Vol. 13 / No. 8 / September 2014

ASBMB TODAY

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

DEFYING STEREOTYPES:

PUNKS WHO PUBLISH

2015 CALLS FOR SUBMISSIONS

HOBBIES

We know that a life in science can be grueling. We also know that some of you have very interesting or unusual ways of blowing off steam or finding your Zen. We would like to feature your essays, poems, artwork or multimedia reflecting on scientists' pastimes. We welcome all creative interpretations of the theme. You could send us a photo of you shooting hoops or jumping out of an airplane. You could send us a video of you jamming with your band. You could send us a poem about a childhood hobby or otherwise abandoned escapes. You could write about a hobby enjoyed by someone else — perhaps a figure in science history or one of your mentors. And you could send us a rant about how you don't have time for such frivolity.

GENERATIONS

This collection of essays, poems and artwork will explore generations in a very loosely defined way. You might have come from a family of scientists. You might have insights about parenting while doing science. You might have something to say about generations of cell lines or scientific lines of inquiry. You might have a story to tell about a line of researchers mentored by one scientist. Interpret the theme as you will. It is not a boundary but rather a springboard for the making of meaning.

DEADLINES FOR HOBBIES AND GENERATIONS: Dec. 31, 2014.

FORMAT: We'll print some; others, we will post online. Some might appear both in print and online.

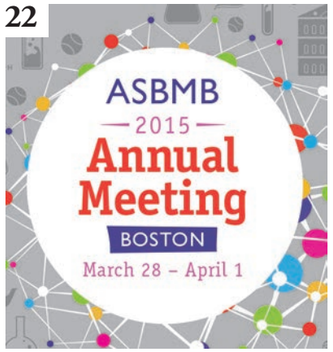
SUBMISSIONS: Email (to asbmbtoday@asbmb.org) your manuscripts as Word documents, static images as JPEG or TIFF files (the higher the resolution the better), audio as mp3 or mp4 files, and videos in something like QuickTime, Vimeo or YouTube. Please indicate to which series you are submitting in your email subject line.

CONTENTS

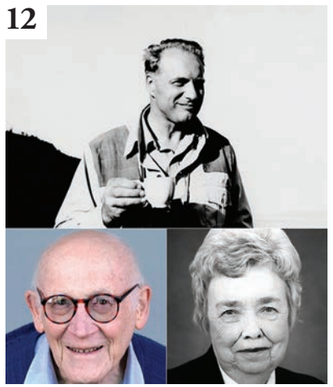
NEWS

FEATURES

22



12

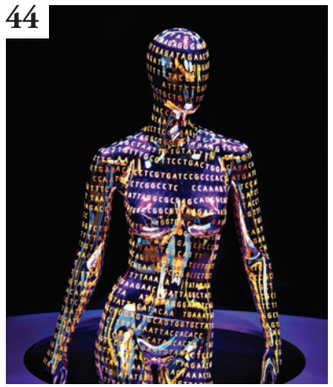


28

In the first part of our "Defying Stereotypes" series, Rajendrani Mukhopadhyay and Geoff Hunt write about three punk rockers who also do science. For image credits see page 36.

PERSPECTIVES

44



38

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

www.asbmb.org/asbmbtoday
PRINT ISSN 2372-0409

Defying stereotypes

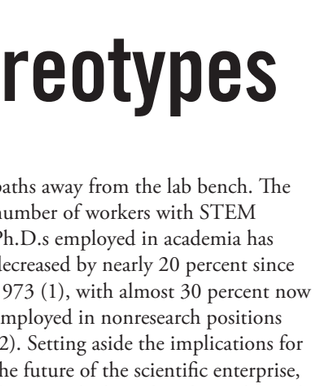
Imagine you are at a social event, such as a wedding reception or a birthday party. Between toasts and appetizers, somebody asks you what you do. For most people, it's not a big deal to answer the question. But for you, as scientists, it's a dreaded question, because as soon as you announce your profession, you pretty much know what the reaction will be.

Scientists are assumed to be socially inept and far too smart for mere mortals. While people in other professions are understood to come in all shapes and sizes, those of us with lives in science are defined by caricature: Only certain kinds of people are scientists, and scientists are only certain kinds of people.

In a series of articles launching in this issue of ASBMB Today, we aim to alter, if not completely vanquish, this stereotypical image of a scientist. The series presents profiles of individuals who have scientific know-how but who have made their names in completely different fields. Some of those featured might be obvious; others might surprise you. In some cases, science clearly has inspired their current work; in others, science has served as only a stepping stone along their career paths. Regardless of how those featured in this series got to where they are now, their stories demonstrate that having a science background doesn't limit the possibilities of what someone can accomplish.

The series comes at a time when scientists increasingly are taking paths away from the lab bench. The number of workers with STEM Ph.D.s employed in academia has decreased by nearly 20 percent since 1973 (1), with almost 30 percent now employed in nonresearch positions (2). Setting aside the implications for the future of the scientific enterprise, these trends show that the traditional, stereotypical view of scientists is crumbling.

The series also will explore how the characteristics and qualities that make scientists who they are also make musicians, athletes, artists and others who they are. Our hope is that nonscientist readers will appreciate that being a scientist doesn't mean anything other than enjoying science and that scientist readers will appreciate that they have what it takes to do anything they want. Hence the name of this series: "Defying stereotypes."



Read our first installment of the series on page 28.

REFERENCES
1. http://www.nsf.gov/statistics/seind14/content/etc/nsb1401.pdf
2. http://acd.od.nih.gov/biomedical_research_wgreport.pdf

Death notices

One important but sobering duty I have as editor of this magazine is to report the deaths of our members. We have thousands of members, of course, and I certainly don't know them all personally, but I appreciate that a stranger to me is a very special person to another.

In most cases, word of a recent death trickles in.

Our executive director, Barbara Gordon, who seems to know just about everybody, often spots death announcements and lets me know. Cindy Whalen, our membership coordinator, periodically checks our list of emeritus members so that she can keep our records updated. And sometimes members will notify us when their colleagues have passed away.

You might wonder how we determine which obituaries to include in the magazine. If the member has made key discoveries or held leadership positions with the society or its journals, we do our best to recognize his or her contributions in a Retrospective article. It's especially helpful when colleagues offer to write it.

Another consideration is how long ago the member passed away. In most cases, if more than a few months have passed, a news magazine like ours has, by industry standards, missed its window. But there are exceptions, like one in this month's issue.

In early July, Cindy sent what I thought at first was a typical death notice, but I couldn't have been more wrong. She provided a link to an obituary, like she usually does. She also provided a link to a Wikipedia page, which was a little odd. And she included a note: "I love this one." I was intrigued.

I clicked the first link. The headline read, "Loch Ness Monster & Mokele-Mbembe Researcher, Cryptozoologist Roy P. Mackal Has Died." It wasn't making sense. This fellow was an ASBMB member?

As a matter of fact, Mackal joined the society in 1953, back when he was a young biochemistry faculty member at the University of Chicago, before he abandoned the bench to track down elusive beasts. He apparently remained an ASBMB member until his death last year.

I found lots of reporting on Mackal's adventures, including a People magazine interview with him before he set off for the Congo swamps to find what might have been "the last of the dinosaurs." I watched videos of him and about creatures I'd never heard of. I cruised cryptozoology websites – some serious and some not so much. (Cryptozoology, by the way, is the study of hidden animals and often derided as a field.)

Mackal passed away on Sept. 13, 2013. I've written an obituary for this longtime member who was not at all representative of our general membership but who was nonetheless a larger-than-life character. You can find the article on page 12. I apologize for its lateness, but I hope you enjoy it.

Sincerely,
Angela Hopp
Editor, ASBMB Today

The curse of committees and clubs

By Steven McKnight

I start this essay by directing you to the lyrics of a song written by Ron Laskey, co-discoverer of nuclear localization signals (see box). In the song, Ron laments about the beating of committees, a necessary evil of governance in most all domains of society. Some people gravitate to committees, yet this is not the natural attraction for most of us who love adventure into the unknown of scientific exploration.

The majority of United States scientists involved in biomedical research must win external grant funding in order to practice our craft. The National Institutes of Health is, by far, our most substantive paymaster. We compose our grant applications and then submit them for evaluation via the Center for Scientific Review. After receipt of an application, the CSR assigns it to a review committee commonly called a study section. The CSR organizes and manages hundreds of study sections such that every slice of the pie of our biomedical research enterprise is covered.

Individual grant applications are typically assigned to three reviewers within a study section composed of 20 to 30 scientists. Reviewers read and evaluate their assigned grant applications before the entire committee meets. The study section then, as a committee, systematically ranks all applications as a means of prioritizing those most suitable for funding.

Two or three decades ago, this system was effective, yet I now judge it to be flawed. What went wrong? I submit that the demise of the review process can be attributed to two changes. First, the quality of scientists participating in CSR study sections two to three decades ago was, on average, superior to the quality of study section participants today. Second, study sections have become highly specialized such that they narrowly define a differentiated club of biomedical research.

Let me first offer ideas as to why and how the quality of our scientific review panels has diminished. Thereafter, I will speak to clubs, including thoughts on how they evolved and how they insidiously poisoned our research enterprise.

Among all problems leading to devolution of CSR study sections, the elephantine expansion of the biomedical research complex tops the list. Biomedical research in the 1960s and 1970s was a spartan game. Prototypically, scientists were employed as teaching faculty members at universities. Carving out what time they could manage relative to their primary roles as educators, scientists worked in a focused manner on discrete problems in biology or medicine. They worked with perhaps a single technician or graduate student and needed modest support from external funding sources. The glory of the experience was straightforward: Could a scientist make a discovery? It was that simple. It was not a high-flying game but instead a relatively modest enterprise composed primarily of men and women who practiced science for the right reason — inquiry into the unknown.

Once the budget of the NIH began to grow modestly in the 1970s, it was easy to find highly qualified scientists to staff the study sections. These were practicing scientists who knew how to perform experiments with their own hands. Given that they were also educators, most such scientists were endowed with a breadth of knowledge in biology or medicine or both.

Between then and now, the size of the enterprise has grown by a whopping degree. The budget of the NIH was roughly $1 billion in 1970. Last year, it was $29 billion — a growth of 2,900 percent. It is self-evident that it takes a whale of a lot more reviewers and study sections to distribute $29 billion per year than $1 billion.

Yes, the CSR is able to corral the personnel required to deal with this huge increase in grant evaluation. I submit, however, that the quality of study section membership has eroded significantly. Here are several reasons to explain the erosion.

First, the average scientist today is not of the quality of our predecessors; it's a bit analogous to the so-called "greatest generation" of men and women of the United States who fought off fascism in World War II compared with their baby boomer children. Biomedical research is a huge enterprise now; it attracts riff-raff who never would have survived as scientists in the 1960s and 1970s. There is no doubt that highly capable scientists currently participate in the grant-review process. Likewise, unfortunately, study sections are undoubtedly contaminated by riff-raff.

A second cause of the demise in study section quality can be attributed to the fact that it is a thankless task balanced by few benefits. Three to four decades ago, it was a feather in one's cap to be appointed to an NIH study section. When I joined the molecular cytology study section in the 1980s, Bruce Alberts was chairman, and the committee included the likes of Tom Pollard and all kinds of superb scientists. To spend three meetings per year with an esteemed group of scientists was both inspirational to me as a young scientist and of tangible value to my maturation as a researcher.

There are many reasons things have changed. Government restrictions mean that study section participants can hardly get a cup of free coffee. The pay, especially when factoring in the time required to properly review dozens of applications, is pathetic. Career benefit from study section participation for top-tier scientists, young or old, is marginal. Finally, as study sections have become ever more dedicated to thin slices of the biomedical landscape, participants are exposed to less and less science outside of the narrowly defined disciplines covered by their individual study sections. As such, one rarely learns much of anything new by participating in an NIH study section meeting.

Before turning from committees to clubs, let's consider what might be expected from a grant review committee composed largely of second-tier scientists with limited knowledge of the breadth of biology and medicine. I propose that these committees are equally good at ensuring that the worst and best applications never get funded. They can see a terrible grant wherein the science is flawed and the investigator has no track record of achievement. These committees are, unfortunately, equally good at spotting and excluding the most creative proposals — the grant applications coming from inspired scientists whose research is damned because it is several steps ahead of the curve and damned because it comes from an applicant not blessed with club membership.

Now, to the second of two evils: the evolution of scientific clubs. Back when we used to "walk miles to school," the scientific meetings we attended had some level of breadth. Among all meetings I attended back in the 1970s and 1980s, the two best were the Gordon Conference on Biological Regulatory Mechanisms and the Arolla Workshop. Both were relatively small meetings, including only perhaps 100 to 150 participants. Despite the small size of these meetings, both sported an intellectually thrilling breadth of scientific scope. One might hear about mobile genetic elements in maize, mating type switching in yeast (where sirtuin proteins came from), UV-mediated release of phage lambda from its lysogeic state, or the genetics of pattern formation in fruit fly embryos. Methods of genetics, biochemistry and molecular biology were applied to zoo- or botanical garden-like distributions of animals, microbes and plants. When one left such meetings, horizons of perspective were broadened. Boy, were those meetings fun.

Fast-forward 30 years, and what do we now have? The typical modern biomedical meeting spends a week on a ridiculously thin slice of biology. There are entire meetings devoted to the hypoxic response pathway, sirtuin proteins, P53, mTor or NFkB. If a scientist studies some aspect of any of these domains, he or she absolutely has to attend these mindless meetings where, at most, some miniscule increment of advancement is all to be learned.

CONTINUED ON PAGE 7

Committee Commitment Committed

By Ron Laskey

As I enter the lab every morning
Each time a sad sight makes me stop
An entire European paper mountain
Has piled up upon my desk top.
They want me to join their Committees
And to referee papers as well
To comment on grants and promotions
Endless paper that makes my bin swell.

(Chorus)
Committee, Commitment, Committed
Three words that are tricky to spell.
Committee, Commitment, Committed
Three problems that make my life hell.

But I think that I've just found an answer
To stop all this nonsense I'll try
And next time they ask my opinion
Well here's what I'm going to reply:
So you want me to join your committee
But its members are worse than dead sheep
There's only one reason I'd join
It's the chance to catch up with my sleep.
And you want my review on that rubbish
What they claim in that junk I can't tell
I suggest you accept it without any change
It will fit in your Journal so well.

(Chorus)

So you need a new Head of Department
And you want me to recommend one
I suggest that you try resurrecting
That nice man Attilla the Hun
He'd soon put a stop to your fiddles
And bring all you mavericks to heel
And you asked about hiring that postdoc
So I'll tell you the things that I feel.
That fool needs a transplanted brain
He spends all his time in the bar
I suggest that you hire him without a delay
In your lab he'd shine like a star.

(Chorus)

And now that I've sent off these letters
They won't trouble me any more
So I'll take up hang-gliding and skydiving too
I'll play with my children and show them the zoo
I'll even have time for experiments too
It's a new life I'm starting today
All commitments I'm throwing away.

From CD "Selected Songs for Cynical Scientists"

Crane, Jez and Johnson named HHMI professors

CRANE

JEZ

JOHNSON

The Howard Hughes Medical Institute has awarded $1 million each to three members of the American Society for Biochemistry and Molecular Biology.

Brian Crane of Cornell University, Joseph Jez of Washington University and Tracy Johnson of the University of California, Los Angeles, were among the 15 people named as the 2014 HHMI professors. The awards, which will be dispersed over five years, are intended to support the integration of research with undergraduate teaching.

In a statement, HHMI said: "HHMI professors are accomplished research scientists who are making science more engaging for undergraduates. By providing HHMI professors with the funds and support to implement their ideas, HHMI hopes to empower these individuals to create new models for teaching science at research universities."

The honors resulted from a competition for professors at the 106 research universities deemed by the Carnegie Foundation for the Advancement of Teaching as having very high research activity. In the end, there were 173 proposals judged by a panel of scientists and educators. Finalists were called to make presentations at HHMI in May. (IMAGES COURTESY OF PAUL MORIGI OF HHMI)

Bassler and Dikic win Vallee Foundation visiting professorships

BASSLER

DIKIC

Bonnie Bassler of Princeton University and Ivan Dikic of Goethe University have won Vallee Foundation visiting professorships, which allow senior scientists to spend four weeks in other labs around the world.

Bassler is the chair of Princeton's molecular biology department and a Howard Hughes Medical Institute investigator. Dikic is the director of the Institute for Biochemistry and scientific director of the Buchman Institute at Goethe. They were among six honorees chosen this year for the program.

All of the winners will be supported by the foundation as they embark upon various pursuits of intellectual exchange at institutes worldwide. Dozens of researchers, about a third of them ASBMB members, have won Vallee professorships over the years. The program will begin accepting nominations again in October. Recipients are allowed up to two years to take advantage of the visiting professorships.

Ortiz named editor-in-chief of journal BAMBEd

ORTIZ

Phillip Ortiz, the assistant provost for undergraduate education at the State University of New York, has been named editor-in-chief of the journal Biochemistry and Molecular Biology Education, commonly known as BAMBEd.

