howard K. Schachman Public Service Award from the American Society for Biochemistry and Molecular Biology in 2014.)

But many, my wife among them, will say, "Wise up, hippie free spirit! These are not the '60s. Students have crushing student debt. These are very different times. They are older and have families." And that is the truth. So what to do?

First of all, regardless of time and circumstance, we all have responsibility for our lives. The bold experiment is always the best choice. It may take different forms depending on the times, but those choices are there.

One reasonable choice is one of the forms of national service that is available – Teach for America, AmeriCorps, the Peace Corps and so forth. These are redeeming programs, and many have student-loan repayment opportunities. And they will be life changing.

Student debt is the largest form of citizen debt in the country. If you were designing a country, would you put a $50,000 to $100,000 financial barrier to college entry in the way of the youth of your nation? Would you strap students with essentially a mortgage prior to their first day on the job? I'm not sure. If political activism is an option for you, what about pushing for a national plan to forgive student loans?

There are a lot of things that need help in our country. Probably at the top of the list is primary and secondary education. There are many opportunities there. Or one way to understand the issues around legislative reform in immigration is to work in an immigrant community for a few years. There are many opportunities there also.

I don't mean to speak casually about the issues that our students and postdocs, or our nation, are facing. They are as serious as it gets, and it's not a time to play. It's your life (and maybe your family obligations) we're talking about. But this can be a time to take stock of where we are as individuals and where we are as a nation and to make some courageous decisions.

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Preston Hensley (cphensley@gmail.com) spent 10 years in academia, 20 in big pharma and five in biotech. Today he works in computational biology and is earning his high-school STEM teaching credentials.

How to meet rock stars and pageant beauties

By Eleftherios P. Diamandis

In 1996, I was on a lecture tour to five major cities in India. I gave one lecture in Bombay (now known as Mumbai). While there, I was staying at the famous Taj Mahal Hotel. Returning from a dinner to the hotel one of these nights, my traveling companions and I noticed that there were hundreds of people waiting outside. Curious, we asked the staff why all these people were waiting. We were told that the next evening, the MTV Music Awards were to take place with participation of rock stars from all over the world, most of them staying at Taj Mahal.

Being a music lover and celebrity seeker, I decided to sit in the lobby of the hotel just in case any rocker showed up. It didn't take much time

to hear the roar of the crowd that signaled the entry of a rock star. It was Robert Plant, the lead singer of the legendary rock group Led Zeppelin. He was accompanied by his girlfriend and a couple of others. I asked Robert if he would pose for a picture with me, and he graciously agreed.

I was very excited and asked one of the staff who else was staying in the hotel. She mentioned Bryan Adams, the Canadian rock star. I decided to use an alternative way to reach Bryan Adams. I wrote a letter to him, mentioning how much I liked his music and that I was a fellow Canadian keen to meet him and asking him to autograph two of his CDs, which I happened to have with me at that time. (That was before the iPod was invented.) I put the letter and the CDs in a big envelope, and I requested that a staff member deliver the package to his room. The next day, to my astonishment, I found a voice message from Bryan Adams on my hotel phone noting that he was sorry to have missed me (we had been out for dinner) and that he had signed the two CDs and left them with the concierge.

Around the same time, the Miss World Competition was taking place in Bangalore. During our stay in Mumbai, there was a party in a nearby hotel honoring the winner, Irene Skliva from Greece. Coincidentally, we had dinner at that hotel on that evening. I took my chances and asked the guards of that private party to let me in, showing my business card and claiming that I was a professor of the winner at the University of Athens. To my surprise, the guards believed me and allowed me enter the party, where I had a chance to shake the hand of my compatriot and Miss World 1996.

My India trip was very rewarding for the science and my exposure to the culture of India. But the most exciting moments were in Mumbai, where I met three international personalities under unexpected circumstances.

Eleftherios P. Diamandis (ediamandis@mtsinai.on.ca) is a professor and head of the clinical biochemistry division at the University of Toronto and holds an endowed chair in prostate cancer biomarkers at Mount Sinai Hospital and University Health Network.

From project to runway

By Andrea Hadjikyriacou

As a female scientist who loves to shop while working many hours in the lab, I started a fashion blog in August 2012 called "PhDFashionista" to show others that being a scientist doesn't mean you have to be boring!

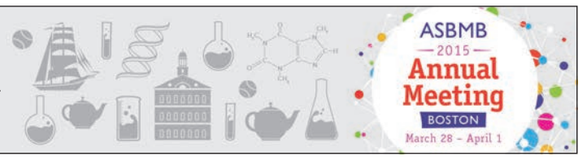
There's a certain stigma that being in science means you are a nerd or awkward, and I am trying to break those expectations by showing that you can still have a great sense of style while being successful and working hard in research. I also find practical outfits to wear to work while still looking fashionable and obeying the rules of the University of California, Los Angeles, for lab-acceptable clothing.

On my blog, I post not only outfit details but also beauty and makeup tutorials, looks, inspiration for various holiday outfits, and more! I love to shop, and this gives me an outlet to post about what I enjoy doing in my free time, when I am not in the lab, and also has helped me build a community with other fashion bloggers who aren't necessarily in science but with whom I have something in common.

Andrea Hadjikyriacou (ahadjiky@ucla.edu) is a doctoral candidate at the University of California, Los Angeles.

One of the many outfits that Andrea Hadjikyriacou wears to the lab. Find details about the clothes at www.phdfashionista.com.

Andrea Hadjikyriacou will be an official American Society for Biochemistry and Molecular Biology annual meeting blogger in Boston later this month. Follow her on Twitter at https://twitter.com/phd_fashionista.



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#protein	What's New in Membrane Transport Proteins
#training	Training the Mind of an Interdisciplinary Scientist
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Bonnie Bassler,
Princeton University


Zhijian James Chen, *University of Texas–Southwestern Medical Center*


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