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ASBMB TODAY

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

Vitamin D

How much is enough?

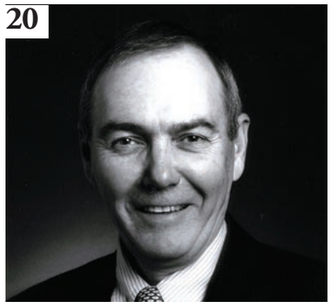
CONTENTS

NEWS

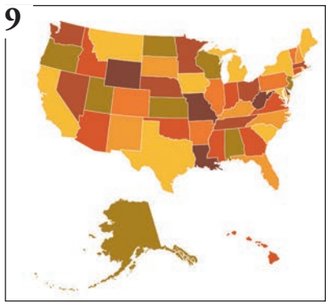
FEATURES

6

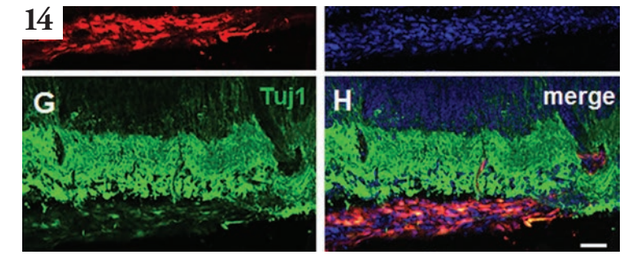
38



20

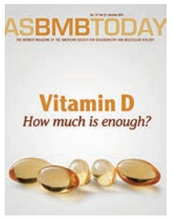


9



14

Science writer Rajendrani Mukhopadhyay explores the debate over how much vitamin D is enough for good health.



24

PERSPECTIVES

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A president's perspective on Experimental Biology 2014

By Jeremy Berg

As a society president, attending the annual meeting is a great pleasure, and this year's Experimental Biology meeting in San Diego was no exception for me. With many events to lead, participate in or at least make an appearance at, the meeting is quite full. However, the benefits of attending many outstanding talks, catching up on science and other activities with old friends and acquaintances, seeing long-planned projects come to their next phase, and meeting young students and excited teachers and hearing them talk about new educational programs make it all worthwhile. This year's meeting also provided many new perspectives on social media that, I believe, were thought-provoking for many involved.

Before the meeting

For the president and other officers and staff members at the American Society for Biochemistry and Molecular Biology, the activities start before the opening of Experimental Biology with meetings of the ASBMB Council and other committees. These meetings allow the groups who are working on both longstanding ASBMB activities, such as publications, and more recent initiatives, such as public outreach, to meet and to update ASBMB leadership on their efforts, get feedback and advice, and plot the paths forward for the next year. Although there are, of course, many challenges, I am pleased to say that the society is in reasonably good shape.

Award lectures

Once the Experimental Biology meeting formally begins, a considerable amount of the president's schedule revolves around the award presentations. The society gives more than 15 awards (1), and the award lectures give the society members an opportunity to hear the winners describe the work that led to their selection. These presentations come from a mix of well-established investigators describing long careers' worth of work and relatively young investigators who have made important contributions early in their careers.

For me, two special treats this year were the inauguration of the Bert and Natalie Vallee Award in Biomedical Science, awarded to Michael Gottesman, and the Ruth Kirschstein Diversity in Science Award presentation by Mike Summers. Bert Vallee was


GOTTESMAN


SUMMERS


HRABOWSKI

one of the early leaders in the field of the biochemistry of zinc (my favorite element), and Gottesman is a cancer biologist I got to know well during my time at the National Institutes of Health who got his start in research as a medical student in Vallee's laboratory. Summers, a professor at University of Maryland, Baltimore County, shared the Kirschstein with UMBC President Freeman Hrabowski III for their development of the Meyerhoff Scholars Program (2), a leading initiative to launch students from diverse racial and ethnic backgrounds into careers in science and technology. Mike gave an engaging presentation about the conceptual framework for the program and presented both anecdotes and data about the program's successes. He concluded with a discussion of efforts to replicate the program at other institutions. I was just sorry that he did not have time to discuss the outstanding research in RNA structural biology that he and his largely undergraduate research team have completed over the years (which also has roots in zinc biochemistry).

The Public Affairs Advisory Committee panel on sustainability

One of my major efforts during my term has been to stimulate discussions about addressing some crucial issues that have made the biomedical research enterprise unsustainable in its present form. I wrote about this effort a year ago (3), and a key next step was a panel discussion at Experimental Biology.

While we were in the final stages of preparation for this, a commentary appeared in the Proceedings of the National Academy of Sciences, written by Bruce Alberts, Marc Kirschner, Shirley Tilghman and Harold Varmus, titled "Rescuing U.S. biomedical research from its systemic flaws" (4), which noted our efforts. This paper, which identified many of the same issues that we had raised and proposed some potential solutions, has led to much discussion in the scientific community.

Our panel discussion at the annual meeting was lively, with different perspectives on these complex issues, as anticipated, and it was covered by official meeting blogger Biochem Belle (5). Spurred by our efforts and the Alberts et al. paper, we anticipate that much discussion and, with luck, some needed action will occur over the next year.

I found it interesting to watch the body language in the room that revealed attitudes ranging from skepticism to confusion to excitement.

The role of social media

Discussions of the role of social media were a thread that ran through the meeting, starting at the ASBMB Council meeting. Social media have potential roles to play in many activities related to the ASBMB, including meetings, publications, education and outreach. Indeed, considerable coverage of the sustainability panel came from tweeting with the hashtag #SBRE, as summarized in the Storify summary by Biochem Belle (6).

Some of the younger ASBMB staff members gave the Council a presentation on the rudiments of Twitter and some other social media tools. I found it interesting to watch the body language in the room that revealed attitudes ranging from skepticism to confusion to excitement. A few Council members moved toward exploring the possibilities of strategic use of these tools and even attended a breakfast meeting built around a Twitter tutorial.

ASBMB staff and others used Twitter as a useful tool for highlighting upcoming events at the meeting and for calling out exciting comments or results in real time. Indeed, the societies involved with Experimental Biology enlisted the services of social-media-savvy individuals to live tweet selected events.

On to Datahound

It has been a great honor to serve as ASBMB president following in the footsteps of many great scientists and leaders. I have greatly enjoyed the opportunity to write these monthly columns and have been gratified by many positive comments that I have received over the years, including some at the meeting.

Indeed, as my term approached its end, I realized that I likely needed to find another outlet, particularly for the data analyses that I find helpful for my own thinking about science-policy issues that also help shape discussions in more productive directions. One of the happy outcomes of the Experimental Biology meeting was a chance to meet with some science bloggers who operate the collective blogging platform called Scientopia (7).

I was invited to join the group and have started a new blog called Datahound (8). I already have posted on many topics, including trends in training stipends, the distribution of indirect cost rates and gaps

CONTINUED ON PAGE 4

CONTINUED FROM PAGE 3

in research funding. I am looking forward to continuing to post and welcome thoughts about topics of interest.

Finally, the meeting gave me a great opportunity to interact with the incoming ASBMB president, Steve McKnight. Steve and I have known each other since I was an assistant professor in the chemistry department at Johns Hopkins University and he was a staff member at the nearby Carnegie Institution for Science. We shared many spirited conversations about the then-unknown structures of zinc finger and leucine zipper DNA-binding domains recently discovered in eukaryotic transcription factors. Steve is one of the most passionate advocates for the science of biochemistry that I have ever known, and I am thrilled to hand over the reins to him.

MCKNIGHT

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7. http://scientopia.org/blogs/about
8. http://scientopia.org/blogs/datahound

Jeremy Berg (jberg@pitt.edu) is the associate senior vice-chancellor for science strategy and planning in the health sciences and a professor in the computational and systems biology department at the University of Pittsburgh.

Experimental Biology 2014 tweet analysis

Shortly after the Experimental Biology meeting ended, Colby Vorland, a Ph.D. student in nutrition science at Purdue University who tweets under the handle @nutsci, created a fascinating analysis of the meeting chatter on Twitter. Here are just a few of his findings. See more of his analysis from this year and his analysis from last year on his blog: http://nutsci.org.

HASHTAGS

In 2013, the meeting hashtag was #EB2013. But this year it was changed to #xBio. Some users just assumed it was #EB2014. Here's what Vorland found:

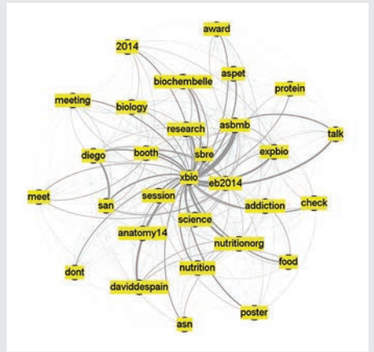
- 83% of tweets contained only the #xBio hashtag
- 12% contained only the #EB2014 hashtag
- 5% contained both hashtags

BIG NUMBERS

In 2013, there were 5,455 tweets with the meeting hashtag (#EB2013) over a 10-day period, and in 2014 there were 6,223 with the meeting hashtags (#EB2014 and #xBio) over an 18-day period.

NETWORK GRAPH

Vorland created a network graph of the relationships among the most common words in tweets and retweets with the meeting hashtags. He explained: "The connections between words are weighted by how common they appear together in tweets."



TOP 10 TWEETERS

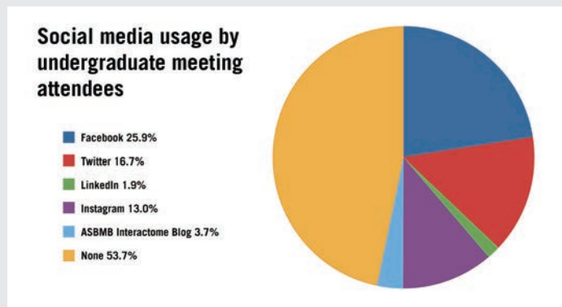
2014	
Handle	**Tweet count**
ASBMB	226
biochembelle	196
daviddespain	190
drugmonkeyblog	159
expbio	112
cjmetzgarrd	104
nutritionorg	88
drdairy50	81
phlane	77
paulaike	74

2013	
Handle	**Tweet count**
biochembelle	292
drdairy50	243
ASBMB	223
daviddespain	211
bwcorb	185
licorbio	122
dramyrd	116
nutritionorg	92
chrispickett5	81
phyziochick	81

Source: Colby Vorland (http://bit.ly/1hJwmeg)

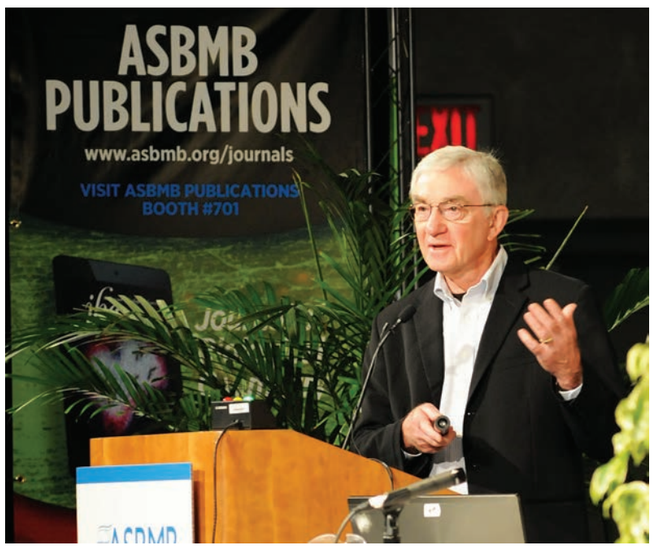
ONE DEMOGRAPHIC SLICE

The ASBMB asked its undergraduate attendees which society social-media channels they used. This is what they reported.



Scenes from the annual meeting

Journal of Biological Chemistry reception



Dana Carroll of the University of Utah School of Medicine gives the Herbert A. Sober Lectureship.

The ASBMB photo booth in the exhibition area was a hit.

Incoming ASBMB President Steven McKnight of the University of Texas Southwestern Medical Center at Dallas chats with Bruce W. Stillman of Cold Spring Harbor Laboratory (left), the winner of ASBMB's Herbert Tabor Research Award.

Jeremy Berg, president of ASBMB

ASBMB travel award recipient Treniqka Walters of Meharry Medical College in Nashville talks about her research with Bettie Sue Masters of the University of Texas Health Science Center at San Antonio.

Muhammad Allele, ASBMB's mascot, is always a sought-after tchotchke.

From left: Phil Ortiz, Tayla Olsen, and Kristin Fox

A challenge reissued

Can the ASBMB membership conduct at least one meeting with federal representatives and senators in each and every state?

By Chris Pickett

You did it! Two years ago, we challenged the American Society for Biochemistry and Molecular Biology membership to conduct 100 or more meetings with U.S. representatives and senators during the summer congressional recess. And last year, you had 105 meetings. Congratulations!

While we are still figuring out the logistics for your ticker-tape parade, we at the ASBMB have started thinking about our next step. One hundred meetings is an astonishing feat, but researchers are still confronted by myriad problems. Despite all of your advocacy efforts, the budgets for the National Institutes of Health, the National Science Foundation and others are not growing fast enough to keep up with the demand for grant money. Jobs for newly minted Ph.D.s are scarce, and legislative issues concerning immigration reform, travel by federal scientists and changes to peer review remain unresolved. And recent events on Capitol Hill indicate that, despite bipartisan support, funding for scientific research is not a high priority for many members of Congress.