In a letter to readers, Ortiz said he, along with the editorial board, will "determine areas that the journal might explore so that it can continue to meet the needs of educators throughout the world."

He continued: "For example, it might be appropriate to focus some attention on emerging pedagogies in distance education, continuing refinements in professional and medical education, strategies for overcoming the challenges faced by underserved students, and the emergence of under-recognized educational committees."

Ortiz is a past member of the ASBMB Minority Affairs Committee.

Belfort, Cuervo and Gierasch named to NIH Council of Councils

BELFORT

CUERVO

GIERASCH

Three ASBMB members were named earlier this year to the National Institutes of Health's Council of Councils, an advisory body that counsels the NIH director. They were Marlene Belfort of University at Albany, Ana M. Cuervo of Albert Einstein College of Medicine and Lila Gierasch of the University of Massachusetts Amherst.

The Council of Councils has 27 members, all of whom are nominated by the NIH institutes, centers and an advisory committee to the director. The councilors are called upon to provide insights with regard to scientific policy and make research recommendations about lines of research that are emerging or deserving of special emphasis.

Nonprofit invests in Gerton's work on Cornelia de Lange syndrome

GERTON

The Cornelia de Lange Syndrome Foundation selected Stowers Institute for Medical Research investigator Jennifer Gerton as the recipient of a research grant. Gerton will use the funding to study Cornelia de Lange syndrome in a zebrafish model of the disease and to determine whether some developmental defects can be ameliorated through treatment with the amino acid L-leucine.

Cornelia de Lange syndrome is a developmental disorder that affects males and females equally across all human populations. Although the symptoms can range from mild to very severe, most affected individuals have similar physical characteristics: stunted growth; small hands and feet; thin eyebrows that meet in the middle; long eyelashes; upturned noses; and thin, downturned lips. Common medical problems include gastroesophageal reflux, bowel malrotation, hearing loss and congenital heart defects.

Gerton and her team recently linked a dampened growth signal to Roberts syndrome, a related condition that responded well to treatment with L-leucine in RBS zebrafish. "Both RBS and CdLS are caused by mutations that affect cohesin, although the molecular basis of CdLS is less well understood," she says. "A logical next step was to determine whether our work on RBS has any relationship to CdLS."

Founded in 1981, the Cornelia de Lange Syndrome Foundation is a national family support organization that exists to ensure early and accurate diagnosis of CdLS, to promote research into the causes and manifestations of the syndrome, and to help people with a CdLS diagnosis and their families to make informed decisions throughout their lifetimes.

A version of this article appeared in the Stowers Report, published by the Stowers Institute for Medical Research. It has been adapted here with permission.

PRESIDENT'S MESSAGE CONTINUED

CONTINUED FROM PAGE 5

Damn the fool who does not attend these meetings: The consequence is failure to maintain club membership. And why is club membership of such vital importance? Yes, precisely, there is nearly a one-to-one correspondence between these clubs and CSR study sections. To think that a grant applicant would have even a prayer of winning a fundable score from a study section wherein the applicant is not a club member is to be equated with idiocy.

Whether clubs came from committees or vice versa matters not – that is where evolution of our biomedical enterprise has taken us. Upon closing out his presidency in 1960, Dwight Eisenhower offered the cautionary statement, "Beware of the military industrial complex." I close with a similar warning: Beware of the biomedical industrial complex. In subsequent essays, I will offer ideas on how we might reverse untoward trends.

Steven McKnight (steven.mcknight@utsouthwestern.edu) is president of the American Society for Biochemistry and Molecular Biology and chairman of the biochemistry department at the University of Texas-Southwestern Medical Center at Dallas.

Researchers reveal important gene in early cilia development

By Elizabeth Meier

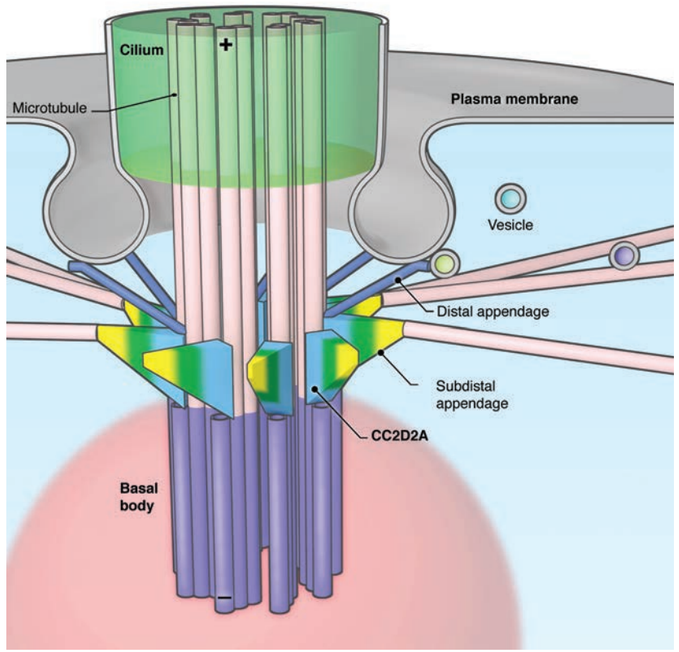
The primary cilium is a microtubule-based organelle with important sensory and signaling functions. These specialized extensions transduce mechanical and chemical stimuli to support cellular functions, such as organogenesis and tissue homeostasis, and the absence or malfunction of primary cilia underlies numerous human diseases, known as ciliopathies.

Considering the demonstrated importance of cilia for human health, many research groups have sought to characterize the molecular mechanisms of cilia biogenesis and function. Recently, researchers at the National Eye Institute identified a gene that plays an important role in cilia development.

Patients with ciliopathies experience a range of effects, and some ciliopathies are fatal. Bardet-Biedl and Joubert syndromes, for example, result in deafness, retinal degeneration and kidney disease. Meckel syndrome, meanwhile, is a severe ciliopathy, and most people afflicted by it die before or shortly after birth due to respiratory problems or kidney failure.

In post-mitotic cells, the primary cilium originates from the mother centriole, which functions as a basal body. The mother centriole also contains distal and subdistal appendages that are important for membrane tethering and docking.

The NEI researchers, led by Anando Swaroop, zeroed in on the gene Cc2d2a, mutations in which are associated with Meckel syndrome.



Previously published in Nature Communications

IMAGE COURTESY OF SHOBI VELERI

The team generated a Cc2d2a-null allele in mice. Loss of Cc2d2a resulted in embryonic lethality with defects in multiple organs associated with cilia biogenesis, consistent with Meckel syndrome phenotypes. Cilia were absent in the tissues of mutant mice during early stages of development, and there was neither subdistal assembly nor microtubule anchoring.

The researchers say the work, published in the journal Nature, demonstrates an essential role for CC2D2A in the formation and/or stabilization of subdistal appendages to initiate the process of cilia biogenesis. The findings are of clinical and biological significance, as they begin to elucidate the molecular basis of the Cc2d2a mutations present in Meckel syndrome.

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

Regular maintenance required

By Benjamin Corb

Last month, it was time to get new tires for my car. A simple tire change turned into a tire change and a brake job, rotors and pads. Five hours later, and with my wallet nearly $2,000 lighter, I was back on the road. Sadly, very few people took the time to compliment me on how fantastic my tires looked or how fresh and smooth my braking was. My costly — yet necessary — maintenance had gone largely unnoticed. That said, the price of doing nothing would have been much higher.

Doing advocacy is like doing regular maintenance on your car. It's not cheap, and at times it's frustrating, but not taking the time to do it can result in catastrophic damage. When your day consists of managing your lab, attending faculty meetings and writing grants (never mind family and other outside-the-lab responsibilities), it may seem nearly impossible to find the time to call your representative, write to your senator or attend an event in the next town over.

But like regular maintenance of your car, advocacy is critical to protecting your personal investment. For every scientist who doesn't make an effort to talk to his or her officials about the importance of supporting research, for example, there are literally dozens of neighbors talking to officials about their policy or funding priorities. Sitting on the sidelines (because of perceived lack of time or a very real lack of interest) and watching the National Institutes of Health's budget erode is the same as driving your car for thousands of miles with the "check engine" light on and then being surprised when the car breaks down.

How Legislators Perceive Issues

POLITICS	POLICY: Connected to legislator's goals/consistent with values	POLICY: Not connected to legislator's goals/consistent with values
Important to constituents	• Issues/projects that impact local economy • Issues/projects that impact or interest many constituents • Issues/projects that have significant impact on state or nation	• Issues/projects important to key political supporters • Issues/projects important to elected officials • Issues/projects with significant coalition support
Not important to constituents	• Issues/projects with personal connection to legislator • Issues/projects on which legislator wishes to demonstrate leadership or associate with	• Issues/projects important to groups/individuals not central to legislator's re-election • Issues/projects without clear connection to congressional district

SOURCE: "THE CITIZEN'S HANDBOOK TO INFLUENCING ELECTED OFFICIALS."

But you don't have to take my word for it.

Congressional Management Foundation President and CEO Brad Fitch has spent 25 years in Washington as a journalist, congressional aide, consultant and college educator. In 2010, he wrote "The Citizen's Handbook to Influencing Elected Officials." In the book, Fitch outlines in a simple chart how legislators perceive issues. Issues that are important to constituents and are consistent with a legislator's values are the issues that are most likely to cause the legislator to take action.

The Harvard University Kennedy School of Government did a study in 2013 to find out if political protests matter and looked at the 2010 Tea Party movement for evidence.

"When they observe a surprisingly large number of protesters, policymakers update their beliefs about preferences and the policy they choose to set," the researchers found (1). To put it more succinctly, the squeaky wheel does, in fact, get the grease!

Biomedical research is likely to be supported regardless of political party, but legislators need to know that it is important to you, the constituent. Together, we certainly can work harder to make sure our elected officials know that an issue like scientific research is a priority for constituents.

Advocating is tiring, frustrating and even, in some ways, costly. But it works. And just like car maintenance, ignoring it will result in the degradation of your investment.

Benjamin Corb (bcorb@asbmb.org) is director of public affairs at ASBMB.

REFERENCE

1. http://www.hks.harvard.edu/fs/dyanagi/Research/TeaParty_Protests.pdf

New JBC/Herb Tabor Young Investigator Award winners

By Laurel Oldach

Andrew DeVilbiss

Andrew DeVilbiss, a doctoral student in the cellular and molecular pathology graduate program at the University of Wisconsin School of Medicine and Public Health, received a Journal of Biological Chemistry/Herbert Tabor Young Investigator Award for his work on transcriptional control of erythropoiesis, the development of red blood cells.

Andrew DeVilbiss received his Tabor award at the Midwest Chromatin and Epigenetics meeting in Madison, Wis., in May. JBC Associate Editor John Denu of the University of Wisconsin–Madison issued the award.

Many changes must occur for a hematopoietic stem cell to become a red blood cell, including removal of the nucleus, alterations to the cytoskeleton and changes in the expression level of the globin genes, heme biosynthesis genes and many other genes. The master agent of this change is the transcription factor GATA-1.

DeVilbiss described a new interaction between the transcription factor and a chromatin-modifying enzyme with the exciting additional discovery that the interaction was context-dependent. That is, GATA-1 required the chromatin-modifying enzyme to repress some but not all of its target genes.

Moreover, the effects of the chromatin-modifying enzyme in combination with other known regulators of GATA function were variable: Some of the shared target genes also were sensitive to a second and/or third coregulator, while others were not.

It previously had been thought that GATA factors mediate transcription using a common cohort of co-regulators at the majority of target genes. However, DeVilbiss and his coworkers found a more intricate mechanism whereby transcriptional repression by GATA-1 is dependent on different combinations of co-regulators at different target genes.

Of his future work, DeVilbiss says, "I am now interested in identifying the unique molecular attributes of (GATA-1 regulated) loci that mandate different coregulator requirements for repression."

Sheila Sadeghi

Sheila Sadeghi, a lecturer at the University of Torino in Italy, was honored with a Tabor award for her work on developing a testing platform for toxic interactions between small molecules that are known to be safe when administered individually.

Sheila Sadeghi received her Tabor award at the 20th International Symposium on Microsomes and Drug Oxidations in Stuttgart, Germany. JBC Associate Editor F. Peter Guengerich of Vanderbilt University issued the award.

Predicting adverse interactions between drugs is difficult; screening all possible combinations in model organisms would be prohibitively expensive and time-consuming. However, one major known source of toxicity is inhibition of the liver enzyme cytochrome P450, which catalyzes the metabolism and clearance of many drugs.

Because P450 is a redox enzyme, its activity is difficult to study outside of its complex biochemical context; however, Sadeghi and her colleagues used a solid electrode surface to immobilize P450 and characterize its catalytic rate in the presence of individual or combinations of drugs. This technology gives a way to predict exactly how two drugs metabolized by P450 will interact with one another and prevent patients from being prescribed deadly combinations.

In the long term, Sadeghi envisions her work leading to high-throughput tests of drug–drug and food–drug interactions and also applications that may use polymorphic P450 variants better to individualize treatment regimens.

Gopal Gunanathan Jayaraj

Gopal Gunanathan Jayaraj, a doctoral student at the CSIR-Institute of Genomics and Integrative Biology in India, received a Tabor award for his work illuminating the reasons that aminoglycoside antibiotics, such as the tuberculosis drug streptomycin, occasionally damage patients' hearing for life.

Gopal Gunanathan Jayaraj received his Tabor award at the International Conference on Chemical Biology – Disease Mechanisms and Therapeutics in Hyderabad in February. JBC Associate Editor Ruma Banerjee of the University of Michigan issued the award.

Jayaraj was studying a previously described effect of streptomycin on microRNAs, a category of small, noncoding RNAs that affect the translation of specific target genes. His colleagues had shown that streptomycin could bind to pre-microRNA21, preventing the microRNA from being completely processed and affecting cells' ability to express microRNA21 targets.

When he followed up with a microRNA-wide screen to determine whether this effect extended beyond miRNA21, Jayaraj found that a large cluster of hearing-related microRNAs also was affected. Jayaraj characterized these interactions biochemically and further showed that streptomycin could repress these microRNAs in a zebrafish system in vivo, offering a tantalizing, though partial, possible explanation for the antibiotic's toxic side effects.

Jayaraj adds that "this study also warrants a cautionary re-evaluation of other RNA-binding drugs for their off-target effects in the context of miRNA and other functional noncoding RNA."

To learn more about the JBC/Herb Tabor Young Investigator award program, visit http://www.jbc.org/site/home/tabor_award.

Laurel Oldach (loldach1@jhmi.edu) earned a B.A. in biology from Reed College and is pursuing a Ph.D. in biological chemistry at Johns Hopkins University School of Medicine.

Roy P. Mackal, 1935 – 2013

Biochemist-turned-cryptozoologist hunted Loch Ness monster and other mysterious beasts

By Angela Hopp

Roy P. Mackal, a retired associate professor at the University of Chicago who began his career studying the biochemistry of bacteriophage infection but who ended up dedicating most of his life to the search for creatures that may or may not exist, died Sept. 13, 2013. He was 88.

Mackal had been a public face in the 1980s for the often-ridiculed but undeniably fascinating field of cryptozoology – that is, the study of hidden animals. From the late 1960s to the mid-1970s, he served as scientific director for an institute formed to research the Loch Ness monster (or monsters) in the Scotland highlands, and he later spent time in the swamps of Congo, following up on alleged sightings of the elusive Mokele-mbembe, which is believed by some to be a living dinosaur.

Mackal was born in 1925 in Milwaukee. His son, Paul Mackal, told the Chicago Sun-Times in December that his father enjoyed reading books as a child about adventure and lost worlds, including Jules Verne's "20,000 Leagues Under the Sea." A colleague who worked with him in Chicago described him as "a romantic."

After serving in the military during World War II, Mackal enrolled at the University of Chicago, earning a bachelor's degree in 1949 and a Ph.D. in biochemistry in 1953 under the direction of Lloyd Kozloff, whose lab focused on virus replication. "The fate of bacteriophage T7," Mackal's first paper, appeared in the Journal of Biological Chemistry in 1954. Mackal ended up joining the lab of Kozloff's collaborator, Earl Evans. His next four papers, with Evans, appeared in the JBC between 1958 and 1964.

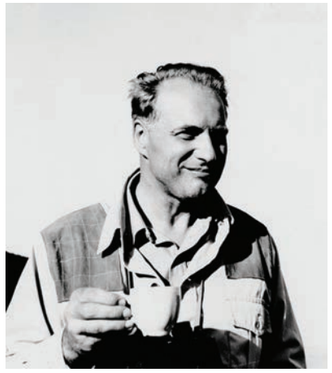


IMAGE COURTESY OF UNIVERSITY OF CHICAGO PHOTOGRAPHIC ARCHIVE, [APF1-04046], SPECIAL COLLECTIONS RESEARCH CENTER, UNIVERSITY OF CHICAGO LIBRARY

As former colleague Ed Brody recalls, by the summer of 1960, Mackal was practically running the Evans lab. "Roy was intelligent, knew a lot of biochemistry and biophysics, and was a wonderful, patient teacher of laboratory techniques," says Brody, now chief medical officer emeritus at SomaLogic Inc. "I never saw him or heard him get angry, which would have scared a lot of people. He was an ex-Marine and physically imposing."

