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ASBMB TODAY

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

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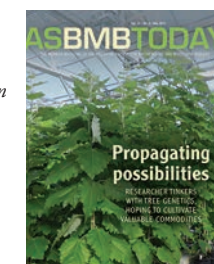
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PRESIDENT'S MESSAGE

Good reads and the power of data

By Jeremy Berg

Curling up with a good book is one of life's great pleasures. Two books that I have greatly enjoyed over my time as president of the American Society for Biochemistry and Molecular Biology are Nate Silver's "The Signal and the Noise: Why So Many Predictions Fail — but Some Don't" (1) and Siddhartha Mukherjee's "The Emperor of All Maladies: A Biography of Cancer" (2).

Although they are very different, these books share three major features. First, each takes a largely historical approach to analyze progress in its respective field. Second, each addresses the roles of careful data collection and analysis in allowing fields to move past strongly held but often incorrect beliefs. Finally, each emphasizes the importance of understanding mechanism to place empirical observations in a robust context that can be extended. These features, of course, are of central importance in biochemistry and molecular biology and also in science advocacy.

'The Signal and the Noise'

Silver is best known for his success in predicting the outcome of recent presidential and senatorial elections based on aggregation and analysis of polling data on his blog FiveThirtyEight (3). In his book, Silver describes the history and bases for predictions in a range of areas including politics but also finance, sports, gambling and earthquakes.

I found the section on weather prediction particularly illuminat-

ing. It includes a discussion of the discovery by Edward Lorenz at the Massachusetts Institute of Technology of so-called "chaotic" behavior in computer-based simulations of weather. Lorenz was dismayed when apparently identical runs of the simulations with the same data produced vastly different results. This is due to the fact that these (and many other) simulations are very sensitive to the data on which they are based. Silver goes on to describe how computer simulations, in conjunction with judgments from human meteorologists, have steadily improved the quality of weather predictions since the 1970s.

This conclusion, of course, depends on tracking the accuracy of predictions. One of the sections that I found most intriguing involves calibration of measures of prediction accuracy, which Silver entitles "How to Know if Your Forecasts Are All Wet." This section highlights the importance of access to many predictions and subsequent outcomes and calibration of predictions to judge how well they do. The predictions of the likelihood of rain by the National Weather Service are remarkably well calibrated; when the NWS forecasts rain with a 50 percent probability, it really does rain approximately 45 percent of the time.

He also presents calibration curves for the Weather Channel and for local television forecasts. Both of these groups have access to the National Weather Service predictions, yet their

calibration curves are much worse. This is particularly true for the local television forecasts: They substantially overpredict the probability of rain. This tendency gets at a key point. What is the best measure of the validity of a forecast?

Citing a study by Allen Murphy (4), Silver notes three possible measures:

1. the "quality" or "accuracy" (How well does the forecast match the actual outcome?)
2. the "consistency" or "honesty" (To what extent was the prediction as accurate as it could be?)
3. the "economic value" (How useful was the prediction in making good policy decisions?)

In this light, it seems that some forecasters decrease accuracy and consistency to increase the economic value of their predictions. They get in less trouble with their audiences if they predict rain and it doesn't occur (and the event is moved to an indoor venue) than if they don't predict rain and all of the guests get soaked.

'The Emperor of All Maladies'

This delightful and thought-provoking book by Mukherjee tracks our understanding of cancer and the development of cancer treatments from ancient times through the present "genomic revolution." Major steps along this path include the appreciation of the nature of cancer as a disease of poorly controlled cell growth, the development of surgical approaches for treatment (including highly intrusive, radical surgeries), the introduction and refinement of chemotherapies based on killing rapidly dividing cells, the elucidation of cancer as a genome-based disease of cell-growth control, and recent advances in the development of specifically targeted anticancer agents.

In this context, I will highlight the development of the radical mastec-

tomy for breast cancer by surgeon William Halsted and the implications of studies of its effectiveness. Moving past surgical treatments that focused primarily on the identifiable tumor, Halsted developed more aggressive surgical approaches that removed considerable additional tissue based on the concept that removing all of the "roots" of a tumor would save more lives than more localized surgeries.

Halsted analyzed the outcomes of radical mastectomy in 1907. Mukherjee writes:

In the summer of 1907, Halsted presented more data to the American Surgical Association in Washington, D.C. He divided his patients into three groups based on whether the cancer had spread before surgery to lymph nodes in the axilla or the neck. When he put up his survival tables, the pattern became apparent. Of the sixty patients with no cancer-afflicted nodes in the axilla or the neck, the substantial number of forty-five had been cured of breast cancer at five years. Of the forty patients with such nodes, only three had survived.