This is why we've decided to renew our challenge to the membership while at the same time setting our sights on a higher target. A thriving local research community provides jobs, encourages entrepreneurship and makes the occasional groundbreaking discovery. *And this happens in every single state in the nation.* That is why we are now challenging you, the members, to demonstrate this to the congressional representatives of every state. A 50-state challenge. Can the ASBMB membership conduct at least one meeting with federal representatives and senators in each and every state? We think you can, but it's up to you to prove it.

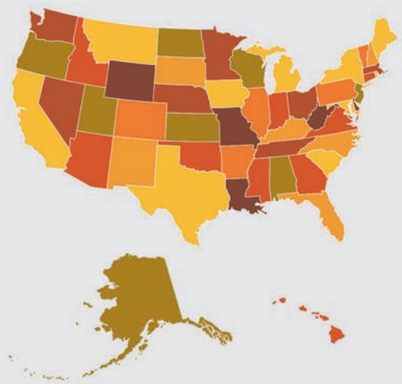
This challenge is issued to all scientists, from undergrads to grad students, postdocs, technicians, staff scientists and faculty members. Your voice is important to your members of Congress, and they need to hear about the benefits your research brings to the states and districts you live in. You are the one working toward breakthroughs in critical issues related to human health. Your work brings federal dollars into the community and improves the economic well-being of surrounding areas. And your discoveries have the potential to make significant change. These are the stories that will motivate members of Congress to raise the profile of science.

Congress will go on recess for five weeks starting at the beginning of August. During this time, federal policy makers and their staffs will be in their states and districts meeting with concerned constituents. This is your window to set up a meeting with your representatives. As always, the ASBMB Public Affairs Office is here to help you as much or as little as you want. We can set up meetings for you and provide you with materials to help you make your points. We will even travel and escort you on your meetings if that is what you want. We are here to make sure that your voice can be heard. And we're challenging the ASBMB membership to make your voice heard in every state in the nation.

A 50-state challenge. Think you're up to it?

How to participate

Do you want to meet with your member of Congress and his or her staff during the summer recess (Aug. 1–Sep. 5)? Register now for the ASBMB 50-State Challenge and help us meet our goal of having members conduct at least one meeting in all 50 states! http://bit.ly/1qwKcEK



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

Protein Society honors White, Hurley and Fierke


WHITE


HURLEY


FIERKE

Three members will be celebrated at The Protein Society's annual symposium in July. Stephen H. White of the University of California, Irvine, won the Carl Brändén Award. Sponsored by Rigaku Corp., the award is issued to "an outstanding protein scientist who has also made exceptional contributions in the areas of education and/or service to the science." James H. Hurley of the University of California, Berkeley, won the Hans Neurath Award, sponsored by The Neurath Foundation, "for his ground-breaking contributions to structural membrane biology and membrane trafficking." Carol A. Fierke of the University of Michigan won the Emil Thomas Kaiser Award for "exceptional contributions to our understanding of the metal homeostasis, and to understanding of the structure and mechanism of ribonuclease P."

IN MEMORIAM: James E. Stowers Jr.


STOWERS

James E. Stowers Jr., the co-founder of the Stowers Institute for Medical Research, died March 17 at the age of 90. He was known as one of the world's biggest philanthropists after giving most of his fortune to the biomedical research institute. Stowers was born in 1924 and, after studying medicine for several years, chose to leave medicine to pursue a career in business. He went on to become the founder of what now is American Century Investments, and it is there that he established his wealth. After several personal health crises, including prostate cancer, Stowers, along with his wife, decided to pour their wealth into biomedical research. This led to the founding of the Stowers Institute in 1994. It opened in 2000 in his hometown of Kansas City, Mo.

The Stowers Institute is the home to many biomedical researchers, including several ASBMB members, and continues to make large contributions to the field. Stowers is survived by his wife, three children and six grandchildren.

Baldwin will be FASEB's next VP for science policy


BALDWIN

Thomas Baldwin, a professor of biochemistry at the University of California, Riverside, has been elected the next vice president for science policy of the Federation of American Societies for Experimental Biology. Baldwin's research primarily focuses on studies of the heterodimeric flavoprotein monooxygenase bacterial luciferase. His lab has studied the mechanism of the bioluminescence reaction, as well as the folding and assembly of the enzyme, both in vitro and in vivo. He also has employed the enzyme to investigate metabolic processes as they occur in the cell by monitoring light emission. Baldwin currently serves as the chairman of the ASBMB Public Outreach Committee and is ASBMB's representative on the FASEB board of directors. He will begin his new term as VP-elect for science policy July 1.

Baltimore appointed co-chair to National Academy of Sciences panel


BALTIMORE

The National Academy of Sciences appointed David Baltimore, president emeritus and Robert Andrews Millikan professor of biology at the California Institute of Technology, as co-chair of its Committee on Science, Technology and Law. The CSTL was established in 1998 to examine the areas where science, engineering and law intersect. CSTL is a unique body where the legal and scientific communities come together for needed discussions. Baltimore is one of the world's most influential biologists. In 1975, he was awarded the Nobel Prize in physiology or medicine for research into viral replication that helped scientists better understand the life cycle of retroviruses. His work has contributed widely to the understanding of cancer, AIDS and the molecular basis of the human body's immune response. Baltimore said he is looking forward to working with CSTL members to identify pertinent issues where a better understanding of the science–law interface can lead to more informed policy decisions. Baltimore will co-chair the committee with Judge David S. Tatel from the U.S. Court of Appeals for the District of Columbia Circuit.

Written by Nicole Parker

New members of American Academy of Arts & Sciences


DILL


GLASS


GOURSE


HUNT


MERCHANT


ROSENZWEIG


SILVERMAN


VAN DER DONK

The Academy of Arts & Sciences announced the members of the class of 2014. The academy has served as the nation's champion of scholarship, civil dialogue and useful knowledge since its founding in 1780. Its members contribute to publications and studies of science and technology, policy, energy and more. The members include some of the world's most accomplished leaders from academia, business, public affairs, humanities and the arts. This class of members includes many winners of notable awards in a wide range of disciplines. The new class includes the following ASBMB members:

- **Ken A. Dill, Stony Brook University**
- **Christopher K. Glass, University of California, San Diego**
- **Richard L. Gourse, University of Wisconsin-Madison**
- **Donald Frederick Hunt, University of Virginia**
- **Sabeeha Merchant, University of California, Los Angeles**
- **Amy C. Rosenzweig, Northwestern University**
- **Richard B. Silverman, Northwestern University**
- **Wilfred A. van der Donk, University of Illinois at Urbana-Champaign and Howard Hughes Medical Institute**

The new class will be inducted at a ceremony Oct. 11 at the academy's headquarters in Cambridge, Mass.

ASBMB wins two NSF grants to support teachers and students

New awards expand and bolster the society's leadership in BMB education and professional development

By Weiyi Zhao

The American Society for Biochemistry and Molecular Biology has won two new National Science Foundation awards to support emerging and ongoing education and professional-development initiatives.

New funding

One initiative that won NSF funding, titled "Creating a Community of Scientists: Supporting PUI Faculty and Undergraduates at the ASBMB National Meetings," is part of a more than five-year effort by the society's Education and Professional Development Committee and Undergraduate Affiliate Network to highlight research conducted at primarily undergraduate institutions.

Each year, students and faculty members from primarily undergraduate institutions are invited to present their work during platform sessions at the ASBMB annual meeting. This year, we expanded our focus to include faculty members and students from minority-serving institutions and community colleges. Additionally, funding was designated to promote greater student engagement and networking at the meeting.

A formal evaluation of this year's efforts will be conducted in the coming months. If you attended the annual meeting in April, please help us in our evaluation by completing the online survey that will be emailed to annual meeting attendees.

The second NSF award supported the "ASBMB Mentoring Program for Early-Career Scientists" project, a grant-writing and mentoring workshop for postdoctoral fellows and assistant professors held in June in Washington, D.C. The project was spearheaded by the ASBMB Minority Affairs Committee under the leadership of Takita Felder–Sumter of Winthrop University; Marion Sewer of the University of California, San Diego; Squire Booker of The Pennsylvania State University; Sonia Flores of the University of Colorado Denver; and David Wilson of the Society for the Advancement of Chicanos and Native Americans in Science.

A precursor workshop in 2013 elicited more than 75 participant nominations, from which 32 were selected to attend. This year, we received 48 nominations, many from leading research institutions, such as the Massachusetts Institute of Technology, Stanford University and Johns Hopkins University.

A student at Hernandez Elementary School participates in a HOPES seed grant project organized by faculty at the school and at Texas State University.

This overwhelming response from the ASBMB community demonstrates that there is a clear need for well-planned and -executed professional-development programs emphasizing grant writing and mentoring for young scientists and that the society is responding to the needs of its members. Learn more at www.asbmb.org/grantwriting.

Existing funding

In addition to the grant-funded efforts noted above, the society won in 2009 a five-year NSF Research Coordination Network Undergraduate Biology Education grant. The RCN-UBE award has funded more than 30 teacher-focused workshops around the country, six in the first half of 2014 alone, which have brought together hundreds of undergraduate biochemistry and molecular biology educators.

As a result of this project, a set of undergraduate biochemistry and molecular biology foundational concepts and skills was developed and published in the journal Biochemistry and Molecular Biology Education, commonly referred to by its acronym, BAMBED. Find out more about the effort at www.asbmb.org/teachbmb.

Finally, another ongoing NSF-funded ASBMB initiative is the HOPES program, which is short for Hands-on Opportunities to Promote Engagement in Sciences and is led by Regina Stevens–Truss of Kalamazoo College and Peter Kennelly of Virginia Polytechnic Institute and State University.

Since 2012, the society has awarded up to 10 seed grants worth $2,000 apiece annually to support faculty and teacher collaborations aimed at bringing real-world, hands-on science into K – 12 classrooms. Find out more about the HOPES grants at www.asbmb.org/hopesgrant.

Along with the programs highlighted above, the society also launched in 2013 the BMB Accreditation Program. Fourteen schools already have received ASBMB accreditation. More information can be found at www.asbmb.org/accreditation.

The continued success of these initiatives is dependent on smart, enthusiastic and dedicated ASBMB committee and staff members. We hope to keep up our funding momentum as the ASBMB firmly positions itself in a leadership role in life-sciences education in the 21st century.

Weiyi Zhao (wzhao@asbmb.org) is the ASBMB manager of education and professional development.

Human retinal progenitor cell transplantation to preserve vision

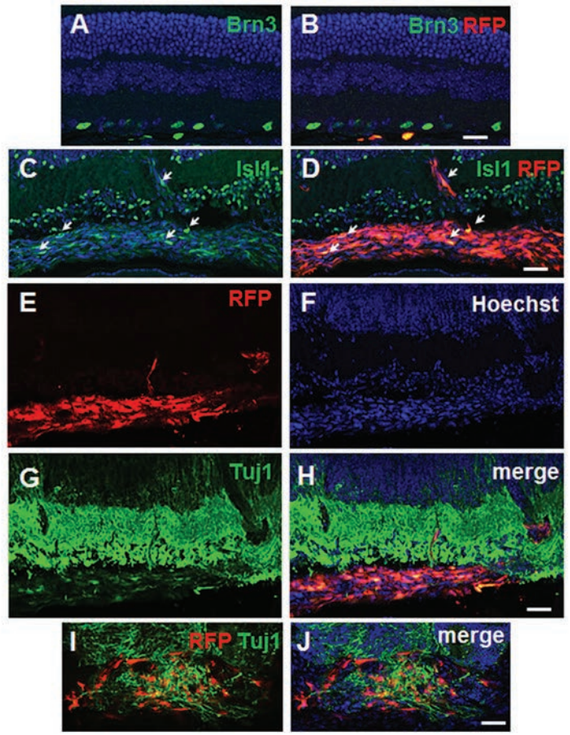
By Lesley Wassef

Photoreceptor cells in the retina are involved in detecting light and converting it into neural signals for vision. Retinal degenerative diseases, such as age-related macular degeneration, are the leading cause of blindness in the developed world. While very few effective treatments exist to slow the progression of these diseases, a new study in **The Journal of Biological Chemistry** provides what the authors say is proof of concept that dying photoreceptors can be rescued by cell transplantation.

The study, led by Kang Zhang at Central South University in China and conducted with collaborators in the U.S. and Europe, set out to determine whether transplanted human retinal progenitor cells, or hRPCs, have protective or restorative effects. After all, many lives have been saved by replacing dying organs through transplantation. In addition, studies in animal models of retinal degenerative diseases have demonstrated that transplanted retinal progenitor cells can migrate into the retina and differentiate into photoreceptor cells.

So the team turned to a widely used animal model for inherited retinal degeneration: the Royal College of Surgeons, or RCS, rat. In one group, researchers injected hRPCs (in solution) into the retina of only one eye per rat, leaving the other eye as a control. Two additional groups of rats were used as well: One group was injected with a vehicle (solution without the hRPCs), and another group was not injected at all.

The researchers report that 12 weeks after the injection, only the eyes that had been injected with hRPCs showed preservation of visual acuity (i.e., clarity), whereas deterioration was seen in eyes of RCS rats that had not been injected.



The transplanted RFP-tagged p53$^{-/-}$ MRPs (red) formed an epi-retinal tissue onto the retinal ganglion cell layer 3 weeks post transplantation. A subset of cells expressed retinal ganglion cell markers such as Brn3 (A and B), Islet1 (C and D, small white arrows) and Tuj1 (E and J). Incorporation of transplanted cells into the retinal ganglion cell layer was also observed (H–J). Scale bars, 25m (A and B) and 50 m (C–J).