Brody remembers Mackal as a "master craftsman" who made instruments for various labs. "If he was not in his office, he usually could be found in the machine shop," Brody says.

He recalls working with bacteriophage lambda: "The standard method to get lysogenic E.coli to produce phage was to UV irradiate Petri plates growing the bacteria, scrape the plate and isolate the induced phage. Roy invented and then built a machine to increase the amount of phage by 100 fold. He grew the lysogenic bacteria in 10-liter flasks, pumped them through quartz tubing surrounded by UV lamps and then incubated the irradiated bacteria until lysis occurred."

Bob Haselkorn, another former colleague at Chicago, also remembers Mackal as an "imaginative" young scientist. In one project, Haselkorn says, Mackal and his group took phage extracts from cells and observed what was at the time thought to be replication. Many years later, a different group armed with new technologies and knowledge used "well-defined mutants blocked at various steps in the assembly of heads, tails and tail fibers" and worked out the assembly pathways.

Mackal "could have scooped the assembly story by decades if he had understood the use of mutants and invested the years it took to isolate and characterize them," Haselkorn says.

He quips that Mackal "was always an adventurer, pretty weak on controls."

Mackal discovered his true calling in 1965 while vacationing in Scotland. There he came upon members of the Loch Ness Investigation Bureau conducting observations. He was hooked. He returned to Chicago and continued to contribute to the endeavors there, publishing another half a dozen or so virology papers through 1971. But at the same time, he was becoming more involved and more prominent in the field of cryptozoology.

Brody recalls: "Cryptozoology – the term didn't yet exist – was already strong, and he used to explain to us paleozoology and the probability of finding coelacanth-like, supposed-extinct species. His reading was deep, and he knew this was not a field that was going to please his peers." But "Roy's approach to cryptozoology was scientific," Brody said. "He studied the subject assiduously and knew that finding positive results would be difficult, even unlikely, but he thought the risk was worth taking, because he was passionate about the subject."

While still employed by the university, Mackal took the post of scientific director of the Loch Ness Investigation Bureau, which he held until 1975. The bureau employed sonar and a biopsy harpoon that Mackal himself had fashioned on the hope of one day getting close enough to Nessie to obtain a tissue sample.

Mackal described in a 1981 People magazine interview the moment when he saw Nessie himself. It was 1970, and the creature was just 30 yards away, he told the magazine. He saw "the back of the animal, rising eight feet out of the water, rolling, twisting. If that's a fish, I thought, it's a mighty fish indeed! To this day, when someone asks me, 'Do you believe there is a monster in Loch Ness?' my stomach does a somersault. I know what I saw."

In 1976, Mackal published the first of three books about hidden animals, "The Monsters of Loch Ness." According to a tribute by Loren Coleman, founder of the International Cryptozoology Museum in Portland, Maine, Mackal "theorized that a population of large invertebrate living fossils were living in the loch" but "later changed his mind and proposed that the creatures were zeuglodons, ancient serpentine whales."

In the 1980s, Mackal went twice to Africa in search of the Mokele-mbembe, thought to be something like a living dinosaur of the smallish sauropod variety. He and his team talked to pygmy locals who reported sightings of the long-necked and -tailed creature in Congo's Likouala swamps.

Around that time, Mackal and others founded the International Society for Cryptozoology at the Smithsonian's National Museum of Natural History. He served as its vice-president until the society was dissolved in 1998.

"Over the years, I saw Roy from time to time. He stayed calm and philosophical about his choices, and I never heard him complain one time" about how his work was viewed by some of his peers and administrators, Brody said. "He was one of the most interesting people I've ever known."

Angela Hopp (ahopp@asbmb.org) is editor of ASBMB Today.

In memoriam

By Mariana Figuera–Losada and Sapeck Agrawal

Thomas C. Alber

ALBER

Thomas C. Alber, 60, a structural biologist and professor of molecular and cell biology at the University of California, Berkeley, died March 28 after five-year battle with Lou Gehrig's disease.

"He was known for his ability to span a wide range of scientific disciplines, to see connections between disparate fields and to extract fundamental insights from complex data sets," Susan Marqusee, a longtime friend and colleague at Berkeley, said in a statement. "In addition to his impact on science, he'll be remembered for his scientific integrity, collegial spirit, mentorship and intellectual enjoyment of collaborations."

Born in Japan, Alber was raised in Southern California and earned his B.S. in chemistry from UC Santa Cruz. His first scientific manuscript was published in the journal Nature, and he then earned his Ph.D. in biology from the Massachusetts Institute of Technology in 1981.

Alber went on to develop innovative computational methods to uncover alternative protein structures with potential biological function from existing X-ray data. He discovered a sophisticated system of protein communication within Mycobacterium tuberculosis and found potential targets against both tuberculosis and HIV. In 2013, The Protein Society honored Alber with its Christian B.

CONTINUED ON PAGE 14

CONTINUED FROM PAGE 13

Anfinsen Award in recognition of "his foundational studies yielding an understanding of the structure/function relationship of proteins."

Alber, the founding director of the Henry Wheeler Center for Emerging and Neglected Diseases, was a faculty affiliate in the California Institute for Quantitative Biosciences and a member of the Lawrence Berkeley National Laboratory division of physical biosciences.

UC Berkeley has established a memorial fund in Alber's memory. It will sponsor an annual lecture on infectious disease. Find out more at bit.ly/TomAlberFund.

Carlos Barbas III


BARBAS

Carlos Barbas III, an organic and biological chemist at The Scripps Research Institute, died from a rare form of medullary thyroid cancer on June 24. Barbas was the Janet and Keith Kellogg II chair professor and a member of The Skaggs Institute for Chemical Biology at TSRI in San Diego.

Barbas was born Nov. 5, 1964, in St. Petersburg, Fla. He received a B.S. in chemistry at Eckerd College in Florida and earned a Ph.D. in organic chemistry at Texas A&M University in 1989. He then did postdoctoral work, first at Pennsylvania State University with Steven Benkovic and later at Scripps with Richard Lerner.

He joined TSRI in 1991 and combined molecular biology, chemistry and medicine to study asymmetric catalysis, zinc finger technology, synthetic antibodies and proteinlike DNA enzymes. He developed the first human antibody phage libraries and synthetic antibodies. His research has contributed to the development of numerous potential drugs and vaccines.

Barbas received many awards in recognition of his contributions. He was a fellow of the American Association for the Advancement of Science and of the Academy of Microbiology. He also was the founder of CovX Pharmaceuticals (acquired by Pfizer) and Zyngeni and a co-founder of Prolifaron (acquired by Alexion).

Herbert C. Friedmann


FRIEDMANN

Herbert C. Friedmann, a pioneer in bacterial enzymes research, devoted and enthusiastic educator to budding scientists, and passionate storyteller on the subjects of biology, history and literature, died Jan. 13. He was 86.

Along with having served the University of Chicago for almost 50 years with excellent teaching and research, Friedmann was known for his book "Enzymes," an article he co-wrote on the life of Theodor Escherich (the researcher after whom E. coli was named), and a short paper titled "Fifty-six laws of good teaching," a guide for any instructor. One of his laws was "Never expect your students to learn or understand anything that you cannot or did not learn or understand yourself."

Friedmann was born June 19, 1927, to a Jewish family in Mannheim, Germany. His mother was a violinist and his father a physician. At age 11, his childhood took an unfortunate turn when his father was arrested for being Jewish and the family residence was ravaged by members and sympathizers of the Nazi party. However, after agreeing to give up their property, the family was permitted to immigrate to Madras (now Chennai, India) in 1939.

Friedmann grew up in India and completed high school in 1943. In 1947, he earned his B.S. in chemistry at the University of Madras and stayed to continue his research on enzymes in the university's biochemistry labs while also earning his M.S.

In 1954, Friedmann won acceptance and a scholarship to a Ph.D. program at the University of Chicago. He conducted his thesis research with Birgit Vennesland and completed his Ph.D. in 1958. For the next year, he worked as a research associate at the university and subsequently moved to Baltimore to complete a two-year fellowship at the Johns Hopkins University, where he met his future wife, Joan Bowerman.

In 1960, Friedmann returned to Chicago as an assistant professor in physiology and began his extensive studies of vitamin B12 and its role in bacterial nucleotide synthesis. He was later promoted to associate professor. In a university statement, Donald Steiner, a former chairman of biochemistry and molecular biology at Chicago, described Friedmann as "one of the department's best citizens." Steiner also added, "He gave more lectures than anyone else. He introduced undergraduates to biochemistry in a way that made it special."

For his exceptional undergraduate teaching abilities, Friedmann won in 1978 the coveted Llewellyn John and Harriet Manchester Quantrell Award for Excellence. Until his retirement in 2009 at the age of 82, he continued to receive glowing reviews from students.

Erich Heftmann

Erich Heftmann, a chemist well known in the chromatography world, died Jan. 18 at his home in Walnut Creek, Calif., at age 95.

Heftmann was born in 1918 in Vienna, Austria, and studied medicine there till 1938. He immigrated to the U.S. in 1939 after the annexation of Austria by Nazi Germany. He earned a B.A. in chemistry from New York


HEFTMANN

University in 1942 and a Ph.D. in biochemistry from the University of Rochester in 1947. He worked at the National Institutes of Health from 1948 until 1963, when he joined the California Institute of Technology. He then worked as a research chemist at the U.S. Department of Agriculture in California from 1969 until his retirement in 1983.

Heftmann used chromatography to study the role of steroids in plant biology and was the first to show the presence of cholesterol in plants. In 1961, he developed a precursor to high-pressure liquid chromatography instruments.

During his career, Heftmann published nearly 200 articles and two books, including six editions of "Chromatography," which has become a standard reference. He was symposium editor of the Journal of Chromatography from 1982 to 2008, handling almost 5,000 papers.

Martin Lackmann


LACKMANN

Martin Lackmann, a leading German-Australian biochemist and associate professor at Monash University who had been spearheading the discovery of several novel drugs against cancer, died suddenly on May 22. Lackmann made major contributions to our understanding of how a family of cell-signaling receptors known as the Eph family of receptor tyrosine kinases regulates cell–cell interactions during normal development and cancer.

More recently, he was committed to exploiting this new knowledge to develop treatments for cancer patients, and this led to the development of new therapeutic antibodies directed against the EphA3 receptor. One such antibody, KB004, is in phase II trials in patients with leukemia. In 2010, his proposed research on KB004 was acknowledged as one of the 10 best research projects of the year by the Australian National Health and Medical Research Council.

Lackmann was born March 11, 1956, in Germany, where he grew up with an affinity for medicine. After completing his B.S. in biochemistry at University of Hamburg, he moved to Australia to pursue a Ph.D. in immunology at the University of Sydney, which he completed in 1992.

For his postdoctoral studies, Lackmann chose the Walter and Eliza Hall Institute of Medical Research in Melbourne and later the Ludwig Institute for Cancer Research. There, with mentorship from the then-director of the institute, Tony Burgess, Lackmann established his own laboratory in 2000 with a focus on translational cancer research. In 2003, Lackmann moved his research program to the Monash University biochemistry and molecular biology department, where he made highly significant discoveries regarding Eph receptor signaling and function and identified several molecular targets for the development of antibody-based anticancer therapeutics. Before his death, he was working on a patented antibody targeting ADAM-10, which is in the preclinical development phase.

Fabian Lionetti

Fabian "Doc" J. Lionetti, professor of biochemistry at Boston University Medical School, died on March 14 at age 96.

Fabian, who held a Ph.D. in physical chemistry from Rensselaer Polytechnic Institute, was a distinguished researcher whose body of work contributed to advances at NASA, the U.S. Department of Energy and the field of blood preservation.

Colleagues and friends recalled him as the author of numerous papers in leading scientific journals, a trusted counselor to students and a nature enthusiast.

Marian Swendseid


SWENDSEID

Marian Swendseid, a prolific and distinguished nutrition scientist at the University of California, Los Angeles, Fielding School of Public Health, passed away on Jan. 19 at age 95 in Irvine, Calif. She had been an ASBMB member for 64 years.

Swendseid was born Aug. 2, 1918, in Petersburg, N.D. She earned a B.S. in chemistry and M.S. in organic chemistry at the University of North Dakota and a Ph.D. in biological chemistry at the University of Minnesota in 1941.

Swendseid pioneered research on protein, choline, folic acid and vitamin B12 metabolism, identified histidine as an essential amino acid for adults and published more than 150 manuscripts. She served as an associate editor of The American Journal of Clinical Nutrition.

A scholarship fund to support students or investigators focused in the area of nutrition and cancer prevention was established with the American Society for Nutrition Foundation in memory of Swendseid. More information is available at www.nutrition.org.


Mariana Figuera-Losada (fmariana@hotmail.com) is a postdoctoral fellow at the Johns Hopkins University. She wrote the briefs on Alber, Barbas, Heftmann, Lionetti and Swendseid. Sapeck Agrawal (sapeck.srivastava@gmail.com) recently earned her Ph.D. in molecular microbiology and immunology from the Johns Hopkins University. She wrote the briefs on Friedmann and Lackmann.

Thematic series on caloric restriction and ketogenic diets

By Mary L. Chang

The September issue of the **Journal of Lipid Research** marks the beginning of a new thematic review series examining how diet modifications improve general health and manage a broad range of chronic diseases.

Caloric restriction, a type of controlled therapeutic fasting, reduces oxidative stress and damage while promoting more efficient energy metabolism. Ketogenic diets — characterized by low carbohydrate, sufficient protein and high fat intake — have been used primarily to manage seizures in epileptic children. However, more recently, these diets have shown promise, along with drugs and hyperbaric oxygen therapy, in managing cancer, and they may have applications in managing certain neurological diseases.

After they are consumed, carbohydrates are broken down to glucose, raising sugar levels in the blood. Because a ketogenic diet minimizes the intake of carbohydrates while also increasing fat intake, sugar levels in the blood are lowered, and the liver is able to take fat consumed and produce ketone bodies, which are released into the bloodstream. As the ketones are taken up by cells of the body, cells break down the ketones instead of sugar for energy, a process called ketosis.

The following JLR reviews address this subject:

Ketone body therapy: from ketogenic diet to oral administration of ketone ester
Sami A. Hashim and Theodore VanItallie

Ketone ester effects on metabolism and transcription
Richard Veech

Ketogenic diets, mitochondria and neurological diseases
Lindsey B. Gano, Manisha Patel and Jong M. Rho

The collective therapeutic potential of cerebral ketone metabolism in traumatic brain injury
Mayumi Prins and Joyce Matsumoto

The ketogenic diet for the treatment of malignant glioma
Eric C. Woolf and Adrienne C. Scheck

Editorial board member Thomas N. Seyfried of Boston College is coordinating the series. In 2012, Seyfried published the textbook "Cancer as a Metabolic Disease: On the Origin, Management, and Prevention of Cancer," which presented methodology and findings of the sources and prevention of cancer.

Mary L. Chang (mchang@asbmb.org) is publications manager for ASBMB.

How a squid forms a relationship with a bacterium

By Rajendrani Mukhopadhyay

How do you get into a mutually beneficial relationship? That is the question researchers asked in a recent paper in the journal **Molecular & Cellular Proteomics**, albeit for a squid and its bacterial partner. The researchers showed that in order for the Hawaiian bobtail squid to form a symbiotic relationship with the bioluminescent Vibrio fischeri, proteomic changes have to occur in a set of cells of the squid.

The Hawaiian bobtail squid, formally known as Euprymna scolopes, has a light organ that is exclusively colonized by V. fischeri. The squid feeds the bacterium a solution of sugar and amino acids and, in return for the steady food supply, the bacterium gives off the light that masks the squid's silhouette while it goes hunting for various species of shrimp for its own meals.

Scientists study the squid and its bacterial partner as a model to understand how beneficial bacteria form associations with multicellular organisms and help animals develop. "Our lab is interested in understanding the role of the host's innate immune system in establishing specificity," says Tyler Schleicher at the University of Connecticut, the first author on the MCP paper. "Each generation of squid is colonized by V. fischeri from the environment, and they must distinguish between the symbiont and a huge background of nonsymbiotic bacteria that are found in seawater." The question is how the squid achieves this feat.

To answer the question, the

The adult Hawaiian bobtail squid with inset scale

IMAGE COURTESY OF WIKIMEDIA COMMONS USER MARGARET-MCFALL NGAI

investigators used two quantitative proteomic techniques to compare a set of special cells taken from squid colonized with bacteria and those that were uncolonized. "This is the first time that two independent, high-throughput proteomic techniques have been applied to the squid–Vibrio association," says Spencer Nyholm, also at the University of Connecticut and the senior author on the paper.

The cells the investigators chose to look at are hemocytes, which are blood cells in the squid's light organ; these cells have properties of the immune system's macrophages and interact with the symbiotic bacteria present at the light organ.