The ultimate survival from breast cancer, in short, had little to do with how extensively a surgeon operated on the breast; it depended on how extensively the cancer had spread before surgery. As George Crile, one of the most fervent critics of radical surgery, later put it, "If the disease was so advanced that one had to get rid of the muscles in order to get rid of the tumor, then it had already spread through the system," making the whole operation moot.

But if Halsted came to the brink of this realization in 1907, he just as emphatically shied away from it. He relapsed to stale aphorisms. "But even without the proof which we offer, it is, I think, incumbent upon the surgeon to perform in many cases the supraclavicular operation," he advised in one paper. By now the

perpetually changing landscape of breast cancer was beginning to tire him out. Trials, tables, and charts had never been his forte; he was a surgeon, not a bookkeeper.

This passage reveals several points. First, the collection and analysis of the long-term outcomes demonstrated a clear but surprising pattern. These observations had implications both for treatment (more and more radical surgery was not likely to lead to improvements) and for the understanding of cancer (it can be a systemic rather than a localized disease). Second, rather than embracing the insights from the analysis, a leading expert applied his tools to other fields; the data had provided the "wrong" answer.

We must all be mindful of our own prejudices and our tendencies to see what we want to see in data or to dismiss data and analyses that come to conclusions inconsistent with our goals as flawed.

The importance of mechanism and rich data sources

Both books highlight the role of mechanistic understanding in driving progress.

Weather forecasting has improved steadily because the basic physical mechanisms of air and temperature flow and related phenomena are reasonably well understood so that models can be based on these mechanisms, even though considerable simplifications and approximations are necessary to produce manageable models (even with the most powerful supercomputers). In contrast, Silver argues that earthquake prediction remains much more problematic because of limited knowledge of mechanisms that promote earthquakes or fault stability. Further-

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more, earthquakes are (fortunately) relatively rare events (in contrast with weather changes) so that limited data are available to test and calibrate predictions.

Mukherjee tracks the mechanistic understanding of cancer throughout his book, ending with the modern discoveries of cancers as diseases of the genome with changes in uncontrolled growth-promoting

oncogenes and growth-controlling tumor suppressors. This mechanistic understanding has transformed some aspects of cancer treatment and prevention but, of course, much remains to be done.

Of course, these mechanistic insights come largely from studies of molecular biology and biochemistry. Progress in both basic science and its applications depends on pushing toward mechanistic rather than

merely empirical understanding and on dispassionate and ruthless analysis of data.

As one might expect based on this discussion, I strongly believe that the same principles apply to policy and advocacy (5). For example, the ASBMB has helped frame discussions of the impact of the sequester with data collection and analysis including surveys (6) and quantitative analysis of available data (7). These efforts should continue as we strive to help develop a more sustainable framework for our enterprise (8).

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Making scientific research a priority for Congress

By Chris Pickett

The Public Affairs Advisory Committee of the American Society for Biochemistry and Molecular Biology conducted a successful day of Capitol Hill office visits at the beginning of April. The 15 members of the PAAC along with 20 students and postdocs from around the country conducted 97 meetings with members of Congress and their staffs. We found overwhelming bipartisan support for increasing funding for the National Institutes of Health and the National Science Foundation. Despite the strong showing of support, however, American research is still not a high enough priority for many in Congress to improve conditions in the research community.

For instance, while on the Hill, we asked legislators to support a funding level of \$32 billion for the NIH and \$7.6 billion for the NSF for fiscal 2015. Concurrently, a "Dear Colleague" letter initiated by U.S. Reps. David McKinley, R-W.Va., and Susan Davis, D-Calif., was circulating in Congress, also urging appropriators to allocate \$32 billion for the NIH. Out of the 435 members of Congress, this letter garnered 190 members' signatures: 165 Democrats and 25 Republicans.

However, this bipartisan support was short-lived. Not too long after the McKinley-Davis letter was submitted, the U.S. House passed a budget resolution that would balance the federal budget in 10 years, in part by slashing nondefense discretionary



SHAILA KOTADIA

programs. Federal science-funding agencies, such as the NIH, are part of the NDD budget and certainly will be cut if this budget becomes law. Unfortunately, 22 of the 25 Republicans who signed the McKinley-Davis letter requesting an increase in the NIH budget also voted to cut the NIH budget via the House budget resolution. All House Democrats opposed the budget resolution.

This is just another example of Congress saying it supports the NIH but subsequently doing little to back it up. In March, President Obama signed into law the Gabriella Miller Kids First Research Act. That law authorizes \$12.6 million annually, through fiscal 2023, for pediatric research exclusively. This money is meant to be an addition to the yearly NIH appropriation. To pay for this increased spending, the law terminates federal funding for presidential nominating conventions, instead putting that money into the NIH Common Fund.