Further testing showed that hRPCs preserved the outer nuclear layer by increasing its thickness, increasing the number of cells and increasing the spread of cells. The results, the researchers say, are believed to be a result of hRPCs rescuing the host photoreceptors through the delivery of the right ingredients (for example, neurotrophic factors) rather than cell replacement.

This proof-of-concept study showed that hRPCs "offer protection of visual function via mechanisms that rescue host photoreceptor cells when transplanted into a degenerative retina," the authors wrote.

Lesley Wassef (lesleywassef@yahoo.com) was a research associate at the Rutgers University Food Science Department and Rutgers Center for Lipid Research. She is now a medical writer.

Two new studies on oral bacterium that causes lethal heart valve infection

By Sapeckshita Agrawal

Two back-to-back studies published in **The Journal of Biological Chemistry** have provided significant insights into virulence of Streptococcus sanguinis, which causes a potentially lethal infection of heart valves.

Infective endocarditis occurs when the otherwise innocuous S. sanguinis, a Gram-positive, facultative aerobic, oral bacterium, enters the blood stream and colonizes vulnerable heart valves or endocardial tissue, an infection that proves to be lethal for more than 20 percent of patients. The severity of this disease and the lack of a vaccine for it make it imperative to understand the mechanism of virulence by S. sanguinis to facilitate the development of potent antimicrobial agents.

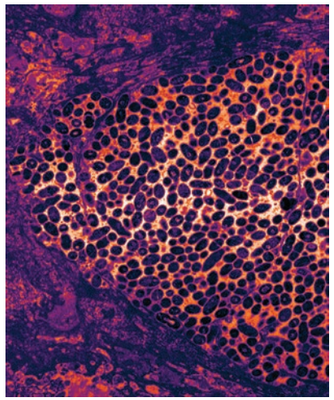
The studies in the JBC resulted from a collaboration between the labs led by Todd Kitten at Virginia Commonwealth University and JoAnne Stubbe at the Massachusetts Institute of Technology.

Two past observations prompted the research teams to examine the activity of the bacterium's class Ib ribonucleotide reductase, or RNR. These essential enzymes rely on metallo-cofactors to convert ribonucleotides into deoxyribonucleotides, precursors for DNA replication and repair. In S. sanguinis, RNRs occur in two forms: the aerobic class Ib and the anaerobic class III.

The first observation was that deletion of a manganese transporter called SsaB drastically reduces the virulence of S. sanguinis and its ability to tolerate oxygen. So the researchers set out to "identify manganese-requiring proteins that would also be required for growth in oxygen," explains Kitten. The second observation was that class Ib RNRs, along with an iron cofactor, also appear to employ a dimanganese-tyrosyl radical cofactor for in-vivo activity. "We wondered whether the oxygen-dependent class Ib RNR might be the manganese-requiring enzyme we were seeking," Kitten says.

In the first study, the researchers demonstrated that the S. sanguinis RNR can not only self-assemble a diferric-tyrosyl radical in the presence of oxygen, but also assemble a dimanganese-tyrosyl radical, if provided with an additional enzyme called NrdI.

"In my view, the main contribution of the first study was that it identified all the components and established that the S. sanguinis RNR had the properties that were expected of it," says Kitten. "We confirmed that RNRs behaved the way we thought they would in vitro, and we provided direct evidence about which components are required for RNR activity."



False-colored transmission electron micrograph of Streptococcus sanguinis cells (purple ovals) encased within an infected heart valve in an animal model of infective endocarditis. Mutants lacking either the NrdEF ribonucleotide reductase or the NrdI protein required for manganese cofactor formation were unable to cause disease.

Emboldened by those findings, the researchers in the second study created mutant strains of S. sanguinis lacking class Ib RNR or other RNR-related enzymes and tested those mutants for growth competency under aerobic and anaerobic conditions.

The authors reported that the mutants lacking the genes for synthesis of class Ib RNRs or the manganese cofactor were unable to grow aerobically (but grew normally under anaerobic conditions) or cause endocarditis in a rabbit model system. This phenotype, however, could be partially rescued by heterologous complementation with a class II RNR gene, which codes for an oxygen-independent, adenosylcobalamin-cofactored RNR.

These results allowed the authors to conclude that manganese was indeed critical for the proper function of RNRs and, consequently, for the virulence of S. sanguinis.

The work is significant because the results provide a novel target — manganese cofactored RNRs — for developing antimicrobial agents designed to treat infective endocarditis, and that is made even more promising by the fact that such RNRs do not exist in eukaryotes. The results also may answer the longstanding question of why some bacteria require manganese for oxygen tolerance and virulence.

Sapeck Agrawal (sapeck.srivastava@gmail.com) recently earned her Ph.D. in molecular microbiology and immunology from The Johns Hopkins University.

Realizing when proteins go bad

By Rajendrani Mukhopadhyay

Just as some plastics warp when left out in the heat and sun, some proteins are destroyed under suboptimal conditions. Knowing when changes in proteins are caused by poor conditions and not disease is critical. In a paper recently published in the journal **Molecular & Cellular Proteomics**, researchers have demonstrated that changes in two major blood proteins, considered by some scientists to be signs of cardiovascular disease, actually correlate with improper handling and storage.

Chad Borges at Arizona State University was interested in albumin and apolipoprotein A-I as possible markers for cardiovascular disease in patients with type 2 diabetes. "There is a track record in the literature suggesting that the oxidized forms of both of these proteins are associated with diseases involving oxidative stress," says Borges. "Some researchers are supporters of this hypothesis for one or both proteins, and other researchers remain unconvinced."

When Borges and colleagues started to look more closely at the changes in oxidation of albumin and apoA-1, they started to notice trends that had nothing to do with patient medical histories or diagnoses. When they analyzed the two proteins by liquid chromatography-mass spectrometry, which are common in clinical analyses laboratories, they discovered that these proteins spontaneously oxidize if they are not completely frozen below -30 °C. "This point will not come as a surprise to most chemists," says Borges. "But it has three major ramifications for clinical investigators."

First, he states, validating protein oxidation as a biomarker of disease requires differentiating between biochemical effects caused by disease from artifacts brought on by improper handling and storage.

Second, says Borges, it would be naïve to think that albumin and apo A-I are the only proteins to get damaged under incorrect storage and handling conditions. It's very likely that most proteins with free cysteine and methionine residues, which are most susceptible to oxidation, will break down under suboptimal conditions. "When these chemical modifications occur on proteins, they may very well affect the manner in which the protein interacts with antibodies employed in clinical test kits designed to quantify the protein," explains Borges. "In other words, protein oxidation may invalidate some clinical assays — and it may be the molecular root cause behind the eventual disappearance of other candidate markers of biospecimen integrity that simply disappear when a sample has gone bad."

Third, Borges says the oxidation phenomenon could be turned around to benefit clinicians: It could be used to monitor how well blood samples are handled and stored and determine whether results from assays are reliable.

This aspect goes beyond the clinic. Laboratories that test for performance-enhancing substances in athletes have to prove that samples were properly handled and stored whenever their data are disputed in legal courts. The finding by Borges and colleagues that some key proteins oxidize under suboptimal conditions could be applied in sports doping.

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

A critical lipoprotein receptor reduces metabolic disorders brought on by low testosterone

By Rajendrani Mukhopadhyay

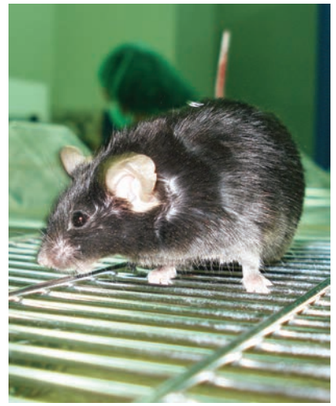
Testosterone is the male sex hormone involved in sex differentiation, libido and erectile function. It's also known to play a role in metabolism and influence obesity, type 2 diabetes and other metabolic disorders. But how testosterone participates in various metabolic pathways is not clear. In a paper just published in the **Journal of Lipid Research**, investigators demonstrate that the effects of testosterone on metabolism may be altered by the low-density lipoprotein receptor, a critical protein for the transport of lipid-modified proteins and the regulation of blood cholesterol levels.

The study is important, says lead author Kyriakos Kypreos at University of Patras Medical School in Greece, because it reveals "a novel role of the LDL receptor as a switch for processes associated with testosterone-induced metabolic alterations, such as body weight and body fat content, energy metabolism, and glucose tolerance." Based on this finding, Kypreos adds that scientists can now focus on drugs to treat metabolic disorders that modulate the number of functional LDL receptors on cells.

Kypreos and colleagues have a longstanding interest in metabolic disorders in which testosterone is involved. Testosterone deficiency in men, called hypogonadism, is considered a primary risk factor for a number of disorders. These disorders include obesity, insulin resistance, and dyslipidemia, a condition where LDL-cholesterol and total cholesterol levels in blood are raised.

Kypreos says he and his colleagues came across research that suggested that the LDL receptor was an important receptor in diet-induced obesity. There is also research that shows that mutations in LDL receptor cause coronary heart disease and dyslipidemia.

Putting it all together, Kypreos and colleagues decided to investigate the potential involvement of the LDL receptor superfamily in the metabolic actions of testosterone. The investigators used genetically engineered male mice that were missing the LDL receptor. They surgically castrated these mice to see how low testosterone levels and a lack of LDL receptor affected metabolism. They fed the mice a high-fat diet "to mimic the human situation where obesity develops as a result of disruption of homeostasis between food intake and energy expenditure," explains Kypreos.



A mouse from the Kypreos laboratory study about the role of the low-density lipoprotein receptor in modulating testosterone's effects.

The investigators discovered that the LDL receptor "is a main switch of testosterone actions on body metabolism," says Kypreos. The receptor helps testosterone trigger those pathways involved in maintaining blood sugar and triglyceride levels. The investigators' data also suggest that the receptor affects how testosterone activates fat burning in white adipose tissue. Kypreos says one of the group's aims now is to search for "molecular targets for new pharmaceuticals that will promote fat burning through thermogenesis as a treatment of obesity and obesity-related complications."

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

Intracellular lipid transport

By Frederick R. Maxfield

Although much of my laboratory now works on various aspects of lipid biology, my interest in lipids started accidentally. We were studying membrane protein traffic, and the transferrin receptor and the low-density lipoprotein receptor were the major objects of our interest. While recognizing the importance of membrane lipids, I mainly ignored them. I also assumed that much was known about lipid trafficking — just not by me. Eventually, I realized that much is known about lipid trafficking, but there are fundamental issues in this very important area of biology that are not well understood by anybody.

Basic mechanisms for maintaining distinct lipid compositions in different organelles are only partially understood, which means that this is an area where fundamental principles are still awaiting discovery. In addition to being a fascinating area of scientific inquiry, intracellular lipid transport plays a key role in dyslipidemias, which are a growing health problem throughout the world.

My first foray into lipid transport was using fluorescent lipids as a control for a membrane protein trafficking experiment. We found that, after endocytosis in fibroblasts, the recycling of the lipid analog was kinetically and morphologically indistinguishable from the recycling of the transferrin receptor (1). This supported our hypothesis that specific protein-protein interactions were not required for rapid and efficient recycling of transferrin receptors.

This satisfying result was published, but it left some gnawing questions. The lipid analog we studied recycled to the plasma membrane with nearly 100 percent efficiency, but obviously some lipids were required to form the membranes that went to late endosomes. Were there lipids that would be targeted preferentially to these organelles? If so, how? While we did make some progress on this by showing that some fluorescent lipid analogs could be sorted efficiently to late endosomes (2), this type of sorting remains poorly understood for natural lipids in cells.

In addition to being a fascinating area of scientific inquiry, intracellular lipid transport plays a key role in dyslipidemias, which are a growing health problem throughout the world.

Our results with fluorescent lipids were an example of one mechanism for lipid sorting: segregation of a subset of lipids during the formation of vesicles and tubules in membrane vesicular trafficking. In a recent Lipid News column (3), Patricia Bassereau discussed the role of lipid curvature induced by proteins on the selection of lipids into highly curved membranes, such as those formed in vesicular membrane trafficking. While the preference of individual lipid molecules for curved regions does not impose a strong selection, curvature can contribute to lipid sorting in lipid mixtures in which the composition is close to a phase separation boundary (4, 5).

Just as lipids are recycled at the plasma membrane, there must be similar mechanisms to sort lipid components in anterograde and retrograde transport at each step of the biosynthetic pathways. While general principles based on lipid phase separation and curvature preferences also are likely to play a role in these secretory pathways (6), much remains to be learned about how this works.

The second major mechanism for lipid sorting involves nonvesicular transport processes that exchange lipids among membranes. There are several examples of lipids that are delivered from a specific donor organelle to a specific acceptor, based in large part on binding specificity of the carrier proteins (7).

One example is the transport of ceramide by the ceramide-transfer protein, CERT, which has a ceramide-binding START domain. A pleckstrin homology domain can target CERT to Golgi membranes, and a FFAT motif binds the endoplasmic reticulum protein VAP (8). Thus, CERT can shuttle efficiently ceramide from its site of synthesis on the cytoplasmic side of the ER to the cytoplasmic side of the Golgi, where it can be converted to glucosylceramide. This type of selective nonvesicular transport process plays a role in determining the specific membrane composition of different organelles. However, in general, we do not know the relative contributions of vesicular and nonvesicular transport pathways to the flow of lipid between organelles.