From the investigators' analyses of the differences in protein expression in hemocytes taken from colonized and uncolonized squid, they saw that the presence of V. fischeri in the light organ induced changes in the hemocyte proteome to promote the cell's tolerance of the bacteria and favor symbiosis. The changes involved the cytoskeleton, lysosome function, proteases and receptors. Because scientists still don't understand the precise mechanisms that contribute to host–symbiont specificity, the investigators are now focusing on studying several proteins identified in this study that appear to influence the bacterium's adhesion to the squid's light organ.

"A growing body of evidence from a variety of animal model systems suggests that beneficial microbes influence a host's innate immune system to foster these associations," says Nyholm. Because macrophagelike cells similar to hemocytes are found in almost all animals, he adds, "our study may provide insight into other host–microbe associations."

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

Thematic series on phospholipase D and cancer

By Indumathi Sridharan

A new thematic minireview series in the **Journal of Biological Chemistry** focuses on phospholipase D and its role in cancer. PLD signaling controls a variety of cellular activities (namely, proliferation, migration and lipid metabolism) and thus plays a key role in cancer invasion and metastasis. The series highlights PLD's tumorigenic potential, tools to study its in-vivo function, its putative role in inflammatory diseases, and regulation of levels of the signaling metabolite, phosphatidic acid. A deeper understanding of PLD has broad applications in developing targeted drug therapies for cancer.

In the first article, Julian Gomez-Cambronero briefly describes the various mammalian isoforms of PLD and discusses mechanisms by which PLD1 and PLD2 affect cell migration, cell adhesion and proliferation. In light of these activities, PLD has a direct impact on cancer growth, invasion and metastasis and is therefore a therapeutic target in cancer treatments. The author points out recent developments in PLD research and their implications in cancer treatments. For example, combining radia-

CONTINUED ON PAGE 18

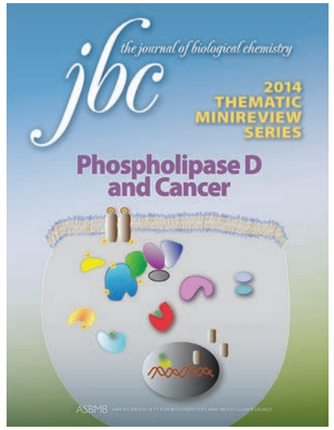
CONTINUED FROM PAGE 17

tion with PLD-inhibitor drugs is an effective strategy to treat chemotherapy-resistant and radiation-resistant cancer cells. The author concludes by specifying the challenges remaining in PLD research, such as defining the in-vivo mechanisms of PLD signaling and establishing the crystal structure of PLD.

Yi Zhang and Michael Frohman in the second minireview discuss the tools used to study the physiological role of PLD1 within a tumor and its microenvironment. The authors describe how small molecular inhibitors and cell lines were used to define PLD's function and PLD1's role in cancer. However, these in-vitro approaches suffer from limited physiological relevance. Alternatively, studies using animal models (particularly PLD1-deficient mice) provide better insight into the in-vivo role of PLD1 in cell metabolism, tumorigenesis, angiogenesis, autophagic response and therapy resistance. The authors also mention new techniques, such as genetically encoded phosphatidic acid sensors and advanced intravital imaging, that can elucidate the impact of PLD1 in early steps of tumor development and metastasis.

Dong Woo Kang and colleagues focus on regulation of PLD expression and its implications in cancer and inflammation in the third minireview. Cancerous phenotypes and inflammatory diseases are characterized by aberrant PLD expression. In this article, the authors elaborate on the dysregulation of PLD expression and activity in cancer, the use of PLD-selective inhibitors and microRNA for cancer therapeutics, amplification of PLD expression resulting from genomic alterations in PLD gene and dynamic control of PLD signaling by transcription factors in cancer. The authors also discuss PLD regulation in various inflammatory conditions and the mechanisms by which PLD-selective inhibitors, such as triptolide and rebamipide, exert antitumorigenic and anti-inflammatory effects. The authors emphasize that PLD-selective inhibitors have great therapeutic potential for treating cancers and inflammatory conditions.

In the fourth and final minireview, David Foster and colleagues highlight the intracellular regulation of phosphatidic acid and its implication in cancer-cell survival via mammalian/mechanistic target of rapamycin, or mTOR, activity. The ability of mTOR to integrate nutrients and growth-factor signals during cell-cycle progression depends heavily on intracellular phosphatidic acid levels. Phosphatidic acid is a signaling metabolite produced by three major metabolic sources: enzymatic action of PLD on phosphatidylcholine, the diacylglycerol kinase pathway and the lysophosphatidic acid acyl transferase pathway. The authors discuss how compensatory pathways maintain intracellular levels of phosphatidic acid when one pathway is compromised. Given mTOR's dependency on phosphatidic acid and strong mTOR activity in cancer cells, the authors suggest that interfering with phosphatidic acid metabolism could prove to be an effective therapeutic strategy for cancer treatments.



In the introductory commentary for the collection, series organizers Julian M. Gomez–Cambronero and George M. Carman remark that, despite the evident advances in PLD research, many issues need further investigation. Realizing the full potential of PLD inhibition in cancer therapeutics requires a better understanding of various PLD isoforms, their role during cancer progression and the evaluation of isoform-specific PLD inhibitors in clinical trials.

Indumathi Sridharan (sridharan.indumathi@gmail.com) earned her bachelor's degree in bioinformatics in India. She holds a Ph.D. in molecular biochemistry from Illinois Institute of Technology, Chicago. She did her postdoctoral work in bionanotechnology at Northwestern University and is now an intern at the Office of Technology Transfer at the National Institutes of Health.

Thematic series on prions

By Thomas E. Schindler

More than 30 years ago, Stanley Prusiner at the University of California, San Francisco, coined the term "prion" and began to develop evidence to support his radical hypothesis for a new kind of infectious agent.

Since then, the prion hypothesis — that scrapie, a fatal neurodegenerative disease in sheep and goats, is caused by a misfolded protein devoid of a genomic component — has been proved. The new dogma that resulted has been fruitful for guiding new approaches to studying Alzheimer's and Parkinson's diseases. In addition, emerging biochemical details of the pathogenesis of misfolded proteins are beginning to provide potential targets for therapy.

In a new thematic minireview series in the **Journal of Biological Chemistry**, Prusiner and other researchers cover prion replication, transmission and neurotoxicity. JBC Associate Editor Paul Fraser of the University of Toronto oversaw the series.

In the first minireview, Joel C. Watts and Prusiner, both of UCSF, discuss the importance of mouse models for studying pathogenesis of prion diseases and developing new therapies. Transgenic mice that overexpress the prion protein, known as PrP, develop clinical signs of disease in less than half the time it takes for normal mice. So-called knock-in mice, in which the normal PrP gene is replaced with a mutant PrP gene, have been used to study pathogenesis of mutations associated with sporadic and genetic human prion diseases. The authors review the drawbacks and limitations of using mouse models to study Alzheimer's and Parkinson's diseases, considered to be prionlike diseases, and predict that the next generation of research may rely on transgenic rats. Rats may be better suited for studying human neurological diseases because of their more complex behaviors and larger brain sizes.

Surachai Supattapone of the Geisel School of Medicine at Dartmouth University summarizes, in the second minireview, studies with synthetic prions and the enhancement of infectivity with cofactors. Supattapone writes, "Recently, synthetic prions with a high level of specific infectivity have been produced from chemically defined components in vitro." These biochemical studies, he emphasizes, provide formal proof that prions are indeed infectious agents lacking a nucleic acid genome and elucidate the roles of the cofactor molecules — such as phosphatidylenthanolamine and RNA — in the propagation and maintenance of infectious prions. Furthermore, Supattapone writes, cofactor molecules "influence strain properties by facilitating specific PrPSc conformations."

In the third minireview, Marc I. Diamond and Brandon Holmes of Washington University in St. Louis review the studies of the prionlike tau protein associated with Alzheimer's disease. Several proteins implicated in the development of Alzheimer's have been shown to aggregate and spread to neighboring brain cells. Although these proteins, notably tau and alpha synuclein, are distinctly different from prion protein, they can undergo conformational changes leading to aggregation and the formation of fibrils in a prionlike manner. Several recent studies have detected the spread of tau aggregates between cells in vivo and in vitro. The ability of tau aggregates to move across synapses could explain the involvement of neural networks in neurodegenerative diseases, the authors say, and interruption of the cell-to-cell propagation of protein aggregates could provide therapeutic benefits. Studies evaluating potential therapies target secretion, clearance or uptake of tau aggregates.

In the final minireview in the series, Giovanna R. Malucci, Mark Halliday and Helois Radford examine how prion generation and spread affects neurotoxicity. Prion diseases, including scrapie, Creutzfeld–Jakob Disease and bovine spongiform encephalopathy (mad cow disease), are transmissible and fatal. In these diseases, prion protein is the infectious agent, and accumulation of prion aggregates leads directly to neurotoxicity and eventual death. In Alzheimer's and Parkinson's, other proteins — including amyloid-beta, tau and alpha-synuclein — aggregate and propagate throughout the brain; however, the spread of these misfolded protein aggregates is not linked clearly to neurodegeneration. Some studies using mouse models of scrapie have found a dissociation between prion replication and neurotoxicity. What is the relationship between prion propagation and toxicity? The authors of this minireview focus on the unfolded protein response, "a protective cellular mechanism that is induced during periods of cellular and endoplasmic reticulum stress, which aims to maintain protein-folding homeostasis with the ER." Therapeutic manipulation of the unfolded protein response, the authors note, appears to provide neuroprotection in animal models.

Thomas E. Schindler (tschindler.phd@gmail.com) earned a Ph.D. in immunology from the University of Illinois Medical Center in 1981. After a postdoctoral stint at Memorial Sloan–Kettering Cancer Center, he joined Xytronyx, a small biotech company in San Diego started by his graduate adviser, Peter Baram. He took a year off in 1992 to move back east and become a high-school science teacher. Since early retirement from full-time teaching in 2007, he has taught biology and microbiology in nearby community colleges. Now he is pursuing a new career: science writing.

Our evolving view of plasma membrane domains

By Mary L. Kraft and Raehyun Kim

We recently used a new chemical imaging technique to visualize the distributions of sphingolipids and cholesterol in the plasma membranes of fibroblasts (1, 2). Our unexpected finding of cytoskeleton-dependent sphingolipid domains that are not enriched with cholesterol has led us to revise our views on plasma membrane domains.

Though the plasma membrane may contain microdomains with a variety of different lipid compositions, cholesterol- and sphingolipid-enriched microdomains, called lipid rafts, have been the most intensely scrutinized. Lipid rafts are defined as small, dynamic and ordered assemblies of cholesterol, sphingolipids and proteins that may combine to form larger structures (3). Rafts are postulated to regulate protein–protein interactions by laterally segregating proteins according to their affinity for ordered membrane domains. Cell signaling and virus budding are among the processes that lipid rafts hypothetically mediate. This potential importance and the simplicity of the raft hypothesis attracted us to the field.

Though membrane organization and function is now our focus, we entered this field as a bioanalytical laboratory that was developing new methods to obtain chemical information from biointerfaces with submicron lateral resolution. At the time, the raft hypothesis was supported strongly by indirect data, including the spontaneous formation of ordered cholesterol- and sphingolipid-enriched domains in model membranes and the cholesterol-sensitive clustering of membrane proteins thought to reside in rafts. Yet domains enriched with cholesterol and sphingolipids had not been imaged directly in actual cell membranes, likely due to a "technical impasse" (4). Techniques for imaging dynamic lipid domains that were smaller than the diffraction limit of light were not yet widespread. Furthermore, cooperative interactions between cholesterol and sphingolipids might be perturbed by labeling them with fluorophores.

To address this challenge, we were developing an approach that used a new surface-sensitive imaging mass-spectrometry technique, high-resolution secondary ion mass spectrometry, or SIMS, to visualize metabolically incorporated, stable isotope-labeled sphingolipids and cholesterol in the plasma membrane with ~100-nm lateral resolution. High-resolution SIMS is complementary to fluorescence microscopy, because stable isotopes do not alter the chemical structure and thus the interactions or trafficking of the lipids they label, but it cannot be performed on living cells.

We obtained our first images of the sphingolipid and cholesterol distribution in the plasma membranes of fibroblast cells in 2009. To our surprise, we saw sphingolipid domains that were too large to be lipid rafts and a relatively uniform cholesterol distribution within the plasma membranes of mouse fibroblast cells. Baffled by these results, we spent the next few years optimizing our approach for imaging sphingolipid distribution. After confirming reproducibility, we performed numerous control experiments that tested for a multitude of potential artifacts.

We ruled out the possibilities that the micrometer-scale sphingolipid domains we observed were induced by cell fixation, the detection of excess lipid material due to vesicles or intracellular membranes adjacent to the plasma membrane, cell topography, nonspecifically adsorbed labels and many other artifacts (1). We also confirmed the existence of micron-scale sphingolipid domains in the plasma membrane by fluorescence microscopy imaging of metabolically generated fluorescent sphingolipids in the membranes of living fibroblast cells (1).

How could our finding of micron-scale sphingolipid domains be correct when it seemed to contradict so much previously reported data? Upon reevaluating the literature, we found that the contradiction was not with previously reported data but instead with the conclusions that had been inferred from the biophysical properties of putative raft components. The few reports in which sphingolipids were imaged directly showed that gangliosides form nanoscale domains (5) but that sphingomyelin forms membrane domains with dimensions similar to those we observed (6).

We next probed the mechanisms responsible for these sphingolipid domains. We found that the abundances of the sphingolipid domains in the plasma membrane were reduced by depletion of cellular cholesterol. However, depolymerization of the actin cytoskeleton abolished the sphingolipid domains. The sizes of the sphingolipid domains and their higher dependency on the cytoskeleton than on cholesterol indicated these domains were not lipid rafts.

After publishing our finding of sphingolipid domains (1), we returned to imaging cholesterol in parallel with sphingolipids. Again, we found that cholesterol was distributed fairly uniformly in the plasma membrane and not enriched within the sphingolipid domains (2). This lack of cholesterol enrichment confirmed that the sphingolipid domains were not lipid rafts. Of course, we cannot rule out the possibility that we did not detect lipid rafts because they are smaller than the 87-nm-lateral resolution we achieved. However, the lack of cholesterol enrichment in the sphingolipid domains indicates cohesive cholesterol–sphingolipid interactions contribute little to plasma-membrane organization, which refutes a major tenant of the raft hypothesis.

Our data argue against the existence of lipid rafts within the plasma membrane (7). Instead, our results support the model of plasma membrane organization in which cortical actin and its associated proteins divide the plasma membrane into distinct domains by establishing diffusion barriers that sustain concentration gradients produced by vesicle transport (8) or lipid-modifying enzymes.

Furthermore, the direct imaging of GM1 and GM3 by others has shown that these gangliosides form separate microdomains that are dependent on the actin cytoskeleton (5). Thus, microdomains consisting of different sphingolipid species are present in the plasma membrane, which suggests an active, energy-dependent mechanism of membrane organization.

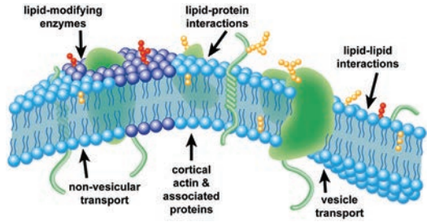


Illustration of factors that may affect the formation of plasma-membrane domains.

Given that many lipids are signaling molecules or their precursors (i.e., ceramide, diacylglycerol, lysophosphatidic acid) (9), cells likely use active mechanisms to segregate each bioactive lipid class within the plasma membrane so that signaling molecules are available when needed. Of course, further studies are required to assess the hypothetical existence of domains of different bioactive lipids and to identify the mechanisms for their formation.

Why do cholesterol levels affect cell function in the absence of cholesterol-enriched plasma membrane domains? Emerging hypothetical mechanisms of cholesterol-mediated cell function involve modulation of protein activity by direct cholesterol binding. Cholesterol binding/unbinding to scaffold protein is hypothesized to regulate the formation of a signaling complex and its function (10).

The cholesterol-sensitive assembly of these signaling complexes could be modulated by the difference in the cholesterol concentrations in the plasma membrane and the intracellular locations where the scaffold protein resides. For instance, cholesterol binding to the NHERF1 scaffold protein regulates its co-localization with the cystic fibrosis transmembrane conductance regulator, known as CFTR, at the plasma membrane and NHERF1-mediated CFTR activation (10).