Similarly, cholesterol, which is mainly synthesized in the ER, reaches organelles, including the plasma membrane, independently of vesicle transport pathways. Our work on LDL internalization naturally led to questions about how cholesterol gets from lysosomes to the ER, where the cell's sterol regulatory machinery is located. Using fluorescent sterols, we have made some progress in identifying nonvesicular sterol transport mechanisms (9), but overall it has been challenging to identify the carriers for cholesterol (or ergosterol in yeast).

In yeast, members of the oxysterol binding protein family have been proposed as nonvesicular sterol carriers, but elimination of many (or transiently all seven) of the OSBPs does not fully block sterol transport between the ER and the plasma membrane (10). In mammalian cells, an additional family of lipid-binding proteins, the START domain proteins, has been proposed to play a role in nonvesicular transport of sterols and other lipids, but much more work is required to understand their role (9, 11).

The third mechanism for regulating lipid composition of organelles is enzymatic transformations in specific organelles. This can include modifications of head groups as well as exchange of acyl chains. These reactions are carried out by enzymes that are localized to specific organelles, which can lead to local changes in the lipid composition. Additionally, these transformations can lead to changes in curvature preference or in the susceptibility to extraction of a lipid and binding to a nonvesicular transport protein. For example, removal of an acyl chain from a glycerophospholipid creates a lysolipid that has different curvature preferences and is easier to extract from the bilayers compared with the parent lipid.

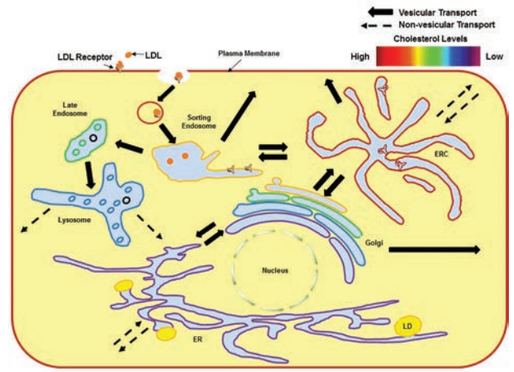


Illustration of some cholesterol trafficking pathways COURTESY OF DAVID B. IAEA

A major challenge in the field is to understand how all of these mechanisms are integrated to maintain the proper balance of lipid compositions in various organelles. An intriguing finding that provides a possible general mechanism for such integration is that several lipid transport proteins also are involved in regulating the vesicle transport machinery. It has been proposed that these proteins may serve as coincidence detectors to ensure that an appropriate set of lipids is available in a donor compartment before allowing the formation of a transport vesicle or tubule (12).

Studies in a variety of yeast mutants have been interpreted as indicating that a phosphatidylinositol transport protein, Sec14, coordinates lipid levels with membrane transport in the trans-Golgi network and endosomal compartments. Members of the OSBP family have been implicated in the transport of sterols and other lipids, but they also can regulate vesicle formation and the structure of the trans-Golgi network. It is unclear if these proteins play a significant role in sterol transport among organelles or if they are primarily lipid sensors that regulate metabolic pathways and membrane trafficking.

New tools, including lipidomics and high-resolution fluorescence microscopy along with genetics and molecular biology methods, finally are allowing us to make significant headway in understanding the details of intracellular lipid transport. It is likely that sophisticated computational modeling and systems biology approaches will be required to develop an integrated understanding of the many processes that play a role in determining lipid distribution.

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Frederick R. Maxfield (frmaxfie@med.cornell.edu) is a professor in the biochemistry department at Weill Cornell Medical College.

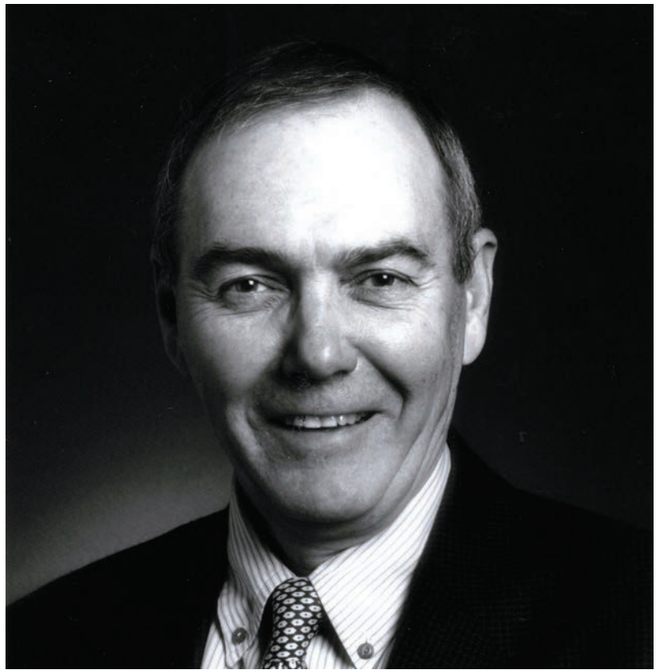
Malcolm Daniel Lane Sr.

(1930 – 2014)

By Daniel M. Raben and Gerald W. Hart

After a long battle with cancer, our friend, mentor, preeminent biochemist and consummate humanitarian M. Daniel Lane passed away April 10 at the age of 83.

Dan was not only a major leader in biochemistry but also contributed substantially to the success of the American Society for Biochemistry and Molecular Biology. He served on the ASBMB Council (1982 – 1985 and 1986 – 1992), as program chairman (1987 – 1989) and as president (1990 – 1991). Dan also served two terms on the editorial board of the Journal of Biological Chemistry, and he won the 1981 William C. Rose Award for his outstanding enzymology and metabolism research.



Dan, the scientist and teacher

The son of Danish immigrants, Dan was born in 1930 in Chicago. After obtaining his B.S. in 1951 and M.S. in 1953 from Iowa State University, he went on to earn his Ph.D. in 1956 at the University of Illinois. Dan's unique scientific talents were so apparent that he was soon recruited to Virginia Polytechnic Institute and State University in Blacksburg, Va., as an associate professor and was promoted to professor of biochemistry in 1963.

After a sabbatical in Munich, he left Virginia Tech to become an associate professor at the New York University School of Medicine, where he was promoted to professor in 1969.

In 1970, Dan moved to the Johns Hopkins University School of Medicine and served as director of the department of biological chemistry (then called the physiological chemistry department) from 1978 to 1997. In 2001, he was named a University Distinguished Service professor, and he became a professor emeritus in 2008.

Dan's scientific career was remarkable, with numerous seminal contributions to our understanding of enzymology of lipid-metabolizing enzymes, insulin signaling, adipogenesis, and the regulation of hunger and satiety.

Dan began his career studying carboxylases. It was Dan's discovery that propionyl-CoA carboxylase is a biotin-dependent enzyme and that the biotin prosthetic group is covalently linked to propionyl-CoA carboxylase. This was a seminal finding that launched our mechanistic understanding of these enzymes.

He then turned his attention to methylmalonyl-CoA:pyruvate transcarboxylase, another biotin-dependent enzyme. He developed an apoenzyme system to investigate the biotin-loading reaction, which stimulated further investigations into these enzymes. It is because of Dan's work that we now have an understanding of the enzymatic mechanisms of these enzymes.

While Dan made seminal contributions to our understanding of other enzymes, he is perhaps best known for his work on acetyl-CoA carboxylase, the key regulator of fatty-acid biosynthesis. His work defined the enzymology, partial reaction mechanisms, and regulation and structure of this enzyme. The importance of this work is underscored by the fact it is now required reading found in most textbooks of biochemistry.

Dan Lane on his boat fishing in the Chesapeake Bay.

Dan's classic work in the enzymology of lipid-metabolizing enzymes (for a recap, see 1) has been complemented by his contributions to our mechanistic understanding of insulin signaling and to the transcriptional regulation of lipogenesis and the role of hypothalamic malonyl-CoA in the control of hunger and satiety. This work led to the identification of genes essential for adipogenesis and the elucidation of the regulation of these genes at a molecular level (for a review, see 2).

Almost from the beginning of his career, Dan maintained an interest in the regulation of hunger and satiety. In an insightful series of studies, Dan discovered that hypothalamic elevation of malonyl-CoA, a key component in fatty-acid synthesis, suppressed hunger. His work on lipogenesis and satiety formed the bases of other studies currently being pursued by other investigators.

Dan's enthusiasm for science was infectious. He often was engaged in scientific discussions that inspired new and exciting hypotheses. Dan always asked insightful and stimulating questions in seminars and journal clubs. This ability to inspire his colleagues spilled over into his formal teaching skills, which remain legendary at Hopkins. Physicians who trained at Hopkins from 1970 until 2006 (when Dan formally stopped teaching) remember the "Lane Lectures" he gave in the metabolism section in medical school. It was not surprising, and it was well-deserved, when he was recognized by the Johns Hopkins community with the Johns Hopkins University School of Medicine Professor's Award for Distinction in Teaching.

Dan Lane's discoveries earned him many honors and awards, including the following:

- American Society for Nutrition's Mead Johnson Award, 1966
- American Society for Biochemistry and Molecular Biology (formerly American Society of Biological Chemists) William C. Rose award, 1981
- Johns Hopkins University School of Medicine Professor's Award for Distinction in Teaching, 1986
- National Institutes of Health MERIT award, 1990

He was recognized by election to numerous societies, including the following:

- American Academy of Arts and Sciences, 1982
- National Academy of Sciences, 1987
- American Society for Nutritional Sciences, 1996

He held numerous leadership positions, including the following:

- President, American Society for Biochemistry and Molecular Biology
- Member, ASBMB Program Committee, Membership Committee and Public Affairs Committee
- Editorial board member, Journal of Biological Chemistry, Biochemistry et Biophysica Acta, the Archives Biochemistry and Biophysics, and Annual Reviews of Biochemistry.
- Executive editor and editorial board member, Biochemical and Biophysical Research Communications

Dan, the humanitarian and mentor

Dan was not only a consummate scientist; he was also a compassionate humanitarian and supportive mentor. Dan always nurtured younger investigators, and this nurturing led to the development of many of our current leading investigators. Virtually everyone Dan recruited to the faculty has had a highly successful and internationally recognized career. He constantly supported his faculty for awards, elections to national academies and even Nobel prizes.

Dan truly believed that a key responsibility of a department chair is to create a supportive environment that promotes creativity, love of science and a vigorous interchange of ideas. Under Dan's direction, the biological chemistry department felt like a family in which we all supported and cared for each other. When faculty members left Dan's department, it was usually thanks, in part, to Dan's unselfish promotion of them to assume leadership positions.

Dan was fearless in his defense of science, science education and training, and scientists. This contributed to his ability to provide a productive and supportive intellectual atmosphere for the scientific community. He and his wife, Patricia Sonquist Lane, were

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true champions of human rights, and their sense of humanity was palpable. Dan was not only aware of violations of human rights and dignities and assaults on the environment, but he also worked hard to alleviate those violations and curb those assaults. Dan fought to maintain voting rights and protect our environment, including efforts to improve the water quality in the Chesapeake Bay.

Any discussion of Dan also must include his personal love for his family, boating and fishing. It was always obvious that Dan cherished his family. For 60 years, Dan was married to Pat, who preceded him in death in 2010. Pat also played a key role in creating a familylike environment in the department. Dan's pride for his family was apparent in his office, which was filled with family pictures.

And it must be said that these pictures were not alone; they were accompanied by photos of his boats and the fish he had caught. Boating and fishing were two of Dan's true joys. Dan was a premier fisherman — of ground-breaking data and young scientists as well as big fish.

The loss of Dan has left a huge void in our scientific community. His warmth, compassion and scientific acumen will be missed by family and colleagues alike. It is sad to realize that future scientists will not have the opportunity to enjoy and be inspired by contributions he would have made if he were still with us. Dan has influenced us all, and for that we can all be thankful.

Daniel M. Raben (draben@jhmi.edu) is a professor in the department of biological chemistry at the Johns Hopkins University School of Medicine and an ASBMB Lipid Research Division leader. Gerald W. Hart (gwhart@jhmi.edu) is director of the biological chemistry department at the Johns Hopkins University School of Medicine and an associate editor for Molecular & Cellular Proteomics and for the Journal of Biological Chemistry.

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Vitamin D

How much is enough?

By Rajendrani Mukhopadhyay

Her body hurt. It wasn't the ache of tired bone and muscle after a long day but severe musculoskeletal pain that had been progressing over five years. The 35-year-old woman underwent extensive medical workups, which resulted in her being offered narcotics and antidepressants. She declined those. She even had a bone scan that showed abnormalities that no one could explain. Finally, the day came when the pain weakened the woman to the point that she couldn't stand at the kitchen counter. Her children were taken away from her because she was unable to fulfill her parental duties.

Then she showed up in Gregory Plotnikoff's office at Allina Health Care in Minneapolis. He noted that the woman had trouble getting up from a chair and the bone abnormalities recorded in her medical reports. He ordered a vitamin-D test. The test results showed that she was profoundly deficient in vitamin D, so he prescribed her supplements. "Truly, $100 worth of vitamin D, and she got her two kids back," he says.

Plotnikoff brings up this anecdote when he argues that we, as a population, need to increase our intake of vitamin D. He is one of several clinicians who are convinced that an unrecognized vitamin-D deficiency is the root of a slew of illnesses that are not limited to only bone. They include cardiovascular disease, various cancers and autoimmune disorders. They say that the current recommendation by the Institute of Medicine that everyone, from toddlers to the elderly, take 600 international units of vitamin D every day is woefully inadequate (1).

Other experts disagree. They say that there is solid evidence to connect vitamin D only to bone health, on which the IOM based its recommendation in 2011. "There's this view that vitamin D is a miracle hormone that does literally everything," says J. Wesley Pike at the University of Wisconsin–Madison. "The fact of the matter is that's just simply not true."

What is vitamin D?

There are two types of vitamin D: vitamin D2 and vitamin D3. Vitamin D2 is generally found in fortified foods, such as milk and some other dairy products, cereals and orange juice. The few natural sources of vitamin D include shitake mushrooms and fatty fish, such as salmon, sardines and mackerel. Vitamin D3 is the product of sunshine. Ultraviolet light from the sun converts 7-dehydrocholesterol in the skin into previtamin D3. The previtamin D3 gets turned into vitamin D3.

But both forms of vitamin D need to be activated to work. Vitamin D2 and D3 get hydroxylated by a P450 enzyme in the liver to be turned into 25-hydroxyvitamin D. This prohormone binds to a protein in the blood called the serum vitamin D-binding protein. Clasped to its binding partner, the prohormone then travels through the blood circulation system for about two weeks. When the bound prohormone gets to the kidneys, an enzyme called CYP27B1 hydroxylase in the proximal tubular epithelial cells turns it into the active hormone 1α,25-dihydroxyvitamin D.

This active form of vitamin D has a fleeting existence in plasma. In the parathyroid gland, bone, kidney and intestine, 1α,25-dihydroxyvitamin D binds to the vitamin-D receptor, which is part of the nuclear receptor family of transcription factors. The transcription factor forms a heterodimer with the retinoid-X receptor. The heterodimer binds to hormone response elements on DNA to turn on or turn off the expression of a variety of genes, such as ones involved in calcium absorption in the intestine.

CONTINUED ON PAGE 26

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When is someone deficient?

Warped bones in children with rickets and adults with osteomalacia are signs of inadequate vitamin-D intake. In 1922, a group led by Elmer Verner McCollum at Johns Hopkins University demonstrated the existence of a fat-soluble nutrient that was involved in calcium absorption (2). They called this nutrient vitamin D. In 1924, Harry Steenbock and A. Black at the University of Wisconsin–Madison demonstrated that irradiating certain foods, most notably milk, and feeding those foods to animals reversed rickets (3). Steenbock patented his discovery, and the 1930s saw the introduction of foods fortified with vitamin D. By the end of the 1930s, rickets was no longer a public health problem.

The definition of a vitamin-D deficiency has morphed over time. Until the 1930s, rickets and osteomalacia were most the visible signs of the deficiency. These days, a deficiency in vitamin D is determined by a blood test. The test, usually based on an immunoassay, measures the level of the prohormone 25-hydroxyvitamin D. It's clear that if someone has a blood level less than 20 ng/mL, that person is in danger of developing a bone disorder or hyperparathyroidism.

The IOM report in 2011 stated that a level between 21 ng/mL and 29 ng/mL of 25-hydroxyvitamin D was considered to be sufficient for maximum bone health. This is the range being disputed between vitamin-D experts. Some believe we need a blood level of more than 30 ng/mL of 25-hydroxyvitamin D; others think the IOM committee behind the report got it right.

The split comes over whether vitamin D does more than maintain bone health. Some experts think that vitamin D plays more roles than we give it credit for and that we should be taking higher doses of it so that it can do all its different physiological jobs. Other experts say the evidence for vitamin D in diseases beyond ones found in bone and parathyroidism is weak; they worry that higher doses may cause more harm than good.

The dispute actually has been going on for decades, and it was further fueled by the 2011 IOM report. Three years after the report, the debate hasn't abated, as evidenced by two meta-analyses published in the British Journal of Medicine in April that attempted to make sense of the vitamin-D literature (4, 5). Based on the conclusions of the two studies, the BMJ editorial urged caution in attributing diseases (besides the ones in bone) to a vitamin-D deficiency (6).

The 2011 IOM report

The IOM report on vitamin D and calcium came about because "the federal agencies that make use of the dietary reference intakes were aware that there was the perception that the public might be becoming more vitamin-D deficient," says A. Catharine Ross at Pennsylvania State University, who chaired the IOM committee for the 2011 report. Data were showing that clinicians and the public were increasingly shelling out money for vitamin D. In a New York Times story published in 2010, journalist Tara Parker Pope noted that in 2008, consumers spent $235 million on vitamin D supplements, compared with $40 million in 2001; orders by physicians for vitamin D tests with Quest Diagnostics dramatically rose in 2009.

So the IOM committee, sponsored by the U.S. Department of Agriculture, U.S. Department of Defense, U.S. Department of Health and Human Services, and Health Canada, was tasked with analyzing the vitamin-D literature and making appropriate recommendations that could be applied to the general North American population.

The committee had to follow a risk-assessment model. In that model, explains Ross, there has to be a causal link between the intake of a nutrient and a physiological outcome, such as a bone disorder. "If you don't have solid evidence that A is causally related to B, then it becomes not appropriate to use it" for establishing a dietary reference intake, she says.

For cardiovascular disease, autoimmune disorders and cancer — physiological disorders suggested to be connected to a vitamin-D deficiency — the committee could not find causal links. "There is quite a bit of literature," acknowledges Ross. "But some of it is of the type where an observation was made in a population with cardiovascular disease, and serum vitamin-D levels may have been measured and were a little bit low. But that's not establishing a link."

Ross says the only clinical outcome that the committee could see where vitamin D had a direct effect was bone health. The literature on that was more extensive and conclusive, so the committee used it to base its recommendation of a daily vitamin D intake of 600 IU.

"It wasn't that we ignored the other studies. It wasn't that we said they were uninteresting or they were not to be considered," Ross says. But in the report, the committee described the problems it ran into in trying to find the connections between vitamin D and other health outcomes other than bone disease:

"These include the difficulty of isolating the effects of a single nutrient under investigation from the confounding effects of other nutrients and non-nutrient factors; the multi-factorial etiology of the chronic diseases the committee considered; the paucity of data from randomized controlled clinical trials, which typically provide the highest level of scientific evidence relevant for (daily recommended intake) development; and the mixed and inconclusive results from observational studies."

Some vitamin-D experts say that the IOM's need to see data from randomized controlled trials is misguided and bewildering. "They said there's not sufficient evidence to suggest that vitamin D has any real effect outside of the skeletal system because there weren't any appropriate randomized controlled trials," says Bruce Hollis at the Medical University of South Carolina. "Randomized controlled trials were designed for drugs, not nutrients."

Both he and Robert Heaney of Creighton University say that randomized controlled trials in nutrition are not feasible in most cases. Vitamin D is an essential nutrient. To test its effects on a certain physiological outcome in a randomized controlled trial, a significantly large group of participants within the study would have to be denied all sources of vitamin D. But this kind of trial simply cannot be done for ethical reasons, explains Heaney, when you know you are depriving people of an essential nutrient. But then organizations like the IOM turn around and say they can't make recommendations for a nutrient without data from randomized controlled trials.

"We've got a catch-22," says Heaney. "Randomized trials are purely empirical, which is fine for

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drugs. They are foreign agents. But nutrients and hormones are not foreign agents. They are native to the body. They should be there."

Critics of the IOM report had other bones to pick. One was the question of sun exposure. Sun-driven production of vitamin D is the most effective source of the nutrient. In the summer, a white person can make 10,000 IU after spending 30 minutes in the early-afternoon sun without sunscreen. But Ross explains that the committee couldn't recommend that people catch more sun because of the relationship between skin cancer and ultraviolet light exposure. "We ended up saying we will try to specify a recommended daily intake in the absence of sun," says Ross. "We realized there really is no such thing as absence of sun, but we called it minimal sunlight exposure." She says the 600 IU recommended for vitamin D was made to maintain an adequate serum level of the vitamin even in the absence of sun "but knowing full well that, for many people, sun adds to that. Chances are their actual total exposure, considering both diet and sun, is actually higher."

Meanwhile, experts point out that black people have different requirements for vitamin D and calcium; melanin absorbs UV light and interferes with its transmission into the skin, reducing the production of vitamin D. Also, black Americans tend to consume less dairy, which is usually fortified with vitamin D. As John Adams at the University of California, Los Angeles, explains, the first values for serum levels of vitamin D were established by studying white people. He says that, if we look at the U.S. population today, about 60 percent of the white population has a serum level of 25-hydroxyvitamin D of less than 30 ng/mL. "If you look at African-Americans who have a (25-hydroxyvitamin D) level less than 30 ng/mL," says Adams, "it's 95 percent of the population."

Sun exposure at different latitudes is another aspect that clinicians say needs to be considered. Plotnikoff says that he and colleagues have observed that Southeast Asians moving from their home countries to higher latitudes in the Western Hemisphere develop cardiovascular diseases and autoimmune disorders like multiple sclerosis. In these studies, patients were shown to have low levels of 25-hydroxyvitamin D.

But Hector DeLuca at the University of Wisconsin–Madison counters those studies. DeLuca, who served as a consultant to the IOM committee, uses multiple sclerosis as an example. "There is clearly a relationship between sunlight and the incidence of this disease. It's been known since, I think, 1964. You know what? There are other things that sunlight does besides produce vitamin D," he says. "But because the vitamin D system is so well-known and we know that it's very important for health, everyone focused on the idea that maybe vitamin D" has something to do with multiple sclerosis. DeLuca says subsequent studies have shown in animal models that a vitamin-D deficiency doesn't cause multiple sclerosis.

The IOM report set the upper limit for taking vitamin D at 4,000 IU for adults and between 2,500 and 3,000 IU for children, based on their ages. Critics say the upper limit could have been higher. They point to a review that showed that doses of vitamin D up to 10,000 IU were not toxic (7).

But Ross explains, "We're making recommendations that might have a shelf life of a decade or more. You have to be cautious under those circumstances. I think that really helps to explain why we stop at 4,000, even though some people might say you could take more and it wouldn't be harmful. We were not so certain."

Pike and Adams both point out that the production of the active vitamin-D hormone is tightly regulated. Popping more vitamin D supplements may not actually affect your level of active vitamin D. The prohormone may just wind up leaving your body through urine. "If you get out in the sunlight, particularly in the equator, and you have a lot of exposed skin, you can make 25,000 or even 50,000 units of vitamin D in an hour," says Pike. "But it's not active because it needs to be converted eventually to (1α,25 dihydroxyvitamin D), irrespective of how much you have. It's very tightly controlled. That's really the key to the vitamin-D system — the hormone is exquisitely regulated."

Michael Holick at Boston University chaired the Endocrine Society's committee on vitamin D (8). The goal was to provide guidance to clinicians for the prevention and treatment of vitamin-D deficiency; the IOM's goal was to provide guidance for the general population. Holick defends the IOM committee, even though he doesn't agree with its recommendation. (He too thinks that the recommended daily intake should have been higher.) "I think they did a great job because, believe it or not, what people don't realize is before they met the actual recommendation for vitamin D in all children and adults was 200 units a day," he says. "They now say no, no, no, it's actually 600. To me, that's a big change."

In the meantime, everyone is waiting to see the results from a large-scale randomized trial now happening under the purview of the National Institutes of Health. The agency is supporting a long-term study of daily intake of vitamin D3 pills of 2,000 IU. Spearheaded by JoAnn Manson and Julie Buring at Harvard University-affiliated Brigham and Women's Hospital, the trial is called the vitamin D and omega-3 trial, from which various letters have been plucked to give the trial the name VITAL.

VITAL is tracking 25,875 men and women across the U.S. The study participants are divided into four groups: One group is taking both vitamin D and omega-3 fatty acid capsules; one group is taking vitamin D and a placebo; one group is taking

CONTINUED ON PAGE 30

CONTINUED FROM PAGE 29

omega-3 pills with a placebo pill; and the final group is taking two placebo pills. Manson explains that the trial has a cost-effective design that allows the investigators to study two separate nutrients efficiently and look at their effects both independently and in combination.

The aim of the VITAL study is to see if taking daily dietary supplements of vitamin D3 or omega-3 fatty acids reduces the risk for developing cancer, heart disease and stroke in people who do not have a prior history of these illnesses. Manson says that VITAL has placed special emphasis on recruiting black participants and has enrolled 5,108, which is 20 percent of the study population. "We're very much interested in whether vitamin-D supplementation may narrow the gap between whites and blacks in terms of cardiovascular mortality, heart failure, prostate cancer, breast cancer mortality, stroke and diabetes," she says. "Many of these outcomes have higher rates in blacks than whites."

But until the study concludes in 2017, Manson says, "The jury is still out on the benefits and risks of high-dose vitamin-D supplementation for nonskeletal outcomes."

Not done with D

Many of the observations of vitamin D affecting the cardiovascular, muscle and liver hepatic systems may be indirect effects, points out Pike. "Vitamin D has a pervasive effect on the maintenance of calcium and phosphorus levels in the blood," he says. When systems go awry in the presence of the vitamin-D deficiency, it is not clear whether the organs are experiencing a direct effect of the deficiency or an indirect effect through the disruption of mineral metabolism brought on by the vitamin-D deficiency.

Experts say that the controversy over vitamin D also highlights the need to rethink using the prohormone 25-hydroxyvitamin D as a measure of the body's overall vitamin-D status. We measure 25-hydroxyvitamin D because it's blood-borne and stable over several days. But just because it's easy to measure doesn't mean it's the right thing to measure. Adams, Hollis and others say that the standard serum measurement is a surrogate measure: It doesn't show how much of the prohormone is free of the binding protein and available to be turned into the active hormone. This is important, says Adams, because some isoforms of the serum vitamin D-binding protein bind more avidly to 25-hydroxyvitamin D. These isoforms are known to be expressed specifically in blacks, once again giving a misleading interpretation of their overall vitamin-D levels.