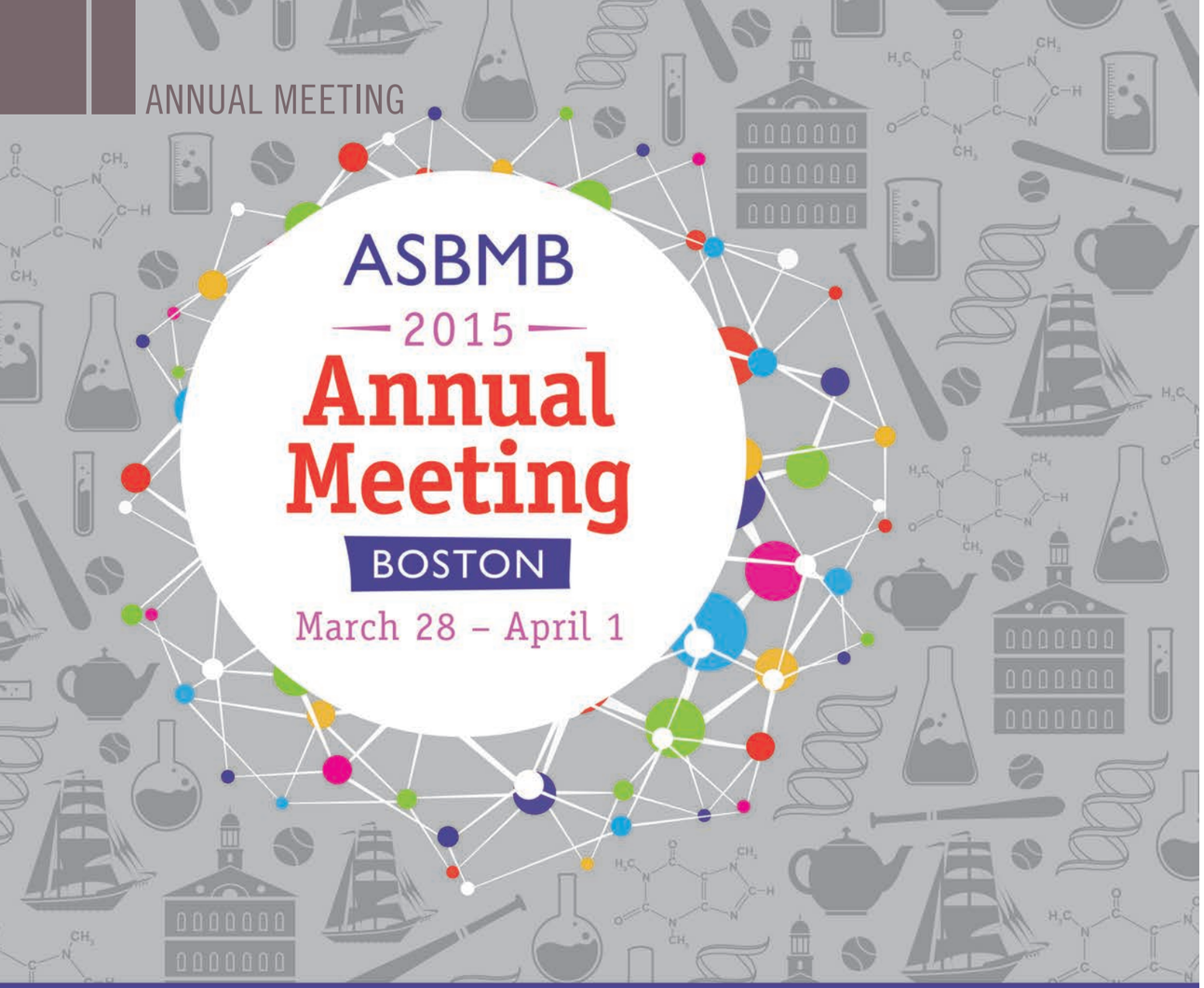
Likewise, oxysterol-binding protein functions as a scaffold protein that requires cholesterol binding in order to complex with two phosphatases, PP2A and HePTP, forming an assembly involved in ERK signaling (11). Cleary, much research is required to assess the roles of specific cholesterol-protein interactions in cholesterol–sensitive cell function.

Identifying the mechanisms that control lipid organization within the plasma membrane and the sources of cholesterol-sensitive cellular processes will require a significant number of new studies. We expect that new efforts to develop and test alternative hypotheses for lipid-mediated biological function are critical to advancing our understanding of plasma membrane domains and their roles in cellular function.

REFERENCES

1. Frisz, J.F. et al. *Proc. Nat. Acad. Sci. U.S.A.* **110**, E613 – E622 (2013).
2. Frisz, J.F. et al. *J. Biol. Chem.* **288**, 16855 – 16861 (2013).
3. Lingwood, D. et al. *Science* **327**, 46 – 50 (2010).
4. Jacobson, K. et al. *Nat. Cell Biol.* **9**, 7 – 14 (2007).
5. Fujita, A. et al. *Biochim. Biophys. Acta – Mol. Cell Biol. Lipids* **1791**, 388 – 396 (2009).
6. Tyteca, D. et al. *Biochim. Biophys. Acta* **1798**, 909 – 927 (2010).
7. Kraft, M.L. *Mol. Biol. Cell* **24**, 2765 – 2768 (2013).
8. Kusumi, A. et al. *Annu. Rev. Biophys. Biomol. Struct.* **34**, 351 – 378 (2005).
9. Wymann, M.P. et al. *Nat. Rev. Mol. Cell Biol.* **9**, 162 – 176 (2008).
10. Sheng, R. et al. *Nat. Commun.* **3**, 1249 (2012).
11. Wang, P.-Y. et al. *Science* **307**, 1472 – 1476 (2005).

Mary L. Kraft (mlkraft@illinois.edu) is an associate professor in the chemical and biomolecular engineering department at the University of Illinois, Urbana-Champaign. Raehyun Kim (kim794@illinois.edu) is a graduate student in the chemical and biomolecular engineering department at the University of Illinois, Urbana-Champaign.



In this issue:

In the October issue:

Molecular mechanisms of infection and immunity

Lipids: in vivo dynamics, protein partners and signaling

What's new in membrane transport proteins

Plant metabolism

Mechanistic impacts of post-translation modifications

RNA expression and post-transcriptional regulatory events

The human microbiome

Microbiome dynamics and health disparities

Careers, mentoring and changes in medical education

Dear readers,

We invite you to attend the exciting 2015 annual meeting of the American Society of Biochemistry and Molecular Biology that will be held from March 28 through April 1 in Boston.

The 14 themes of the meeting cover the broad range of biomolecules and systems that interest the ASBMB membership. We are certain that you will find new twists in the recent discoveries as well as new areas in which the science is advancing rapidly.

Recurring themes include overturning paradigms (such as the fluid mosaic model for membranes and the assumption that protein structure is necessary for function) and expanding dogmas (such as DNA codes for RNA, which codes for protein) to show the beautifully orchestrated complexity of biological processes.

In transcription and translation, this involves RNA and chromatin modifications and modes of crosstalk. The same level of crosstalk between DNA replication and repair now can be visualized in the act through the application of super-resolution techniques. The scientific programming showcases molecular-level studies of complex processes using the newest tools.

Also, we are pleased to return to the tradition of hosting morning plenary sessions by eminent scientists. See the list of plenary lecturers and their tentative talk titles on page 26.

The programming will incorporate short platform presentations selected from the submitted poster abstracts. Each scientific theme will sponsor a poster competition with cash awards for the winners.

Undergraduate and graduate students and postdoctoral fellows are encouraged to apply for generous travel awards. Please check the guidelines, and apply if you are eligible, at http://asbmb.org/meetings/annualmeeting2015/travelaward/.

A unique feature of the ASBMB annual meeting is the breadth of the science covered. Held in conjunction with Experimental Biology 2015, the ASBMB sessions and events represent an unrivaled opportunity to learn about the latest discoveries in the range of subdisciplines that fall under the biochemistry and molecular biology umbrellas. Your participation will be rewarded with exposure to new science, the chance to establish collaborations and network, and access to mentoring and career advice.

You will find, as you read the theme summaries provided in the following pages, that the meeting provides great science for all — new approaches and new systems. Submit your abstracts today, and prepare yourselves to hear about the latest exciting advances in biochemistry and molecular biology!

See you in Boston!
Dorothy Beckett,
University of Maryland,
and Mary Roberts,
Boston College

CANCER: THE WAR AT 44, WARBURG AT 90

Has the tide turned?

By Neal Fedarko

On Dec. 23, 1971, the National Cancer Act was signed into law, beginning what has been called America's War on Cancer. Since then, we have developed an understanding of cancer as a cluster of more than 200 diseases characterized by unrestrained growth and spread of abnormal cells locally, regionally or at a distance, with variable aggressiveness. Despite this daunting complexity and heterogeneity, we are in an era of optimism. This ASBMB annual meeting symposium will provide an update on the theater of operation 44 years on in the war.

The sessions will focus on four arenas that have significantly impacted diagnosis, prognosis and treatment strategies.

"You can observe a lot just by watching."

Where is it? Is treatment necessary? How can we target it? Which therapy will work?

The first session will cover novel imaging techniques, reagents and their application to detection, treatment and subsequent surveillance.

"The future ain't what it used to be."

The second session will bring the young and dynamic fields of microRNA and long noncoding RNA into focus in modulating tumor survival, metastasis and crosstalk with other cells in the microenvironment.

"Déjà vu all over again."

More than 90 years ago, Otto Heinrich Warburg demonstrated that,

CONTINUED ON PAGE 24

CONTINUED FROM PAGE 23

under normal conditions, tumor cells, unlike normal cells, use aerobic glycolysis for energy metabolism. Modern metabolomics has led to a finer understanding of energy metabolism in tumor cells and of therapeutic targets specific for tumor cells.

"It ain't over till it's over."

The idea of stimulating the immune system to fight off cancer has been around for more than 120 years. Advances in biologics — antibodies, inhibitors and immune cell stimulation/modulation — suggest that the potential of immunotherapy finally is being realized.

The quotes above are from Lawrence Peter "Yogi" Berra, who also said, "It's tough to make predictions, especially about the future."

ORGANIZER: Neal Fedarko, Johns Hopkins University School of Medicine

DNA REPLICATION AND REPAIR

Cellular systems for repair

By Michael G. Fried and Myron F. Goodman

In their 1953 paper describing the structure of B-DNA, Francis Crick and James D. Watson recognized that noncanonical base pairs could be sources of mutations. As most mutations are deleterious, the repair of aberrant DNA structures is an essential cellular process. More recently, a vibrant field of research has grown around the discovery and characterization of cellular systems that repair or accommodate noncanonical base pairs. This ASBMB annual meeting symposium on DNA replication and repair will provide a present-day overview of important parts of these systems and the mechanisms by which they operate.

The first session will give a perspective on structural and biochemical mechanisms of aberrant translesion DNA replication.

Structural insights into replication fidelity and mismatch repair will be explored in the second session, as will super-resolution live cell-imaging studies that track the movements of individual proteins involved in replication, repair and recombination.

The third session will explore the range of DNA topologies present in repair complexes and the adaptations that allow repair processes to accommodate them.

Replication and repair complexes often contain many components that interact, sometimes over large physical distances. The fourth session will explore the roles of cooperativity in the function and regulation of these complexes.

ORGANIZERS: Michael G. Fried, University of Kentucky College of Medicine, and Myron F. Goodman, University of Southern California

PROTEIN NONFOLDING AS A REGULATORY PHENOMENON

Challenging the central dogma

By Elizabeth Rhoades and Scott Showalter

Biochemistry students learn that protein folding is required for function. However, over the past 25 years, a group of nonfolding proteins that challenge the structure–function paradigm have been identified and shown to be unexpectedly prevalent.

Intrinsically disordered, or natively unfolded, proteins lack stable secondary and tertiary structures under physiological conditions, and many remain disordered even upon binding to their molecular partners. Their lack of stable structure and highly dynamic nature make them challenging to study.

Given that as much as 40 percent of the eukaryotic proteome is partially or entirely disordered, the scope of the problem and the need for new insights are enormous. This ASBMB annual meeting symposium will highlight computational and experimental advances in this research area.

Flexible recognition of binding partners

Disordered regions in proteins frequently mediate contacts with other proteins or nucleic acids. Reports that partially ordered linear motifs embedded within disordered sequences participate in these binding events are ubiquitous; so are observations of coupled folding and binding. Even so, is folding required for binding? This session will cover the binding mechanisms employed by intrinsically disordered proteins.

What makes a good protein go bad?

Disordered proteins are implicated in many human diseases. Although the loss of native, functional interactions of the disordered proteins is thought to play an important role in disease development, these native functions are poorly understood. The second session will explore the mechanisms of native functions of disordered proteins implicated in amyloidogenic neurodegenerative disease.

What does it mean to be disordered?

The absence of a cooperatively folded native state provides a negative definition for disorder but provides no insight into the diversity of natively disordered states. The third session will cover recent advances establishing clear connections between biological function and native disorder.

Trying to hit a moving target

The prevalence and functional significance of protein disorder are firmly established, but can this knowledge be translated into practical medical intervention? In the final session, we explore recent advances toward directly targeting disordered proteins with small-molecule therapeutics.

ORGANIZERS: Elizabeth Rhoades, Yale University, and Scott Showalter, Pennsylvania State University

EXTRACELLULAR MATRICES IN HEALTH AND DISEASE

What is a matrix?

By Jeff Gorski and Karen Lyons

According to the Wachowski brothers' "The Matrix" film trilogy, a matrix is a slick cyberspace that computer hackers inhabit. For biochemists, it is a far more dazzling structure than that.

In this ASBMB annual meeting symposium, experts on extracellular matrices will enlighten us about how proteases and kinases control extracellular matrix structure and function as well as how the extracellular matrix regulates stem-cell niches, growth factor and integrin function, and cell and tissue behavior in development and disease.

Secret liaisons between growth factors and integrins exposed

The first session will examine how growth factors and integrins interact with specific ECM components and with each other. Emerging studies show that interactions between the ECM and growth factors can be tailored to achieve specific cellular responses.

The good (development), the bad (disease) and the matrix

In the second session, new information on the impact of mutations in ECM components in human development and disease will be presented along with studies on novel ECM components that affect development and disease.

Matrix makeovers: cells, proteases and kinases

The third session will focus on recent developments in understanding interactions between the ECM and growth factors as well as how cells use proteases and kinases to modify the ECM during development and disease.

Design your niche

The final session will present innovative approaches being used to reveal new mechanisms by which cells generate and respond to the ECM niches during development and in disease. Investigations that incorporate mechanical cues and the 3-D microenvironment will receive emphasis.

ORGANIZERS: Jeff Gorski, University of Missouri–Kansas City School of Dentistry, and Karen Lyons, University of California, Los Angeles

NEW DIRECTIONS IN ENZYMOLOGY

Mechanistic enzymology and protein-structure function

By Kate Carroll and Liz Hedstrom

It's been almost 90 years since the isolation of urease, yet a vigorous debate continues about how enzymes impart such large rate enhancements to slow reactions. This ASBMB annual meeting symposium will examine modern issues in mechanistic enzymology and protein-structure function.

Co-opting cofactors

Recent investigations have revealed that even a well-studied cofactor such as NAD has some unexpected tricks up its sleeve. This session will discuss new developments in cofactor biosynthesis, chemistry and dynamics.

Function detectives

In any newly sequenced genome, as many as 70 percent of the genes do not have assigned functions. It is clear, then, that a substantial fraction of biochemical space still remains to be mapped. This session will spotlight recent successes in assigning functions to orphan enzymes, the discovery of new activities and metabolites.

Collective power

Enzymes operate in a crowded milieu that fosters macromolecular complex formation and complicated quaternary behavior. This session will examine new tools for characterizing enzyme complexes and highlight examples of protein oligomerization as a regulatory strategy.

My one and only

Of course, rate acceleration is only part of what is amazing about enzyme catalysis. How enzymes discriminate between substrates is far more complex than the simple lock-and-key model. This session will discuss strategies for substrate recognition and reaction specificity.


ORGANIZERS: Kate Carroll, The Scripps Research Institute, and Liz Hedstrom, Brandeis University

PLENARY LECTURERS

Talks to put on your itinerary

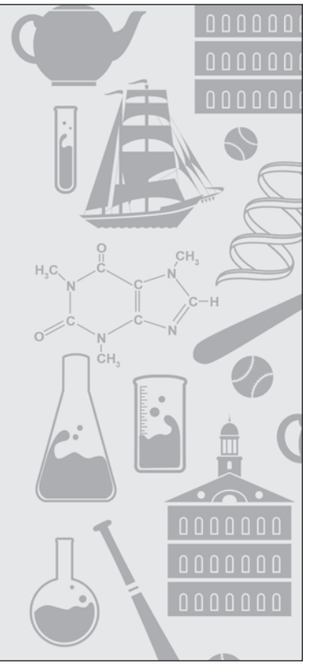
C. David Allis, The Rockefeller University
Beyond the double helix: varying the terrain of epigenetic landscapes in development and disease

Bonnie L. Bassler, Princeton University
Manipulating quorum sensing to control bacterial pathogenicity

Ian A. Wilson, The Scripps Research Institute
Structural basis of broad neutralization of viral pathogens

Zhijian James Chen, University of Texas Southwestern Medical Center at Dallas
Enemy within – immune and autoimmune responses to the cytosolic DNA and RNA (Also ASBMB-MERCK award winner)

Rachel Klevit, University of Washington
Structural, functional and mechanistic diversity in protein ubiquitination (Also Fritz Lipmann Lectureship winner)



Upcoming ASBMB events and deadlines

SEPTEMBER

Sept. 8–10: ASBMB Hill Day, Washington, D.C.

Sept. 23–24: ASBMB exhibits at the National Institutes of Health Research Festival, Bethesda, Md.