Questions also persist about the vitamin-D receptor, which are as simple as "Where is it found?" Some experts, like Plotnikoff, say that vitamin D's far-reaching effects in the body make sense because the receptor is found in every tissue. But others disagree. "Some of us are not convinced that significant levels of vitamin-D receptors are routinely expressed in many of those cells and tissues" in the cardiovascular and muscle systems, says Pike. "Try as we might, but over literally 30 years we have never been able to show vitamin-D receptors present in gross muscle tissue."

Pike says some claims have been made in the literature about finding the vitamin-D receptor in all kinds of tissues but the data are generally weak. In those cases, investigators studying skeletal muscle, as an example, "grind up tissue, let cells grow in culture and then measure the vitamin-D receptor. Sure enough, there it is," explains Pike. "The reality is growing those cells causes them to differentiate and change. Smooth muscle cells are notoriously able to differentiate into other cell types. The presence of receptor in those cell lines just doesn't cut it. It's just not right."

Plotnikoff, Hollis and others who think we should be taking in higher doses of vitamin D are frustrated. They believe that scientific and health authorities have paid no heed to their warnings. Plotnikoff says it's heartbreaking to see patients, like the woman he took care of, suffer. "People are miserable. They are put on all kinds of medications and misdiagnosed with metastatic breast cancer or depression or something else," he says. "Vitamin D is cheap and easy."

But observations like this are not yet backed up by large-scale studies, says Pike, and lead to problems: "Clinicians see one patient that happens to take a vitamin D pill and the next day, they get over the flu. Vitamin D treats the flu! This is nonsense."

The need for more research is a unifying sentiment. Experts say that, despite vitamin D being discovered a century ago, research into it lapsed once rickets was cured. The field saw a resurgence once DeLuca and colleagues demonstrated in 1968 that vitamin D required activation inside the body to work (9) as well as after the cloning of the vitamin-D receptor in the late 1980s. But fundamental gaps in understanding remain. For instance, researchers still don't know the molecular details of how the vitamin-D receptor heterodimer complex works at regulatory sites to influence gene expression.

So when Plotnikoff says "It's mind-boggling that there isn't more attention to be paid to vitamin D," that's a statement all vitamin-D experts can agree on.

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

Location, location, location!

Graduate school and postdoctoral stints offer a nice change of place, so choose wisely

By Shaila Kotadia

Young scientists repeatedly hear that they will not have the freedom to be selective about where they live when they are searching for faculty positions. Unfortunately, this is true in most cases, especially now, with only about 20 percent of Ph.D.s obtaining academic, tenure-track positions. But this is also great motivation to put a lot of thought into where you will live during graduate school and during your postdoctoral training years.

Since location can influence your happiness, here are stories of scientists who determined their paths partly by location and have never looked back.

Justin Crest is a postdoctoral research fellow at the University of California, Berkeley. He started his higher-education path on the California coast, attending graduate school at the University of California, Santa Cruz. But before accepting UCSC as his graduate school of choice, he was offered a fellowship at Columbia University in New York that would cover five years of funding. Despite the wonderful offer from Columbia, he says, location was key to making his decision:

"Graduate school is a difficult initial step into academic research. Choosing the wrong program can make this step even more difficult, which is why I considered many factors — from prestige, to class size, to distance from my family. Not to mention, living in a beautiful location like Santa Cruz makes every failed Western blot sting a little less."

Respondent	Location	Salary Comparison*	Difference
Justin Crest	Santa Cruz, Calif.	$40,000	32.1%
	New York	$58,952	
Shondra Miller	Dallas	$40,000	26.7%
	La Jolla, Calif.	$54,607	
Mark Chen	San Diego	$40,000	-28.1%
	Ann Arbor, Mich.	$31,224	
Shaila Kotadia	Santa Cruz, Calif.	$40,000	-52.6%
	Kansas City, Mo.	$26,214	

*All data collected on CNNMoney with closest comparable city: http://money.cnn.com/calculator/pf/cost-of-living/

Having grown up and completed her undergraduate studies in Arkansas, Shondra Miller had become accustomed to a reasonable cost of living. Regardless, she applied to graduate schools across the U.S. She was fortunate enough to get accepted to several schools, including The Scripps Research Institute in La Jolla, Calif., and the University of Texas Southwestern Medical Center in Dallas, Texas. Ultimately, she says, the decision came down to affordability of each location:

"I considered my options. I could go to Scripps and live with four other people in a studio apartment, or I could go to UTSW and actually own a two-bedroom, two-bath home. I figured I could do excellent science at either school, but I would be happier doing it with a little space to call my own."

After completing his Ph.D. in Dallas, Mark Chen considered his options for his postdoctoral research. He had grown up in Michigan and Southern California and was fond of both locations. Knowing that he would be happy in either place, he limited himself to Ann Arbor, Mich., and San Diego for postdoctoral labs. In the end, he decided to live in San Diego and enjoyed his time back on the West Coast. He explains:

"I was very interested in the work of both labs, in Michigan and San Diego. Ultimately, I wanted to experience not just science but life in a new location. While I had a soft

CONTINUED ON PAGE 33

The cool professor

By Prof-like Substance

When I started my lab, I had a very distinct idea of the type of principal investigator I wanted to be. I had experienced some different styles and observed many others. I knew what my needs were as a graduate student and as a postdoc and recognized gaps in what my mentors had provided for me. Above all, I thought I could navigate that line between friend and boss where all my trainees would both respect me and want to hang out with me.

Oh, and I wanted to ride a unicorn to work every day.

I'm soon to finish up my sixth year as a PI and have mentored two cohorts of students at this stage. I'm hardly a grizzled vet of the mentoring game, but I've had enough experience to change my views on my role. There's been a discussion on Twitter recently about whether someone is a mentor or a boss. It's a false dichotomy. An effective mentor is both. Sometimes you can spend your time leading your people in the general vicinity of water, and sometimes you have to hand them a cup and tell them to drink.

When I say that, I often hear people tell me, "Well, my adviser was totally hands-off, and it helped us be independent and successful!" Whereas I won't dispute that many people can do well in that environment, it's often convenient to leave out the long list of those who flounder in those conditions and spend years of their lives without advancing their career goals.

There are times when certain things need to get done for the lab and the trainee alike, and there are times when the fostering of independence yields tremendous results. To pretend that a PI never has to act like a boss to make sure the bills get paid and the science gets done is a ridiculous view of how a lab functions. If a student comes in with all his or her own funding, then he or she can be free from the lab's reporting, publishing and proposal-writing needs. Otherwise, as the lab goes, so go one's opportunities.

I still care that I have a good relationship with my people. I still hope that they like me and that we can sit down over a beer and enjoy the time spent together. But I'm far less concerned about blurring the line between personal and professional relationships. I want to put people in the position to succeed at doing whatever it is they want to do while advancing the lab's overall agenda. If that sometimes means pushing people to get certain things done, so be it.

Editor's note: This piece originally appeared April 14 on the author's blog and has been reprinted with permission.

Prof-like Substance (proflikesubstance@gmail.com) is an evolutionary biologist and blogger. Visit scientopia.org/blogs/proflikesubstance for more viewpoints and commentaries.

CAREER INSIGHTS CONTINUED

CONTINUED FROM PAGE 32

spot in my heart for Ann Arbor, I felt going to San Diego would be new and exciting. It didn't hurt either that the average temperature of San Diego was 70 degrees. Looking back, I think choosing a location that you are happy outside of work is very important to your mental well-being. In the end, your experience is what you make of it, but there are certain characteristics of a location that appeal to your interests that makes the grind of a postdoc more bearable."

And then there's me. When choosing my postdoctoral lab, I had it narrowed down to the Stowers Institute for Medical Research in Kansas City, Mo., or the University of California, Santa Cruz. Both offered wonderful mentors who I knew would help me flourish as an independent scientist. The faculty members I spoke to encouraged me to go to Stowers, given its prestige and limitless resources. My friends didn't understand why I was even thinking about it; clearly, Santa Cruz was the city for me.

As much as I struggled with the decision, and while Kansas City was unexpectedly charming, it took just one look at the ocean to know that I was moving to Santa Cruz. It was the best decision I've ever made and an experience I never will forget.

Shaila Kotadia is the education and outreach manager for the Synthetic Biology Engineering Research Center (Synberc) and the California Institute for Quantitative Biosciences (QB3) at the University of California, Berkeley.

Quick guide to career fairs

By Donna Kridelbaugh

You may be hesitant to attend a career fair if you are not formally in the job market, but I would encourage you to reconsider the value of these events for your personal career development. A career fair is an interactive way to assess the job market and build connections with future employers.

A few summers ago, I attended a small career fair hosted by the national lab where I worked that was attended by numerous employers. I went armed with copies of my résumé and a mindset that was different from that of most attendees: I used the event as a career-exploration exercise to evaluate how my skills and qualifications might fit into the future employment needs of research institutions.

By chance, a senior scientist from another national lab was in attendance because the lab recruiter had a travel conflict at the last minute. The scientist took the time to listen to me explain how I like to manage technical projects and then suggested that project management would be an ideal career path. (He also stared at me like a weird specimen under a dissecting microscope, because most scientists are not known for their love of staying organized!) In the end, I left the career fair with a renewed sense of purpose and the realization that I could take control of my career.

Career fairs are just networking events. My best advice is to avoid even asking about jobs and instead to focus on building rapport with the exhibitor by asking engaging questions: How do you like the company? What is the future direction of the company? Who is your ideal employee?

Varieties of organizations run career fairs and advertise these events on their websites, including the following entities:

1) career centers at universities, postgraduate offices, community colleges and state governments;

2) local chambers of commerce and newspaper groups;

3) professional science conferences and societies; and

4) private recruiting companies (e.g., BioSpace.com).

Also, online career fairs are becoming more common. The virtual format is a more affordable and convenient option for both employers and job seekers. These online events provide an extra opportunity to network and job hunt on a geographically limitless basis and allow job seekers to maintain privacy if desired.

Both in-person and virtual career fairs require preparation. I have compiled a few general tips, based on my own experiences, along with advice specific to a virtual environment. If you're not sold on attending a career fair any time soon, then I definitely encourage you to at least stop by a virtual career fair for an hour or two to experience it for yourself.

Lastly, remember that any professional venue can serve as an informal career fair. Once when I volunteered as a poster judge during a national research conference, I inquired about whether any institutions had research programs starting up that would need managers. I was surprised at the level of positive feedback I received, including invitations to apply for future positions.

Donna Kridelbaugh (@science_mentor) is a communications consultant and founder of ScienceMentor.Me. Her mission is to create an online field guide to self-mentoring in science careers. She offers writing, editing and marketing services for early-career professionals who are ready to advance their career to the next level. Learn more at http://sciencementor.me/.

Selected upcoming career fairs and resources events*

Aug. 11 – 12: American Chemical Society Career Fair *(Virtual and San Francisco)*

Sept. 19: STEM Diversity Career Expo *(New York City)*

Sept. 23: National Organization for the Professional Advancement of Black Chemists and Chemical Engineers Annual Conference *(New Orleans)*

Oct. 15 – 18: Society of Mexican American Engineers and Scientists Symposium *(San Diego)*

Oct. 16 – 18: Society of Asian Scientists and Engineers National Conference *(Philadelphia)*

Oct. 16 – 18: Society for Advancement of Chicanos and Native Americans in Science National Conference *(Los Angeles)*

Oct. 18 – 22: American Society of Human Genetics Annual Meeting *(San Diego)*

Nov. 2 – 6: American Association of Pharmaceutical Scientists Annual Meeting *(San Diego)*

Nov. 13 – 15: American Indian Science and Engineering Society National Conference *(Orlando, Fla.)*

Nov. 15 – 19: Society for Neuroscience Annual Meeting *(Washington, D.C.)*

**This list is not all-inclusive, and information is subject to change.*

Career-Fair Preparation Guide

What to do	Virtual tip
Résumé: Design a one- or two-page résumé for a broad audience and include a clearly defined objective statement. Check deadlines for submitting your résumé to employers before the fair. Also, consider making a detailed LinkedIn profile with a custom URL and bringing along a business card that includes that link with a corresponding quick reference code.	As soon as you create your account on the virtual fair website, upload a résumé, add URLs for your public LinkedIn profile or personal website, and complete your profile.
Elevator pitch: Craft a three-sentence statement that includes one sentence each on your background, skills and career objectives. Remember to use complete sentences, proper grammar and professional language!	Cut and paste this statement into a chat box or recite the words during a video chat. Pay attention to character limits in the chat box.
Time off: Schedule time away from work to participate in the career fair and consider making up the hours in the evening or using vacation time.	Find an area clear of distractions (not your desk at work).
Appearance: Wear business or business-casual dress. Wear comfortable shoes in case the lines are long.	Use a blank wall as a backdrop, turn on adequate lighting, use a headset and test equipment with the help-desk tech.
Navigation: View the agenda for the event and map out an itinerary for your activities. Know where each event will be held, arrive early if possible and take advantage of the information desk if you need accommodations.	Orient yourself with each virtual room, take advantage of tutorials and ask questions at the help desk.
Research: Look through the list of employers, research their open positions and company profiles, and narrow down the list of ones in which you're interested. Sign up for an appointment with each targeted employer as early as possible.	If you don't hear from the recruiter at your scheduled time, send a polite message to the booth to confirm.
Network: Introduce yourself to other job seekers so that you can share notes and strategies for the job search. Peers can be a great source of support and encouragement.	Search profiles of attendees, find people with related interests and introduce yourself through private chats.
Resources: Take advantage of free career-development services offered during the fair (e.g., seminars, résumé reviews and one-on-one counseling).	Save links and files for download.
Follow-up: Thank each recruiter after the fair in a short email or handwritten note via snail mail. Reiterate why you are interested in the company and remind him or her of your skills and qualifications. Plus, send emails or LinkedIn connect requests to other contacts that you met.	

The measure of success

By Andrew D. Hollenbach

I was sitting in my office one day when a student poked his head around the door and asked, "Andrew, do you have a minute? I'd like to talk to you about something."

Even though I was behind on deadlines (nothing new in my world), I said, "Of course!"

He started talking about what he wanted to do once he defended his thesis. With hesitation (and with what he later told me was concern about disappointing me), he mentioned that he wasn't sure he wanted to go into academic science, to which I responded without hesitation (and with what I must admit was a little relief), "Well, what do you want to do when you grow up?"

It's important that our students be made aware that academic science is not the only career path available to them.

I always say that it takes a special kind of crazy to go into academic science. I have that special kind of crazy. However, I realize that not all of my students have it, will have it or even want to have it.

I do my best to be transparent — to let my students see what I deal with as an academic research scientist. Granted, I don't let them see all of the warts (no need to scare them unnecessarily); however, I make sure that they see the reality of being a faculty member in the academic world, and I let them decide if that is what they want to be too.

I also let them know about career paths that are available to them. I've been in the academic world for nearly 25 years. Along the way, I have made many friends who have followed many different paths. They have become faculty members at teaching colleges, high-school science teachers, administrators in curriculum development, researchers in industry, entrepreneurs for startups, program officers at federal agencies, scientific writers and editors, lawyers specializing in intellectual property, activists in scientific policy, sales representatives for scientific companies, and — yes — even faculty members at research universities.

'This is your degree. You do with it exactly what you want.'

All the people on this diverse list identified career paths for which they are passionate, developed the skills they needed, took advantage of opportunities (both planned and serendipitous) and, most importantly, applied the critical-thinking skills they developed in graduate school and their postdoctoral positions to bring a new depth and vitality to their chosen careers.

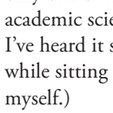
A big part of being a mentor, for me, is getting to know my students and figuring out exactly what it is that they want to do once they earn their Ph.D.s. I tell them, "This is your degree. You do with it exactly what you want. Ultimately, it's your life, you're the one that has to go to work every day, and you have to be happy!"

I also make a point of telling them what I see as their strengths and weaknesses and of telling them what I hear them saying over a beer at the local bar on our regular lab outing. My students have gone on to become, among other things, a translational research physician, a technology transfer and intellectual property specialist, a burgeoning scientific writer and editor, a future director of a molecular genetics diagnostics lab, and even an assistant professor.

To the members of a Ruth L. Kirschstein training grant study section, I would not necessarily be considered a successful sponsor, because only one of my five students stayed in academic science. (Trust me, I know. I've heard it said many, many times while sitting on these study sections myself.)

However, to me, I am successful beyond measure, because I have molded minds that can think critically about science and about their lives. I have tried, as a mentor, to give them the confidence, freedom, support and opportunity to follow whatever paths make them happy. I'm extremely proud of every single one of my students — or, as I call them, my kids — and rejoice whenever they excel in their careers and in their lives. This, to me, is success. And this is what we, as mentors, need to do for our students.

Students, you also must realize that once you have your degree, the sky's the limit. It's up to you to figure out what makes you passionate, follow that passion, never give up fighting until you achieve your goal and, most importantly, understand that you can achieve whatever you put your mind to.



Andrew D. Hollenbach (aholle@lsuhsc.edu), author of the book "A Practical Guide to Writing a Ruth L. Kirschstein NRSA Grant," is an associate professor in the genetics department at Louisiana State University Health Sciences Center in New Orleans.

The road to professor

By Bill Sullivan

Author's note: If I were an undergraduate today writing a letter informing my parents that I want to become a professor and conduct research, I imagine it would go something like this.

Dear Mom and Dad,

I've decided that I want to go to graduate school to get my Ph.D. in the biological sciences. I want to make a real difference in the world by contributing to society's understanding of the cells that make up our bodies and hopefully make a discovery that helps ease suffering or even saves lives.

While this sounds like a noble endeavor, I've heard that it doesn't come without challenges and consequences.

For example, I'm probably going to be behind on the usual timeline for things like financial independence and starting a family. I'm looking at roughly five more years of school to get the Ph.D. — the amount of time depends on whether my experiments are successful, which is impossible to predict. Nature is a tricky beast, and most of our guesses about how things work are wrong. But it's those unexpected results that usually lead to something amazing, and I want to be on the front lines of those breakthroughs!

I hope that my research mentor stays funded, which I understand to be nearly impossible these days. The major source of research funding is the National Institutes of Health, which has struggled with more than a decade of stagnant funding. If my mentor loses funding or decides to leave academia, I will have to find a new lab and go back to square one.

The good news is that we do not pay for graduate school! In fact, I get paid to attend! But don't put your checkbook away yet: The stipend I receive will be only $24,000 a year. I know it sounds crazy for a college graduate to be making such a low amount of money for working 80-plus hours a week on projects that may one day benefit millions of people, but I'm not in this for the money. Oh, and don't expect me home on most weekends and holidays. The cells and mice I must tend to won't care what day it is. Not sure how I am going to afford rent unless I live in one of the most dangerous parts of the city, but since I will be working in the lab so much, perhaps I can just live there. (Kidding!)

So let's say all goes well and I earn my Ph.D. in less than six years. I still won't be able to get a "real job" just yet, because to be competitive for an assistant professor position, I will need to complete two — maybe three — postdoctoral fellowships. "What is that?" you ask. Well, it is kind of like an apprenticeship, during which I get even more training in experimental techniques, critical thinking and, importantly, how to communicate my research to attract research funding as a principal investigator one day. As a postdoc, I will be working even harder than as a graduate student, if you can imagine that, pushing the frontiers of knowledge and making remarkable, original discoveries.

You would think this sort of effort would be rewarded with a substantial paycheck. Well, compared with graduate school, it is a decent increase, somewhere in the range of $35,000 to $40,000 a year if I'm lucky. I might finally be able to start a family on that kind of dough, but please understand if I postpone that, because the next stage of my career will be the most challenging yet.

After the postdoctoral fellowships, I'll have to hope that I can find a tenure-track position somewhere. These are extremely hard to come by right now, but since I won't be on the market for more than a decade, I remain optimistic that the situation will change. I'll be 30-something at this point and probably a little burnt out, but I will need to dig deep as I approach this critical moment of truth. Did all of my hard work and many years of training and sacrifice pay off? Will I be able to launch my own research program, attract funding, recruit a top-notch staff to help in my lab and make fundamental new discoveries that will benefit society for years to come?

Well, I must admit that the high failure rate is daunting. The NIH is rejecting about 85 percent of grant applications, because the agency is not sufficiently funded, although I will get a bit of an advantage for being a newbie. Again, I am hopeful that a decade from now our government will support basic biological research with a realistic budget that helps our country capitalize on the creative talents that it invests so much time and money into training. Our politicians love to declare war on cancer, Parkinson's disease, diabetes, etc. — but they have not yet realized that they need to fund it like they do a real war.

Can you imagine me — your wide-eyed little kid who loved taking things apart to see how they work, the one who used to drive you nuts with endless questions — as a professor? While that sounds like a secure and even somewhat glamorous position that any parent would be proud of, many people don't realize that I will have to pay some — maybe most — of my own salary! Most people assume that the university pays its faculty members, but in reality a substantial part of my salary will come from my research grants. I guess getting a raise will be a mixed blessing — my salary will increase, but I'll have to work even harder to get grants to pay for myself. It's crazy, I know. But hey, I love science.

I sincerely hope the system evolves to allow me to focus on making innovative scientific discoveries rather than how I'm going to feed my family. And keep my students and postdocs employed, as their salaries will be my responsibility too. And fulfill my teaching obligations as I train the next generation of young scientists. And meet university service obligations. Oh, and I'll have to review grants and manuscripts for the research community. But when I think about the euphoria of being the first to figure out how something works, and how it may lead to the next big cure, I just can't put a price on that.

After writing all this down, the perils of my quest are coming into focus like never before. I'm a little apprehensive. Maybe even a little scared. I know there are far easier ways to make a living, but I want to study biology and understand how our cells work. I strongly believe acquiring such knowledge is important in its own right, but it also could lead to revolutionary new treatments for diseases that affect millions, maybe billions, of people. I'm not sure why the road ahead has been littered with so many obstacles. But you know me. I am determined. I am passionate. I will do my best.

Love,
Your Budding Scientist

Bill Sullivan (wjsulliv@iu.edu) is a professor at the Indiana University School of Medicine. Follow him at www.twitter.com/wjsullivan.

Science communication training for graduate students

Two-part course at UC Riverside instructs and inspires young scientists to tell stories that provoke 'meaningful exchange of ideas' with the public

By Thomas O. Baldwin

Three years ago, when the chair of the biochemistry department of the University of California, Riverside, asked me to teach a graduate seminar course, I was somewhat unsure and took some time to think about the request. These generally are considered to be plum teaching assignments, because they require minimal preparation and grading involves listening to students deliver short seminars on their research. Still, my hesitancy was due to my belief that, while most graduate departments of biochemistry do offer some sort of training in how to deliver a seminar, such courses in fact do little to prepare our students to give effective seminars.

To better inform my decision, I read a few books on the subject of science communication — specifically, Randy Olson's "Don't Be Such a Scientist," Cornelia Dean's "Am I Making Myself Clear?" and Nancy Baron's "Escape from the Ivory Tower" — that left me energized and ready to take on the course. I elected to do the course as a two-quarter sequence rather than in a single quarter as it always had been.

The first quarter focuses on the mechanics of delivering a strong research seminar. Students sit together and discuss what makes a seminar good and memorable. From these discussions, the students develop a scoring rubric with which they evaluate all seminars in the department for that quarter. Little do our visitors realize that they are being scored by the graduate students!

The first 15 minutes (of the two-hour class period) each week is devoted to discussing that week's seminar — not just the science but the mechanics as well. Did the speaker tell a story with a beginning, a middle and an end? Did the speaker lead the audience on a memorable journey? Or was the presentation more of a chronology — "we did this and then this and then this"? This exercise does more to enlighten the students to what makes a seminar good, or not so good, than any amount of lecturing by me or reading of experts in the field.

Then the students develop and deliver three presentations: first, a 15-minute narrative that would be fitting for the third-year undergraduate biochemistry course; second, a 15-minute discussion appropriate for a senior-level high-school science class; and finally, a 30-minute research presentation appropriate for first-year graduate students. The students grade each other using the rubric they used to score the visiting speakers.

The second quarter focuses students' attention on the problems associated with communication with nonscientists. After several weeks of reading and group discussion, we invite guests to join the class to allow the students to experience firsthand the issues involved in communication with various audiences.

Our visitors have included reporters who write about scientific topics; the chief science writer for the university; U.S. Rep. Mark Takano, D-Calif.; California State Assembly Rep. Jose Medina and information-technology professionals who talked about use of social media.

Thinking back on my initial hesitancy in taking on the assignment, I am somewhat amused. I now have taught these courses three times, with each experience being enormously rewarding to me. The students leave the course with a totally different feeling about the importance of mastering the skills of communication. Equipped with these new skills, they are aware that for any form of communication to be successful they must first develop a good understanding of their audience. Only then can they bring forth a meaningful exchange of ideas.

Thomas O. Baldwin (thomas.baldwin@ucr.edu) is a professor at the University of California, Riverside, and chairman of ASBMB's Public Outreach Committee.

'To create a new voice'

By Sarah Reinhard

Sarah Reinhard is pursuing a Ph.D. in neuroscience.

Seven years ago, when I was struggling to decide on my college major, I was torn between psychology and writing. Eventually, psychology won out, and I put my writing career on hold — hoping that one day I could integrate writing into some other career.

Now I'm in graduate school, where science and research take up the vast majority of my time. I was excited recently to take a class in which I could polish my writing skills and use my newly acquired skills in science to create a new voice as a science writer … I have had the opportunity to meet with several local science writers and to collaborate with fellow students on two articles. In addition, through the course, I was introduced to an opportunity for a summer science-writing internship — an opportunity I actively sought. This course has taught me new techniques on packaging the science I write about to make it relevant and interesting to others. These are skills I will take with me throughout my career.

'My responsibility'

By Shirin Mesbah

Shirin Mesbah is pursuing a Ph.D. in bioengineering.

My interest in science communication was sparked at a young age — while listening to National Public Radio on long car rides with my parents as well as impulsively oohing and aahing as Bill Nye, a.k.a. the Science Guy, explained the inner workings of the natural world on PBS. My father, an avid amateur astronomer, introduced me to the likes of Carl Sagan, known for both his brilliant scientific work and his effective and engaging communication style.