OCTOBER

Oct. 2–6: Special symposium, Transcriptional Regulation: Chromatin and RNA Polymerase II, Snowbird, Utah

Oct. 15: Fall application deadline for ASBMB degree-accreditation

Oct. 16–18: ASBMB exhibits at the annual meeting of the Society for Advancement of Hispanics/Chicanos and Native Americans in Science, Los Angeles

NOVEMBER

Nov. 6: Deadline for volunteered abstracts for the 2015 ASBMB annual meeting in Boston

Nov. 7: The ASBMB and Florida Biomedical Career Symposium, Jupiter, Fla.

Nov. 11: Deadline for travel-award applications for the 2015 ASBMB annual meeting in Boston

Nov. 11–15: ASBMB exhibits at the Annual Biomedical Research Conference for Minority Students, San Antonio, Texas

DECEMBER

Dec. 1: Deadline for proposals for ASBMB 2016 special symposia

December 7–9: ASBMB exhibits at the American Society for Cell Biology annual meeting in Philadelphia, Booth 1004

"Punk rock, at its best, embraces an openness to experience, a reliance on reason and evidence, and a questioning of received wisdom. Science, which is based on the naturalist perspective, is also about questioning and not settling for dogma."

– GREG GRAFFIN, "ANARCHY EVOLUTION"

DEFYING STEREOTYPES:

PUNKS WHO PUBLISH

By Geoffrey Hunt and Rajendrani Mukhopadhyay

Is there something inherent to punk rock that attracts scientists? At first blush, there would seem to be little overlap between the methodical deliberation of science and the loud aggression of punk. Yet, upon deeper inspection, the similarities start to become apparent. Both are magnets for individuals willing to question convention. Both involve a search for truth. And both rely on creative insights and breakthroughs that spur passion and excitement.

"If I write a song, to me, it's no different than if I make some discovery in the lab," says Milo Aukerman, a plant biochemist working at DuPont who also fronts the punk-rock band Descendents. "Your heart races, and you have this sense of exhilaration."

Bad Religion lead singer Greg Graffin, who also is an evolutionary biology lecturer at Cornell University, agrees: "I think there's a tremendous similarity in creativity in science and in music or art."

So what is it about punk that makes it so amenable to creative people? Punk is "thinking for yourself and doing what you want – and not accepting something as truth just because someone else says it," explains Dexter Holland, the lead singer for the Offspring, who is working on his Ph.D. at the University of Southern California. He says that the "attitude of questioning things" appeals to people who like to think deeply about issues.

The profiles of Aukerman, Holland and Graffin featured in this issue explore how each musician-scientist has used his creative energy to foment successful forays in the lab and on stage. Moreover, what they have to say about the juxtaposition of their scientific and musical careers goes a long way toward erasing the stereotypes of the geeky, introverted, lab coat-clad scientist and the angry, impulsive, Mohawk-sporting punk.

Holland captures it best when he says, "Something that is established doesn't necessarily mean it's true."

A champion of the nerds

Milo Aukerman is a molecular biologist as well as the lead singer of the punk-rock band Descendents

By Geoffrey Hunt and Rajendrani Mukhopadhyay

I want to be stereotyped /
I want to be classified.
– DESCENDENTS, "SUBURBAN HOME"

Whatever inspired Milo Aukerman to write those lyrics, he has spent the past three decades doing everything not to live up to them. As both the lead singer of the seminal Los Angeles pop-punk band Descendents and a plant molecular biologist at DuPont, Aukerman has followed a decidedly nontraditional career path, one that allows him to embrace the most dynamic qualities of his two passions. Both a scientist and a musician, Aukerman blurs the lines between conventional definitions of these two professions.


AUKERMAN

As a high-school student fascinated by the discovery of the structure of DNA and the recombinant DNA experiments of Stanley Cohen, Paul Berg and Herbert Boyer, Aukerman defied the science-geek stereotype by joining up with Tony Lombardo, Frank Navetta and Bill Stevenson in Descendents in 1980 to make a splash in the punk-rock scene. "My parents definitely had an expectation that I would be an academic-type person," recalls Aukerman. However, "I needed a place to get my ya-ya's out and actually be different."

Growing up in Los Angeles, Aukerman had punk rock right on his doorstep. "In the late '70s and early '80s, LA punk rock was just blossoming," he says, listing Black Flag, the Germs, X and the Minutemen as his musical inspirations back then. "It was a pretty amazing time just to be involved in that (scene) and play on the same shows as some of these bands."

Torn between his dual loves of music and science, Aukerman crafted the perfect compromise, now immortalized in the title of the band's debut album, "Milo Goes to College," which was released in 1982. Inspired by his actual departure from the band to study biochemistry at the University of California, San Diego, the album cover featured a caricature of Aukerman, complete with a white button-down shirt, black tie, thick-rimmed glasses and buzz cut, cementing the band's iconic nerd image. "Punk provided me that avenue to be different," says Aukerman, who earned his bachelor's degree in biology in 1986.

For the next several years, Aukerman bounced between touring and recording with the band and working at UCSD to get his Ph.D. in biochemistry. The two lifestyles might seem to be conflicting, but Aukerman sees them as complementary. "Sometimes when the science is getting (to be) a little more of a drudge, that's when I just turn to music and figure, well, now I'm going to take my creative energy and focus on music for a while," he says. "Then maybe a couple of months later, the science takes the driver's seat, and that ends up being where my creative energies go."

From left: Milo Aukerman (IMAGE COURTESY OF AUKERMAN). Descendents band members Milo Aukerman and Stephen Egerton (IMAGE COURTESY OF CHAPMAN BAEHLER). Descendents' logo and "Cool To Be You" album cover (IMAGES COURTESY OF FAT WRECK CHORDS). Milo Aukerman in a greenhouse (IMAGE COURTESY OF AUKERMAN). Descendents members, from left, Karl Alvarez, Stephen Egerton, Milo Aukerman and Bill Stevenson (IMAGE COURTESY OF TONY NELSON). The band's "'merican" abum cover (IMAGE COURTESY OF FAT WRECK CHORDS).

Aukerman's scientific career has challenged his own ideas about stereotypes within the research enterprise. After going along the traditional scientific academic path, including two postdoctoral fellowships, Aukerman had his heart set on a faculty position at an academic institution. By the time he followed his wife, Robin Andreason, to Delaware, where she was about to take up a faculty position at the university's department of philosophy, "I was really on the academic track," he says. But friends who were already working at DuPont suggested that he consider applying there.

He accepted a job at DuPont as a principal investigator and admits thinking, "Oh, great. Here we go, into corporate research." However, Aukerman discovered that the research environment at DuPont is very much like the one he was used to in academia "but in a corporate setting, without all the headaches of grant writing and teaching and all that kind of stuff."

"In fact, the first few years were an amazing time for me," he says. During his time at DuPont, Aukerman and his colleagues have made several important discoveries, including uncovering that microRNAs are involved in controlling flowering time.

These days, as part of the DuPont Crop Genetics group, Aukerman is studying the model organism Arabidopsis thaliana to understand the genetic players for traits such as drought tolerance and nitrogen assimilation that will aid engineering hardier strains of maize. He has no ambition of climbing the corporate ladder. "I just want to have a really fascinating problem to work on," he says. Immersed in research for now, Aukerman sees the band as "a hobby that allows me to maintain (a) youthful outlook on life and a freshness in life."

Despite the unconventional shifting that he does between the worlds of molecular biology and punk rock, Aukerman says he's never suffered "any kind of fallout." Fellow scientists, he says, "are very interested in someone who's not just stuck at the lab bench all day and who can actually go out and do something completely different, something wacky and bizarre." Likewise, for peers in punk rock, "even if they don't really understand what I do necessarily, it's so different to them that it becomes more of a facet that can be fascinating," he says. Even Aukerman's parents have come around to supporting his career decisions. "Whenever I hang out with my mom, she's trying to introduce me as 'my rockstar son,'" he says with a laugh.

You might think that Aukerman is unique in his ability to rise above classifications and challenge the assumption that a scientist or a punk has to look or act a certain way. But he doesn't think so. "There's a stereotype of a punk being this tough, tattoo-laden meathead," says Aukerman. "But in fact, many nerds ended up turning to punk, because it was a way of releasing some of that frustration that they had for being nerds."

Having spent a lifetime avoiding being stereotyped or classified, Aukerman does defy the way labels are applied. As he proudly puts it, "Punks are the champions of the nerds."

Keep 'em separated

Dexter Holland, the lead singer of the punk-rock band The Offspring, has a lot of different interests. One of them is biology.

By Rajendrani Mukhopadhyay and Geoffrey Hunt

Before he became famous as the lead singer for the punk-rock band The Offspring in the mid-1990s, Dexter Holland was just another graduate student toiling away in a laboratory at the University of Southern California. One day, he pulled two five-liter Erlenmeyer flasks full of steaming hot LB broth out of the autoclave and put them in the safety hood to cool down. But the cooling process was taking forever. "They were right next to each other," remembers Holland. "I thought, 'These things are never going to cool off. I've got to keep 'em separated.'"

HOLLAND

The phrase struck Holland. "I thought that was a funny line," he recalls of what would become the signature hook for the band's breakthrough hit, "Come Out and Play." "It was literally a biology inspiration."

Finding inspiration from different areas is integral to Holland's psyche. As a singer, a licensed pilot, and a certified hot-sauce maker, Holland is continually finding new creative outlets for his seemingly boundless energy. "I like making things happen," he explains. "I like to do a lot of stuff." Next up on his list: to finish that Ph.D. in virology he started two decades ago. "It's been a long road," admits Holland.

A native of southern California, Holland formed The Offspring with Greg Kriesel, Ron Welty and Kevin "Noodles" Wasserman in high school. As the band struggled to make it big in the early 1990s, Holland started a Ph.D. at USC and got as far as passing his oral qualifying exams. But in 1994, The Offspring's third album, "Smash," exploded onto the charts, soaring to No. 4 on the U.S. Billboard 200 and catapulting the band into superstardom.

At that point, it was clear to Holland what he needed to do – he had to put his academic pursuits on hold. Others were not as sure. One of his thesis advisers, completely befuddled as to why Holland wanted to take a leave of absence from graduate school, suggested Holland take time out from the band instead. "This is when we were on MTV!" says an incredulous Holland. His parents were equally confounded. "You have this great opportunity of getting a grad degree, and you're throwing it away to go play in a punk rock band?" Holland remembers them saying. "I think they secretly hoped it was a phase."

Clockwise from top: Dexter Holland helps ready Gringo Bandito hot sauce (IMAGES COURTESY OF CHAPMAN BAEHLER). A bottle of Gringo Bandito hot sauce. Band logo for The Offspring (IMAGE COURTESY OF THE OFFSPRING). The Offspring's "Smash" album cover (IMAGE COURTESY OF EPITAPH RECORDS). Dexter Holland stands with his prop plane (IMAGE COURTESY OF CHAPMAN BAEHLER).

IMAGE COURTESY OF THE OFFSPRING

The Offspring band members, from left Greg Kriesel, Dexter Holland, Kevin "Noodles" Wasserman and Pete Parada

In a way, they were right. After 20 years of touring and recording with The Offspring, Holland's focus has finally come back to his Ph.D. "If I don't do it now," Holland says, "I'm not going to do it 10 years from now." Working with Suraya Rasheed at USC, Holland is studying the roles of microRNA sequences in influencing the infectivity of the human immunodeficiency virus. "I'm not predicting necessarily making (science) a career," says Holland. "But I did want to finish something that I started."

Thankfully for Holland, his music career is going pretty well. "Smash" has sold more than 6 million copies in the U.S. and more than 12 million copies globally, qualifying it as the best-selling independent-label album to date. More platinum-selling albums have followed, establishing The Offspring as one of the most successful bands in music history. "I've been very fortunate to be able to pluck an electric guitar for a living," acknowledges Holland. The band continues to be active, and Holland spent this summer touring with his bandmates around North America and Europe.

The band's long-lasting success has afforded Holland the freedom to indulge his passions and explore a variety of distinct pursuits. Hot sauce is a case in point. As someone hailing from southern California, Holland is well acquainted with what makes a good hot sauce and wanted to cook up his own. "I thought it would be cool, because it sounds funny and sounds fun," he says. Holland spent two years crafting his sauce, admitting that he took "a little bit of a scientific approach" in perfecting the recipe. Gringo Bandito Hot Sauce is now available for sale in grocery stores in various states and online.

It's anybody's guess what Holland might do next. He already devotes some of his time to the Innocence Project, an organization that works to exonerate wrongfully convicted prisoners through DNA testing. In this regard, having a Ph.D. at the end of his name adds "a legitimacy" that could help people listen to what he has to say about his favorite charity. After that? "Maybe Bono will give me a call, and I can help him fight AIDS in Africa," he jokes.

Against the grain

Whether he's fronting the punk-rock band Bad Religion or delivering a lecture on evolution, Greg Graffin is constantly challenging his audiences to question convention

By Geoffrey Hunt and Rajendrani Mukhopadhyay

"Early man walked away as modern man took control / Their minds weren't all the same, to conquer was his goal / So he built his great empire, and he slaughtered his own kind / Then he died a confused man, killed himself with his own mind / We're only gonna die from our own arrogance."

– BAD RELIGION

If you're hoping to get a punk-rock performance in his evolutionary biology class, Greg Graffin is quick to dash your hopes. "You can't slam dance when you're listening to me lecture," says the Cornell University lecturer and lead singer for the legendary punk band Bad Religion.

GRAFFIN

For more than thirty years, Graffin has been studying, researching and teaching evolutionary biology while simultaneously fronting one of the most influential bands to come out of the hardcore punk scene. Moving back and forth between these two identities, Graffin seeks to inspire his audiences to question orthodoxy and search for truth, whether in a lecture hall or in a music club.

Graffin's dual lifestyles trace back to his high-school days in the late 1970s in California's San Fernando Valley. A Midwestern transplant with a fondness for progressive rock bands like Utopia and King Crimson, Graffin became fascinated by evolution in his biology class. "My parents never raised me with any religion," he says. Evolution "gave me a mythology of where I came from that wasn't based on any stories in the Bible."

His decidedly unpopular interests drew him to punk rock, which at that time was a refuge for all types of outcasts. "These unpredictable things came together [at] that time in my life," he remembers. Inspired by the poetic lyricism of punk rock peers like The Germs as well as the intellectual freedom he found in the theory of evolution, Graffin teamed up with fellow misfits Jay Bentley, Brett Gurewitz and Jay Ziskrout to form Bad Religion, a punk band that has deliberately defied and offended convention but in a decidedly philosophical way. "My personal discovery of evolution and starting a punk band called Bad Religion – they were nicely harmonious," states Graffin.

One of the first songs Graffin wrote for Bad Religion, titled "We're Only Gonna Die," was directly inspired by the final sentences of Charles Darwin's "Origin of Species." Since then, his interests in music and science have continued to grow in parallel. "They became the two threads of my life," says Graffin, who first began his instructional duties in 1987 as a graduate teaching assistant for a comparative anatomy course at University of California, Los Angeles, around the same time Bad Religion began to achieve a degree of prominence within the punk-rock community.

As the band's fortunes continued to improve, science got temporarily pushed to the side, with Graffin putting his academic pursuits on hiatus for several years before finally obtaining his Ph.D. in zoology from Cornell in 2003.

In the interim, Bad Religion's growing popularity resulted in an ever-expanding audience becoming aware of the sophisticated brand of intellectualism that the band was promoting. Graffin says Bad Religion's mantra has been to "liberate the closed-mindedness of punk rock" by rejecting the vacant anarchism and brutal nihilism often associated with the genre. "Part of the beauty of punk tradition is not giving into stereotypes," he says.

Jumping back into academics as a full-time lecturer at UCLA in 2007 was therefore a relatively smooth transition for Graffin. "I think there's a tremendous similarity in creativity in science and in music," he says.

As an instructor, Graffin readily admits that "my reputation precedes me sometimes," leading to potential confusion and disappointment for his students who sign up for his class in hopes of seeing an exhilarating punk-rock performance. "It's nowhere near as exciting," says Graffin. "I'm not a loud, boisterous lecturer."

Yet keeping his audience members on their toes is something Graffin excels at. "I know people look at me as some kind of schizophrenic person who's doing these two things but not focusing on any one," claims Graffin. But as he sees it, the process of constructing and then delivering a lecture on evolutionary biology relies on a similar approach to songwriting, one that is based primarily on storytelling. "How you approach a subject like extinction or the fossil record, there's really a story to be told there," Graffin says. Similarly, the "songs that I've written are stories in themselves."

The nature of those songs is what sets Graffin and his band apart. Johnny Ramone supposedly once described The Ramones' songs as being "fairly long songs played very, very quickly." In much the same vein, listening to Bad Religion songs is like listening to a lecture given very, very quickly.

The wide-ranging subject matter and extensive vocabulary in Bad Religion lyrics demand concentration, attentiveness and even research, something that Graffin says is consciously part of his songwriting and lecturing processes. "Certainly one of my interests in songwriting is to challenge people to think," he states. "Similar to my goals in lecture."

Graffin uses his songs to inspire his audience to question and analyze the validity of conventional institutions. Topics drawing Graffin's discerning ire include pop culture, religion, government, and even science and technology.

Targeting science may seem to

CONTINUED ON PAGE 36

"We are One People, and we can all strive for one aim: the peaceful and equitable survival of humanity. To have arrived on this earth as the product of a biological accident, only to depart it through arrogance, would be the ultimate irony."

– CHARLES DARWIN, ON THE ORIGIN OF SPECIES

From left: Bad Religion "Crossbuster" logo (IMAGE COURTESY OF EPITAPH RECORDS). Bad Religion performing live (IMAGE COURTESY OF ROBERT GASPARRO). Bad Religion's "Suffer," "Against the Grain" and "True North" album covers (IMAGES COURTESY OF EPITAPH RECORDS).

IMAGE COURTESY OF MYRIAM SANTOS

Bad Religion band members, from left, Brian Baker, Greg Hetson, Brett Gurewitz, Greg Graffin, Jay Bentley, Brooks Wackerman

CONTINUED FROM PAGE 35

conflict with Graffin's proclamation to be a naturalist, but he sees it as a healthy part of the scientific process. "You can't just have blind faith in something," he cautions. "You need to temper it with evidence." Sticking with his nonconformist approach, Graffin even prefers Charles Darwin's "Voyage of the Beagle" to the canonical "Origin of Species," which he considers "pretty dry reading."

Currently, Graffin co-teaches an introductory course on evolution at Cornell during the fall semester, leaving him plenty of time, as he puts it, to "take care of band business." Graffin acknowledges that his musical forays outstrip his efforts in the classroom, at least for now. "I've performed far more concerts than I have given lectures," he says.

While he looks forward to continuing with both his passions, what matters to Graffin, ultimately, is the impact his work is having on his audience. For Graffin, "the astonishing phenomena that come from the connection you can make with an audience member is something that I want to tap into and try and find."

Graffin says he strives to improve his own performances. "I've written something like 300 songs in my life," he says. "I think I've gotten better and better as I've done more of them." Likewise, Graffin continues to improve his teaching skills. "My [class] reviews have all been good," he says, but "I'm trying to get more experienced at lecturing."

Here, finally, Graffin notes a small disconnect between his two passions. "I'm not going to clubs every night, because I'm preparing for lecture," he says. Though it may be blasphemy to his punk-rock peers, this is a statement with which most professors can empathize.

IMAGES COURTESY OF: 1. EPITAPH RECORDS, 2. ROBERT GASPARRO, 3. CHAPMAN BAEHLER, 4. FAT WRECK CHORDS, 5. CHAPMAN BAEHLER, 6. ROBERT GASPARRO, 7. CHAPMAN BAEHLER, 8. EPITAPH RECORDS, 9. TONY NELSON, 10. CHAPMAN BAEHLER, 11. EPITAPH RECORDS, 12. ROBERT GASPARRO, 13. CHAPMAN BAEHLER, 14. FAT WRECK CHORDS, 15. THE OFFSPRING, 16. KATIE HOVLAND, 17. EPITAPH RECORDS, 18. EPITAPH RECORDS, 19. ROBERT GASPARRO, 20. MYRIAM SANTOS, 21. MILO AUKERMAN, 22. EPITAPH RECORDS, 23. CHAPMAN BAEHLER, 24. EPITAPH RECORDS

Geoffrey Hunt (ghunt@asbmb.org) is the ASBMB's public outreach coordinator. Follow him on Twitter at www.twitter.com/thegeoffhunt. Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the senior science writer and blogger for ASBMB. Follow her on Twitter at www.twitter.com/rajmukhop.

Open letter to the incoming cohort of graduate students

By Kelly Hallstrom

Dear newbie graduate students,

To all of you about to start on the exciting, confusing, roller-coaster-of-emotions path of graduate school, I'd like to share some advice and lessons I've learned (and am still learning!) during my own experience as a graduate student in biological sciences.

Own your project

Graduate school is going to be vastly different from your undergraduate experiences. As an undergrad, you most likely helped out on another person's project, running a few PCRs here, taking population samples there. You were a helper of sorts, learning a little of this and that as you went along. It was a great opportunity to get your feet wet in research. If you worked in a lab after your undergraduate studies, you probably had more responsibilities but most likely were still an assistant to someone else.

As a graduate student, however, you transition from being a helper to having ownership over an entire project. This situation was new to me. I inherited my project from a postdoc, and it took some time for me to stop thinking about my work in terms of what I needed to do to finish this project he started and start thinking everything from that point forward was my project.

This ownership is exciting. Your ideas, perhaps for the first time in your research experience, are given weight and consideration. You are involved in the decisions of which experiments to do and which to shelve perhaps for later.

This responsibility also can be daunting at times. You are in charge of understanding the how and why of every step, technique and experiment. You are expected to know the state of the art of the field surrounding your project, to remain up to date on new relevant findings and to contribute new ideas.

It might take a little time to embrace fully this new responsibility. Don't be afraid of it, though. Instead, learn from it. Become the expert. Own your project.

Swallow your pride

You've been warned: You are going to be criticized. A lot.

When you give presentations at department seminars or at conferences or meet with your thesis committee, your approaches and conclusions are going to be targets for questioning and criticism. But this is part of science. Science is constantly self-checking and self-correcting. That can't happen without criticism.

As much as you may think you're doing everything right, it's easy to develop tunnel vision and to forget to approach your work from different perspectives. This may cause you to miss an alternative explanation or key experiment. Without those people in the crowd to point out your errors, your work (and the science behind it) can't improve.

Most people who will criticize you are going to do it from a place of well-meaning — with the goal of helping you and your work to progress in the right direction. Always be open to considering what those people have to say.

Explore all career options

Though you may enter graduate school with a clear plan of what career lies ahead for you, be open to that plan changing a little or a lot. It is not uncommon for people to enter graduate school with the goal of becoming an academic researcher or executive of a biotech company and realize halfway through that those career paths are not right for them after all.

That is OK, and that's why it's good to explore as many career options as possible while you are still a student. Do your homework, and find out what career-development opportunities your school provides and take advantage of them. On the flip side, don't feel limited by the opportunities for growth available at your school. You may have to seek out volunteering or networking opportunities beyond your campus.

For example, if you decide during your graduate studies that you'd like to teach but your school offers few ways to gain teaching experience, contact nearby schools. In short, no matter what your reason for choosing to enter graduate school, continue to explore all of your interests.

Live your life

Finally, I urge you to remember to have a life outside of the lab. Becoming engrossed in your project is important (own it!), but you don't want to live in a vacuum and cut off all social down time.

Breaks are important for allowing your brain to rest. Often, time away from the lab brings you out of the tunnel for long enough that when you return to work you spot issues you otherwise wouldn't have noticed.

Aside from giving you and your brain a break, having outside interests ensures that your life in general doesn't stop just because you're in graduate school. I know people who have lamented over "wasting their youth" in graduate school while their friends' lives progressed into promotions, marriages and other accomplishments and milestones.

Just because you're in graduate school doesn't mean the rest of your life has to stop. In fact, it's the other parts of your life that often will save your sanity when lab life is giving you trouble. So go on dates, go to hockey games (go Bruins!), have karaoke nights — do whatever it is you have to do to stay connected to the outside world.

In closing, graduate school is your opportunity to hone your skills as you transition from a classroom student to an independent researcher. This time marks the start of you shaping your unique career path, and it is a time of immense professional and personal growth.

Learn as much as you can, and enjoy the ride!
Kelly

Kelly Hallstrom (kelly.n.hallstrom@gmail.com) is a Ph.D. candidate at the University of Massachusetts Medical School.

Last call for open letters!

Dear readers,

If you've enjoyed our "Open Letters" series and have contemplated contributing a piece to it, the time has come! We will accept open letters through Sept. 30. After that, we'll be gearing up for our 2015 series (described on the inside of the cover of this issue). Send your submission to asbmbtoday@asbmb.org.

Also, I'd like to express how grateful I am to those contributors who have brought the "Open Letters" series to life. On behalf of our readers, thank you for your courage, humor and sincerity.

Best,
Angela Hopp
Editor, ASBMB Today

Read the series online

Rajendrani Mukhopadhyay, *"An open letter to a professor who once comforted me"* (December)

Michael Mira, *"A belated love letter to my first-grade science teacher"* (January)

Akshat Sharma, *"An open letter from a not-so-good Brahmin boy"* (February)

Paul Sirajuddin, *"An open letter to my younger self"* (March)

Harvey J. Armbrecht, *"Thank God for overlapping genes"* (April)

Philip Yeagle, *"On hindsight and gratitude"* (May)

Bill Sullivan, *"The road to professor"* (June/July)

Angela Hopp, *"An open letter to press officers who won't promote unembargoed research papers"* (August)

A response to the NIH Biomedical Research Workforce Working Group Report

Biochemistry department leaders offer praise, criticism and recommendations

By Bruce J. Nicholson and Richard L. Eckert

Biomedical research in the United States is in crisis as the international leadership the nation has enjoyed for decades is eroding in the face of economic austerity and competition from other countries that have made research a higher priority. This crisis has arisen as universities and research institutes, which have based strategic plans on assumptions of continued growth, are faced with the reality of shrinking federal research budgets and sharp reductions in state funding for higher education. These pressures demand a critical self-analysis as to how we can preserve the vibrant and creative U.S. scientific environment while also devising new strategies for training the next generation of scientists for a job market offering fewer opportunities in academia.

A National Institutes of Health advisory committee headed by Shirley Tilghman made several recommendations addressing these issues in the NIH Biomedical Research Workforce Working Group Report published in June 2012 (1). Bruce Alberts, Marc W. Kirschner, Shirley Tilghman and Harold Varmus recently revisited the report in a "Perspective" article in the Proceedings of the National Academy of Sciences (2). While researchers support some viewpoints expressed in both of these documents, particularly the recommendation that the NIH return to a focus on funding basic science, other opinions in the report have not been universally embraced.

Some of the recommendations in the Tilghman report already have been implemented by the NIH. As we stand poised for implementation of additional steps that could affect graduate and postgraduate training and research for decades, the Association of Medical and Graduate Departments of Biochemistry convened a working group to consider the repercussions of the Tilghman report from the perspective of department chairs who work at the interface between faculty and institutional administration. While we concur with some of the recommendations in the Tilghman report, we have serious reservations about others.

Graduate education

A primary premise in the Tilghman report and recent PNAS editorial is that too many biomedical Ph.D.s are being issued in light of the number of jobs available. However, this is true if one focuses only on traditional academic careers.

Between 2002 and 2008, despite a 50 percent increase in biomedical Ph.D. holders, unemployment remained constant at 2 percent for that segment of the workforce, much lower than the 7.5 percent national average at that time (1). However, there is a shift within this segment, with employment opportunities in academic research decreasing steadily while opportunities in industrial and government research, administration, teaching, scientific writing, advocacy and other areas that demand people trained to think in an analytical manner are increasing. Thus, we disagree with strategies that seek to reduce this pool of highly educated and in-demand individuals. We do, however, enthusiastically endorse the idea of expanding training opportunities beyond the traditional academic track. However, this comes with a specific proviso.

We must not dilute the fundamental goal of graduate training, which is to develop outstanding research scientists who think independently and analytically, as this is precisely what is valued by employers, academic or otherwise. Moreover, training highly competent researchers is essential if the U.S. is going to maintain its international leadership role in the biomedical sciences. For this reason, we disagree with the Tilghman report recommendation that we reduce the time it takes to earn a Ph.D.

Instead, we recommend that the emphasis be placed on shortening how long it takes for a graduate to enter the job market. Permitting students to explore multiple career options during training may actually extend the training period but to good effect. Thus, we propose the focus should move from minimizing time to graduation to minimizing time to career.

We also support tracking graduates to understand how they are moving into the job market, provided that this does not increase investigator administrative burden or increase institutional administrative costs.

We view as flawed the recommendation in the Tilghman report, reiterated in the recent PNAS editorial, that the fraction of students supported by training grants be increased to enhance the quality of training and shorten the time to degree. Our own ad hoc survey of 26 universities revealed no differences in time to degree when comparing students supported on training grants with those supported on individual RO1 grants (see table). The enhanced performance of students supported by training grants, cited in the Tilghman report, is likely the result of institutional selection policies that place the best students on training grants rather than an inherent difference in the quality of training.

We are concerned that training grants have been concentrated disproportionately in elite institutions and that this concentration will increase. Graduate education must serve a range of academic institutions with broad geographical distribution to empower the broadest base of talent. We argue that this can be achieved best and most efficiently by linking student salary support to individual R01s.

Having all students on training grants carries the additional cost of additional administrative burden on investigators and institutions. Thus, rather than expanding training grants, we propose expanding Ruth L. Kirschstein National Research Service Award fellowships, as those awards encourage student initiative and quality and provide student salary support linked to R01s. An example of this strategy, which we endorse, is the recent plan for all NIH institutes to offer F-series grants.

Postdoctoral training

We oppose increasing the number of postdoctoral fellows supported through training grants. Postdoctoral salary support, linked to R01 grants, is a historically effective mechanism that easily and efficiently accommodates productivity and achievement. We support increasing the number of fellowships given to postdocs and making them available to foreign trainees. We also agree with the Tilghman report authors that postdoctoral stipends should be increased, but those increases should be linked to a concomitant increase in modular R01 budgets.

In the recent PNAS perspective it is noted that increasing stipends without increasing grant support will reduce the number of postdocs, which was presented as a positive outcome, but we question if this should be our goal, given the employment opportunities that exist for this group described above! We propose, instead, limiting the time that postdocs can be supported, which can be achieved through enhancing career training and developing additional academic career options.

We also support enhanced tracking of the career outcomes for postdoctoral fellows so long as it doesn't overburden principal investigators or increase institutional administrative costs.

We have significant concerns about the recommendation in the Tilghman report to increase K-type transition awards designed to accelerate movement of postdoctoral trainees toward independent positions. The problem is that it must be done in conjunction with increases in R21 and R01 support available to investigators. Otherwise, increasing K awards amounts to pushing the employment bottleneck down the road.

A better option is to expand opportunities for postdoctoral trainees who may not want faculty positions but aspire to be long-term staff scientists. Staff scientist positions allow these individuals to pursue research careers within other labs without the responsibility of garnering their own funding. Their experience typically enhances the overall competence of laboratory staff. For this staff scientist position to be a viable career path, the NIH and academic institutions would have to accept and put in place a promotion-and-salary structure that endorses and supports these positions analogous to what exists for research-track faculty.

Faculty support

The Tilghman report described a proliferation of what are known as soft-money positions at academic institutions. The reduced job security associated with these positions has created a negative image for research science as a career. As a response, the report recommended limiting the percentage of faculty salary paid for by the NIH.

AMGDB members are in a unique position to understand the impact of soft money on investigators and institutions under pressure to reduce hard-money budgets. We feel that limiting faculty salary coverage on grants should not be achieved by reducing the salary cap, as this will reinforce the image that an academic research career is low paid and unstable. Instead, we favor establishing limits for principal investigator effort on individual grants (e.g., 25 percent for RO1s, 15 percent for R21s and so forth).

In addition, limiting the number of NIH grants that a single investigator can hold, which the NIH has contemplated, also will help. Implemen-

CONTINUED ON PAGE 42

CONTINUED FROM PAGE 41

tation of such a limit must coincide with the recognition by institutions and the NIH that many functions of faculty members — including teaching, committee and professional service, exploratory research, and writing of grant applications in new research areas — should be supported by the institution.

Given the impact these changes will have on our medical schools and research universities, a movement of faculty salaries from grants to institutional budgets needs to be phased in gradually. The NIH may consider incentivizing this transition by directly linking institutional indirect-cost recovery levels to the progress institutions have made in covering higher portions of faculty salaries.

In their PNAS commentary, Alberts and colleagues called for open discourse. We hope this editorial contributes a useful perspective to this conversation and motivates the NIH to reconsider some of its actions. American science has made great progress — which was built upon the success of the R01 award mechanism and the partnership between individual investigators/mentors and their students. We need to continue to foster this relationship but do so in creative ways that adapt to our rapidly changing landscape. We need to avoid the temptation to reduce the training of creative scientists but embrace that their opportunities in different areas have expanded.

Editor's note: The authors of this article wrote on behalf of the AMGDB leaders who contributed to and endorse the report, including David Harris, Boston University School of Medicine; Michael Ostrowski, The Ohio State University; Jane Azizkhan-Clifford, Drexel University College of Medicine; Vadivel Ganapathy, Georgia Regents University Cancer Center; Kevin Raney, University of Arkansas for Medical Sciences; Leslie Parise, University of North Carolina School of Medicine; and Michael Mathews, Rutgers New Jersey Medical School.