Today, living in Southern California, I find myself in slow-moving traffic far too often. And I have found solace in NPR once again — in shows such as Radiolab and Science Friday — and I am pleasantly surprised at how the hosts raise awareness of scientific issues without compromising the science or baffling their audiences. We are fortunate to have a course in science communication … This class not only has allowed me to learn and practice various mediums of communication (oral and written) but also has given me the opportunity to meet with my local representatives, Congressman Mark Takano and Assemblyman Jose Medina, as well as other important figures of the community, including the editor of our local newspaper, the Press-Enterprise, and members of the local school board.

More than ever, I have realized my responsibility as a Ph.D.-in-training to communicate and share the implications and importance of my work in a manner that is engaging for scientists and the public alike. The pressures of competition, lack of resources and slim job prospects after graduation contribute to a cruel reality for the younger generation of scientists. One way to ameliorate this gloomy future is to reignite the conversation between scientists and the public. We must find a way to regain the public's interest in and support for our work by focusing on one of our most important tasks as scientists: outreach.

'This situation is not the politicians' fault'

By Jon Sudduth

The state of California has 80 members in the state assembly. The members have varied backgrounds … They vote on up to 75 bills a day, some of which they don't see beforehand. This pace makes careful study of the issues impossible. Of these 80 men and women, only one has a Ph.D. in the sciences. The idea of the 80 members of the state assembly voting on issues such as climate change, (genetically modified organism) laws or the energy crisis without time to study the bills

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and with only one scientist in the assembly is perhaps cause for concern.

This situation is not the politicians' fault. Rather, it is the responsibility of scientists to bridge this gap. An important responsibility of scientists is to inform their colleagues and the public about what they discover. For this to be done effectively, scientists need training in the art of communicating with the public and with our elected representatives. Stimulating discussions that eschew scientific jargon can convey the story of scientific discoveries and technical advances in a way that empowers the officials in state and federal governments to make informed decisions.

Last quarter, when I heard about a class in science outreach and communication, I was thrilled and signed up. The class has given me a chance to speak with science journalists, a state senator and our local congressman about spanning the gulf between scientists and the public. Offered only once a year, the class should be a requirement for every graduate student.

Jon Sudduth is pursuing a Ph.D. in biochemistry and molecular biology.

With the decline in federal funding for the sciences, it never has been more critical for the public to be aware of the importance of our work. Research funding in the United States has built the strongest economy in the history of the world, a status that is at risk if we lose the trust and support of the public. As the scientists of tomorrow, current graduate students bear the responsibility to seek training in the art of science communication with a broad audience. Such communication needs to be both constant and effective.

'The importance of personal branding'

By Cole Symanski

I registered for a course in science communication this quarter to develop the skills required for effective communication. Over the past several years, it has become increasingly clear to me that communication is not a well-polished skill of most scientists; nor is effective communication commonplace in academic circles. As a graduate student, I suffer through many poorly prepared and delivered research presentations. I often have trouble understanding the scientific content of these seminars. This should not be the case. So my goal in taking the science communication class was clear — learn how to present my own research simply and with meaning.

Cole Symanski is pursuing a Ph.D. in entomology.

Almost immediately, I learned that the greater science community suffers from a more important problem. Scientists do a poor job engaging the public in discussions of what they do, why they do it and why it is important. Tom Baldwin, who teaches the science-communication course, stressed early on why we should want to do this: It affects our careers! Basic-research funding often is a function of public trust and interest in science. And just as important, the inherent value of scientific discovery is reduced greatly when the information is poorly disseminated.

In this class, my peers and I have been able to discuss the process of advocating for science with several important class guests. One of these guests, Congressman Mark Takano, related his own experience of addressing issues of vital importance, like climate change, through, of all things, social media. His visit opened my eyes to the importance of personal branding when advocating for an issue. I know I will benefit professionally and personally by continuing beyond this course to develop the skills required for effective communication with broad, nontechnical audiences. I also plan to integrate public-policy training into my graduate studies.

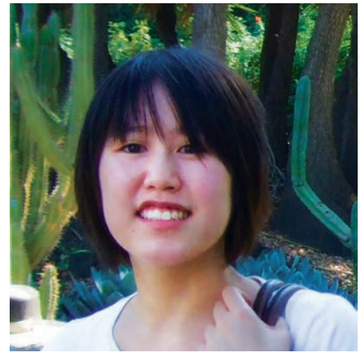
'Know your audience'

By Lisa Tang

The idea of science outreach is important but not new. But let's be honest. Many scientists, including me, don't think about outreach until faced with writing the "broader impacts of research" section of a grant or fellowship application. Lack of time and lack of training in communication are major hurdles that limit our engagement in outreach activities.

We talk science every day — in the lab discussing research data with colleagues, in the classroom teaching undergraduate students or in the auditorium giving a scientific seminar. Yet when it comes to communicating with nonscientists, we are ill-prepared.

As graduate students, we fail to explain our research adequately to our parents when they ask about our work. It is frustrating to receive limited support and appreciation from the public for the work we dedicate ourselves to due to our inability to communicate. The problem, however, resides with us, not the public.



Lisa Tang is pursuing a Ph.D. in botany and plant science.

We are fortunate to have a course in science communication taught by Tom Baldwin … (He) emphasizes that the key to effective communication is to know your audience — who they are and what matters to them — and then to choose your approach carefully. When communicating with the public, scientists often use too much jargon, which, instead of fostering a reciprocal conversation, deepens the gulf between them. Another common mistake scientists make is that they fail to address why the story they are telling matters to the nonscientific community, perhaps under the assumption that it is all obvious.

Science is a way to describe the world we live in, and it is scientists' responsibility to step out of their ivory towers to share with the public how their discoveries elucidate the world. By taking this class, I have learned not only the skills of communication but also the importance of scientists engaging in outreach. The next time my parents ask me about my research, I will be able to explain it with a better storytelling approach without losing the science. I will add, too, that science really isn't that difficult. The difficulty lies in the words we use.

The art of science communication

VOLUNTEERS NEEDED FOR NEW ONLINE SCIENCE COMMUNICATION TRAINING COURSE

The American Society for Biochemistry and Molecular Biology is seeking participants to take part in a pilot version of "The Art of Science Communication," an online course being developed by the ASBMB Public Outreach Committee as part of its science communication training program.

The course will be about eight weeks long, starting in September. During that time, we will cover the important components of what makes for a successful presentation, such as messaging, generating interest and engaging your audience. Training will be provided via a combination of lectures, live mentoring sessions and virtual discussions. The course will culminate with each participant giving his or her own live presentation, utilizing the skills learned in the course.

We expect participants will spend two to three hours on the course each week. As this is a pilot version, we want, and expect, participants to provide extensive feedback, both good and bad, on the content, format and merits of the course. Those insights will greatly assist the development of both this course and our science communication training program, helping us to grow the community of scientific communicators.

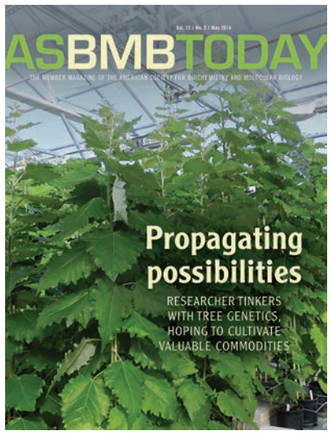
Interested in participating in our pilot program? Contact us at outreach@asbmb.org.

Reader comments

Re: "Give credit where credit is due," May issue

I liked (Eleftherios P. Diamandis') article in ASBMB Today. I concur with (his) observation in the last paragraph as I have transitioned from postdoc to (principal investigator). One thing I take away … is how important it is for PIs to acknowledge the people who did the work when they give talks to large audiences. Some PIs do a really good job of showcasing it as the work of one or more trainees, either with pictures of the trainees or "he/she did this or that key experiment," especially when they want to illustrate the talent/creativity of the individuals involved. This is in contrast with having a laundry list of people at the end of the talk with a couple of names highlighted in bold font. Thanks!

– JUNIOR INVESTIGATOR



Re: "Desperately seeking Sputnik for fundamental science," May issue

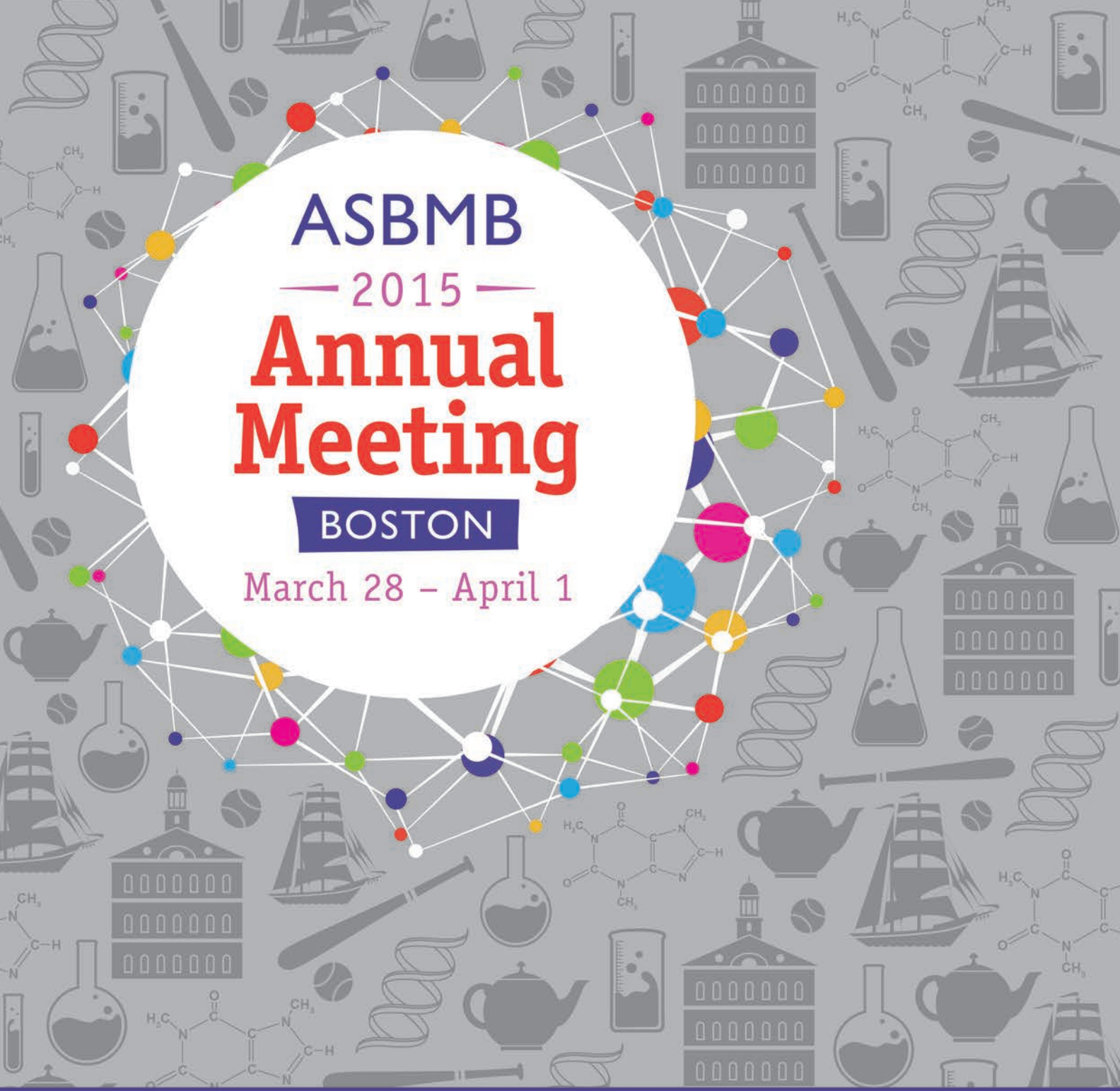
Dear Drs. (Daniel) Raben and (Joseph) Baldassare: I guess many of us are thinking along similar lines. I recently did a radio show on Wisconsin Public Radio (http://bit.ly/1il2hgd) and posed the very same question by recalling how effectively (President John F. Kennedy) rallied the country to achieve an ambitious scientific goal. I think the big difference is that now Americans don't want to invest public money for the greater good. I do think the next Sputnik might be a public health crisis. In the show, I invited people to imagine what would have happened if the AIDS epidemic had struck in 1950 instead of 1981. It's not an exaggeration to estimate that it might have killed a quarter of the world.

– ALAN D. ATTIE, UNIVERSITY OF WISCONSIN–MADISON

Re: "Grant-writing advice," May issue

Dr. (Andrew) Hollenbach's piece on grant-writing advice offers helpful information. But, let me offer one additional piece of advice: Get your message out there early and emphatically. During my tenure as chair, I read many drafts of grant proposals. Too often I would find a statement such as "This disorder affects 20 million Americans..." resting serenely in the middle of a paragraph far into the proposal, when it should have been given top billing. Donald Newlove's "First Paragraphs: Inspired Openings for Writers and Readers" provides helpful (and entertaining) insight into ways to capture the grant reader's tired eyes.

– M.W. ANDERS, UNIVERSITY OF ROCHESTER MEDICAL CENTER



ABSTRACT SUBMISSION DEADLINE
November 6, 2014

TRAVEL AWARD APPLICATION DEADLINE
November 11, 2014

PLENARY SPEAKERS

C. David Allis, The Rockefeller Univ.
Bonnie Bassler, Princeton Univ.
Zhijian James Chen, UT Southwestern Med Ctr.
Rachel Klevit, Univ. of Washington
Ian Wilson, The Scripps Res. Inst.

MARCH 28 – APRIL 1, 2015

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