TOP 30 INSTITUTIONS:
Graduate Student T32 Positions Versus Time to Degree

Institution	TG Slots[1]	Median[2] Years to Degree	NIH Rank[3]
Johns Hopkins	327	5.5	2
Washington	278	6.13	5
Wisconsin-Madison	261	5.73	21
Michigan	259	5.9	6
Penn	258	5.7	3
UC-San Diego	231	6	8
Yale	213	5.5	10
UCLA	209	6	11
UNC-Chapel Hill	197	5.5	13
UCSF	196	6.29	4
Stanford	186	6	14
Univ. Chicago	174	5.88	27
Harvard + MGH	164	6	1
Cornell	163	6	28
UC-Berkeley	160	5.6	53
Wash U	158	5.74	9
Minnesota	142	5.3	20
Columbia	134	6.5	18
Duke	131	5.45	12
Vanderbilt	130	5.75	16
Pittsburgh	123	5.2	7
Northwestern	121	5.7	29
Case Western	117	5.74	39
Emory	111	5	19
MIT	110	6.3	22
Baylor	101	5.6	17
Colorado	97	5.05	26
Virginia	86	5.5	44
Iowa	85	5.7	36
UAB	78	6	25
Total	**5000**		
% of Slots Nationally	**66%**		
Median YTG Top 30		5.73	
Median YTG Top 10		5.81	

[1] See http://grants.nih.gov/training/outcomes.htm#fundedgrants; data are from the version posted in 2009; 7,583 total TG slots nationally.

[2] National Research Council, 2011. Research Training in the Biomedical, Behavioral, and Clinical Research Sciences. The National Academies Press.

[3] See http://www.brimr.org/ data from 2009.

Bruce J. Nicholson (nicholsonb@uthscsa.edu) is a professor and the chairman of the biochemistry department at the University of Texas Health Science Center at San Antonio and president-elect of the Association of Medical and Graduate Departments of Biochemistry. Richard L. Eckert (reckert@umaryland.edu) is a professor and the chairman of the biochemistry and molecular biology department at the University of Maryland School of Medicine and the president of the Association of Medical and Graduate Departments of Biochemistry.

REFERENCES

1. Alberts, B. et al. P*roc. Nat. Acad. Sci. USA* **111**, 5773 – 5777 (2014).
2. http://acd.od.nih.gov/biomedical_research_wgreport.pdf

Passive obstructionism

By Andrew D. Hollenbach

I really don't have a lot of pet peeves. OK, maybe that's a lie; but most of the ones I have are the common ones. You know, people who don't use their turn signals, people who chew with their mouths open and something specific to the New Orleans region, people who say, "ax" instead of "ask." However, my biggest pet peeve when it comes to my job is the people who say something is impossible before even thinking about how to make it possible.

You know people like this: the person who, when you talk to him or her about an experiment, tells you all of the reasons why the experiment won't work instead of simply doing the experiment; the person who, when you discuss a large-scale experiment, states that it shouldn't be done because it is so large instead of simply rolling up his or her sleeves and doing it; or the person who, when you talk about implementing policy changes, tells you all the reasons why it can't be done instead of raising valid concerns and then working with you to figure out how these concerns can be taken into consideration while planning the changes. All of these different scenarios ultimately result in inaction, which causes projects, labs and institutes to stagnate.

The word "impossible" can be very surreptitious and insidious, and it comes in various active forms, which include the words "can't" and "shouldn't." However, it also comes in many passive forms, veiled in statements like "That's not the way things have always been done," or "Well, nobody has ever shown this before," or, at worst, "Nothing ever changes around here, so why even bother?" These latter forms are examples of what I like to call passive obstructionism; people aren't actively saying that something is impossible or trying to prevent something from happening. Instead, their adherence to the status quo, overt dependence on the literature or outright apathy make it impossible to make something happen.

Don't get me wrong; there are many valid reasons that easily could make someone slip into the passive obstructive mentality. Sometimes, a person may simply be afraid of doing an experiment for fear that the results will disprove a hypothesis. Other times, someone may be afraid of doing that large experiment for fear that, if it doesn't work, money and time will have been wasted. Regarding policy and change, some people just don't like or are afraid of change, regardless of whether it's for good or bad.

Finally, it's possible that academic politics may be at play, and no matter how good a plan may be, these politics will work against you simply because someone doesn't want to relinquish power. Regardless of how infuriating these passive obstructionists may be, these situations should not deter us from pushing forward.

One of the many valuable lessons I learned in graduate school was that there is always a way to get an answer to a question or to make something happen. I didn't learn this lesson only from my adviser but also from the faculty members in our department. They told me that if you know what the question is that you are trying to answer, and if you know what techniques are available to develop an experiment to address the question, then there should be nothing standing in your way of getting that answer. If there are technical difficulties, then it is your job to think creatively about the process, talk to others to get input and devise a way to approach the question from a different perspective. Sometimes you are not able to get a direct answer, but

CONTINUED ON PAGE 45

Scientists talking genetics with the public

By Joseph P. Tiano

I am a second-year postdoctoral fellow at the National Institutes of Health and one of two dozen scientists from around the Washington, D.C., area who have volunteered at the National Museum of Natural History's genomics exhibit.

I have learned a lot from my time as a genome exhibit volunteer. From interacting with 1,500-plus visitors over the past year, I have gained unique insights into the lay public's understanding of genetics and expectations for how genetics will shape the future. And I have to say that, as a Ph.D. scientist who spends a lot of his time inside a scientific bubble with other Ph.D.s, I was surprised to realize just how far out of touch I had become with the lay public's knowledge and views of science. (And I have been inside my scientific bubble for only eight years!)

In the summer of 2013, to commemorate the 10-year anniversary of the sequencing of the human genome, the NIH and the museum partnered to put on the entertaining and highly educational exhibit titled "Genome: Unlocking Life's Code." The 4,400-square-foot exhibit features seven areas of genomic science, exploring what a genome is, the role of genomics in understanding human evolution and the role of genomics in reshaping medicine.

What really makes this exhibit special, I think, is the Genome Zone area, where hands-on activities teach kids and adults alike about genetics and how it is shaping all of our futures. It is also my favorite area in which to volunteer, because I enjoy teaching and it is very rewarding to watch kids have fun while learning genetics.

A couple of the hands-on activities the Genome Zone offered were

• the phenylthiocarbamide, or PTC, taste test to identify which variant of the taste receptor TAS2R38 the visitor has and

• the trait tree to identify monogenic traits (dimples, widows peak, tongue rolling) that the visitor may or may not share with other visitors.

The trait tree is most fun with children and their parents, because it usually ends up turning into a competition between the parents to see who shares more traits with their kids. But it is also the perfect opportunity to break out the Punnett square and teach inheritance.

The most popular — and most difficult — hands-on activity is known as Genes in a Bottle. It involves making a necklace with DNA extracted from a visitor's cheek cells. Imagine 20 visitors of all ages who have never been in a lab before sitting around three tables with 50-ml conical tubes, Pasteur pipettes and small cups of their spit. It can get a little messy, but it is worth it when they say in amazement, "You mean this white, gooey-looking stuff is my DNA?"

Museums are great venues to communicate science to kids and the public because they are fun and low-pressure environments. They also offer great opportunities for scientists to learn how to communicate science to the public — a skill most scientists lack — in an engaging, exciting and easy-to-understand manner. The most important lesson I learned was how bad I actually was at communicating science to kids and nonscientists. I am happy to say that, thanks to volunteering, I have dramatically improved my communication skills.

Exhibit calendar

Sept. 27, 2014 – Jan. 4, 2015
Reuben H. Fleet Science Center
San Diego

Jan. 22, 2015 – April 27, 2015
The Tech Museum of Innovation
San Jose, Calif.

May 15, 2015 – Sept. 10, 2015
St. Louis Science Center
St. Louis, Mo.

Oct. 2, 2015 – Jan. 3, 2016
Oregon Museum of Science & Industry
Portland, Ore.

Jan. 28, 2016 – April 25, 2016
Discovery World Milwaukee
Milwaukee, Wis.

Sept. 30, 2016 – Jan. 1, 2017
Exploration Place
Wichita, Kan.

Jan. 28, 2017 – May 29, 2017
Peoria Riverfront Museum
Peoria, Ill.

Sept. 30, 2017 – Jan. 1, 2018
Science North
Sudbury, Ontario

IMAGES COURTESY OF DONALD E. HURLBERT AND JAMES DI LORETO, SMITHSONIAN

I feel very fortunate to have been employed at the NIH during the year that the genome exhibit spent in Washington. Had I not received NIH e-mails asking for employee volunteers, I never would have thought to seek out volunteer opportunities at museums. In fact, I enjoyed volunteering so much that as the genome exhibit in D.C. came to a close, I asked to be transferred to the museum's Hall of Human Origins. I look forward to the new challenges it presents.

While the exhibit left D.C. earlier this month, it will travel around the U.S. for the next four years. If you are lucky enough to live in one of the cities hosting the exhibit, I highly recommend reaching out to that institution and asking about volunteer opportunities. For the majority of you living in other cities, seek out opportunities at your local museum or science centers. Chances are good they will be glad to have your help and your expertise.

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

PROFESSIONAL DEVELOPMENT CONTINUED

CONTINUED FROM PAGE 43

instead the answer is derived circumstantially from multiple experiments. However, it is still an answer.

The same can be said for ideas and change. People see what policies they would like to implement or change. They know the processes they need to use to implement the change. Sometimes there are valid reasons why the processes originally thought of are not feasible. However, that is when communication needs to happen to reveal what these reasons are and to think creatively about other avenues to achieve the desired change.

We need to ban the "I" word in all of its forms. This will not be easy. It has infiltrated our lives and our mentality too deeply, and rooting it out will take serious attitude adjustments for many of us.

Of course, it is easier to sit back and say something can't be done rather than actually rolling up your sleeves and doing the hard work, be it that scary experiment, that labor- or time-intensive experiment, or working for institutional change. Also, sometimes it means that you have to be willing to listen to people who oppose change or have competing interests, communicate with them and then work with them to derive a compromise that incorporates ideas from both sides.

By putting our fear aside, by dedicating ourselves to the hard work, by developing a positive attitude, and, when necessary, by putting our pride on the shelf to compromise and work together, great changes and great advancements can and will happen.

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.

ASBMB grants help UAN chapters do outreach

By Geoffrey Hunt

The American Society for Biochemistry and Molecular Biology Public Outreach Committee has undertaken a number of initiatives to promote and organize science-outreach activities in communities across the country. The most recent venture was a novel partnership with the ASBMB Undergraduate Affiliate Network, a chapter-based consortium of more than 90 institutions. Participation in science outreach is a requirement for UAN chapters, so the partnership was a natural fit. But to spice the pot, the outreach committee worked with the UAN to develop a grant program that would allow chapters to apply for up to $500 to facilitate student participation in outreach activities.

Ultimately, chapters at seven schools won funding this year. Some are continuing programming that they have been part of previously, while some are starting new programs:

Hendrix College will bring student presentations and biology tutoring sessions to underserved students at Wonderview High School in Hattieville, Ark.

Northeastern University will work with the Northeastern Program for Teaching by Undergraduates, known as NEPTUN, to organize and teach a series of science-themed classes aimed at local high-school students.

Otterbein University will host a molecular biology-themed exhibit at the annual Westerville (Ohio) Starry Night Family STEAM Festival.

Purdue University will host molecular biology-themed exhibit booths at Purdue Spring Fest and Celebrate Science Indiana and will make regular visits to local K – 12 science classes.

The University of Tampa will conduct molecular biology experiments alongside students from Tampa (Fla.) Preparatory High School.

The University of San Diego will use amino-acid builder kits to teach fundamental concepts in biochemistry to local middle-school students from underserved communities.

Wisconsin Lutheran College supported student attendance at its annual Synthetic Biology Summer Camp in Milwaukee.

While this grant program is only one part of a broader effort to involve ASBMB members in science outreach, the dedication and passion of our undergraduate members are encouraging indicators for success. Even better, participation in these activities will instill an interest in outreach that will (hopefully) endure throughout their careers, wherever they end up. Read more about the undergraduate outreach grant program at http://bit.ly/Wj5CI5.

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

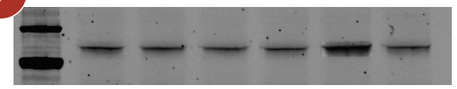
HEY, RESEARCHER! LEAVE THAT BLOT ALONE!

Good practices for preparing publication-quality figures

1. **Before preparing figures, read the Journal's Instructions for Authors.**

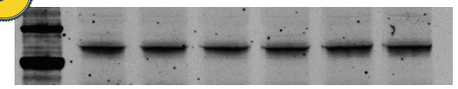
2. **Adjust brightness/contrast equally across image.**

BAD — *Enhanced contrast of one area*



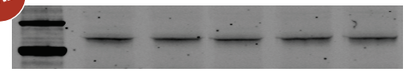
increased contrast ↑

GOOD — *Enhanced contrast equally across image*



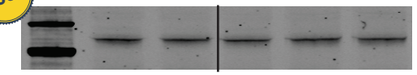
3. **Spliced image must include dividing line at the splice junction and be described in the Figure Legend.**

BAD



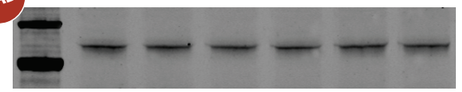
splice ↑

GOOD

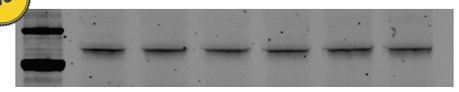


4. **Do not make adjustments that hide any part of the image, including erasing background.**

BAD



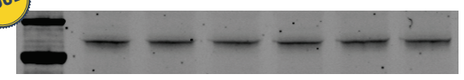
GOOD



5. **Avoid excessive contrast adjustment that removes background.**

BAD

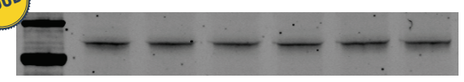
GOOD



6. **Final figures must be high-quality TIFF or EPS files. Avoid preparing figures in PowerPoint to avoid loss of image resolution.**

BAD

GOOD



ASBMB
American Society for Biochemistry and Molecular Biology

Bench Posture – It Matters!

Pipetting involves long hours and a lot of repetition that, over time, can cause chronic musculo-skeletal disorders. But with good pipetting technique and good body mechanics, you can significantly reduce your risk of pain or injury and increase accuracy.

SITTING

Adjust your chair before starting work, making sure your feet rest firmly and comfortably on the floor or footrest, and that you have adequate back support.

POOR

- Neck and back bent
- Elevated shoulders
- Upper arms too high
- Elbow extended
- Wrist not straight

GOOD

- Back and neck in neutral position
- Upper arm relaxed and near vertical
- Wrist and forearm straight
- Thighs parallel with floor and feet firmly supported

STANDING

Periodically rest one foot on a step or stool, and be sure to alternate your weight between feet. When standing for prolonged periods, use a padded anti-fatigue mat.

POOR

- Neck, shoulders and back are stooped
- Elbow is flexed

GOOD

- Neck, shoulders and back are upright
- Upper arm is near vertical
- Elbow at 90°
- Forearm is parallel and aligned with wrist

PIPETTING

Whether sitting or standing, be sure the bench is a comfortable height and that frequently used items are within easy reach.

More good pipetting ergonomics:

- Avoid awkward, twisting movements
- Don't over reach
- Switch hands periodically
- Keep your grip loose
- Vary pipetting with other tasks
- Take frequent breaks
- S T R E T C H !
- Choose ergonomic pipettes, like Rainin Pipet-Lite™ XLS+™ and E4™ XLS+

POOR

- Upper arm flexed
- Elbow extended
- Wrist not aligned with forearm

- Wrist extended backward
- Forearm contact stress on the bench

GOOD

- Forearm parallel to the floor
- Wrist and forearm aligned

For technical papers and other pipetting ergonomics information, please visit www.mt.com/gpp

METTLER TOLEDO

ASBMB 2015 Annual Meeting

BOSTON

March 28 – April 1

ABSTRACT SUBMISSION DEADLINE
November 6, 2014

TRAVEL AWARD APPLICATION DEADLINE
November 11, 2014

PLENARY SPEAKERS

C. David Allis, *The Rockefeller University*

Bonnie Bassler, *Princeton University*

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

Rachel Klevit, *University of Washington*

Ian Wilson, *The Scripps Research Institute*

ASBMB ABSTRACT TOPIC CATEGORY TITLES (#2000-2390)

2000-ASBMB	*DNA Replication and Repair*
2040-ASBMB	*RNA Expression and Post-transcriptional Regulatory Events*
2090-ASBMB	*Intrinsically Disordered Proteins: Protein Nonfolding as a Regulatory Phenomenon*
2110-ASBMB	*Channels and Transporters: What's New in Membrane Transport Proteins*
2140-ASBMB	*Lipids: In Vivo Dynamics, Protein Partners and Signaling*
2180-ASBMB	*Extracellular Matrices in Health and Disease*
2200-ASBMB	*Molecular Mechanisms of Infection and Immunity*
2270-ASBMB	*Enzyme Mechanisms and Chemical Biology*
2290-ASBMB	*Mechanistic Impacts of Post-translation Modifications*
2310-ASBMB	*Human Microbiome / Microbiome Dynamics and Health Disparities*
2330-ASBMB	*Cancer: The War at 44, Warburg at 90*
2350-ASBMB	*Plant Biochemistry*
2370-ASBMB	*Education and Professional Development*

THE ABSTRACT SITE IS OPEN!
WWW.ASBMB.ORG/MEETING2015

ASBMB
American Society for Biochemistry and Molecular Biology