Sounds good, right? Unfortunately, the act is about as effective as using

bubble gum to repair a crumbling dam. The NIH lost \$1.55 billion as a result of sequestration in 2013, which is more than 12 times the amount of money Congress authorized in the Kids First Research Act. The ASBMB supports all forms of research, including pediatric research, but the truth is that this act does very little to help a research enterprise that has stagnated during a decade of flat budgets and sequestration.

The passage of yet another well-intentioned but fiscally irrelevant NIH funding bill and a House budget that doubles down on austerity demonstrates that much of what Congress does for scientific research is lip service. While many value the contributions of scientific research to the country, the needs of the research community are not a top priority for most members of Congress.

This is why the PAAC and ASBMB members continue to conduct Hill Day events, summer recess visits and other advocacy activities. Constantly showing Congress how important scientific research is to the health and economic well-being of America is the only way to raise the priority level of scientific research. Only then will members of Congress consider the well-being of the research enterprise when they vote.



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



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ACS honors nine ASBMB members

The American Chemical Society bestowed a number of its annual awards on ASBMB members. Most were honored at the organization's national meeting in Dallas in March. The Arthur C. Cope Scholar Award winners will be recognized during the organization's meeting in the fall in San Francisco.

ACS Award for Creative Invention	Marvin H. Caruthers , University of Colorado, Boulder	For his invention and development of phosphoramidite chemistry as used to synthesize DNA, RNA and many other macromolecules.
ACS Award in Analytical Chemistry	Jonathan V. Sweedler , University of Illinois, Urbana-Champaign	For his research that emphasizes analytical neurochemistry, involves the development of small-volume methods to probe individual neurons, and uses these techniques to discover novel neurochemical pathways.
Alfred Bader Award in Bioinorganic or Bioorganic Chemistry	Laura L. Kiessling , University of Wisconsin-Madison	For her deft and imaginative use of chemical tools to probe and elucidate diverse biological processes.
Arthur C. Cope Award	Stuart L. Schreiber , Howard Hughes Medical Institute, Harvard University, Broad Institute of Harvard and Massachusetts Institute of Technology	For small molecule-based discoveries concerning signal transduction by calcineurin and mTOR and gene regulation by histone deacetylases, and for advancing the field of chemical biology.
Arthur C. Cope Scholar Award	Richard N. Armstrong , Vanderbilt University	For creative contributions in the use of physical organic chemistry and related disciplines to understand the mechanisms of enzyme-catalyzed detoxification reactions.
Arthur C. Cope Scholar Award	Hung-wen (Ben) Liu , University of Texas	For being a world leader in studying nature's strategies for making secondary metabolites, an expert on natural product enzymology, and a pioneer in glycodiversification with unusual sugars.
Priestley Medal	Stephen J. Lippard , Massachusetts Institute of Technology	For mentoring legions of scientists in the course of furthering the basic science of inorganic chemistry and paving the way for improvements in human health.

In addition, the ACS Division of Biological Chemistry recognized two other ASBMB members, who will present at the fall meeting:

The Repligen Award in Chemistry of Biological Processes	John Lipscomb , University of Minnesota	For outstanding contributions to the understanding of biological processes with particular emphasis on structure, function and mechanism.
Gordon Hammes ACS Biochemistry Lectureship	Thomas L. Poulos , University of California, Irvine	For outstanding contributions in scientific research at the interface of chemistry and biology, particularly in the realm of biochemistry, biological chemistry and molecular biology.

Thematic minireview series highlights phosphorylation in prokaryotes

By Jenna Hendershot

A new thematic minireview series entitled "Prokaryotic Protein Phosphorylation" appeared in a recent issue of the **Journal of Biological Chemistry**. Signal transduction mediated by reversible protein phosphorylation has been studied intensely for more than 50 years in eukaryotes. Sadly, understanding the role of prokaryotic protein kinases in phosphatase signaling has come much slower. Elucidation of the pathways in prokaryotes may be of considerable clinical and industrial importance. This minireview series provides an overview of different prokaryotic protein kinases and discusses the wide conservation of protein phosphorylation as a mode of cellular regulation.

In the first minireview, Yossef Av-Gay and colleagues at the University of British Columbia discuss prokaryotic protein Tyr kinases. This review focuses on the bacterial tyrosine kinases, or BY-kinases, and the atypical or "odd" tyrosine kinases that show no homology to eukaryotic or BY-kinases. The BY-kinases are involved in many diverse functions in bacteria, including biofilm formation, virulence, spore formation, DNA replication and antibiotic resistance. The *M. tuberculosis* Tyr kinase PtkA gets special attention in this review, as it is a representative example of an "odd" tyrosine kinase. Phosphorylation of a key virulence factor in *M. tuberculosis* by PtkA highlights the involvement of tyrosine kinases in microbial pathogenesis and represents an unexplored area for drug discovery.

Virginie Molle and Marc Canova at the Universités de Montpellier explore in the second minireview

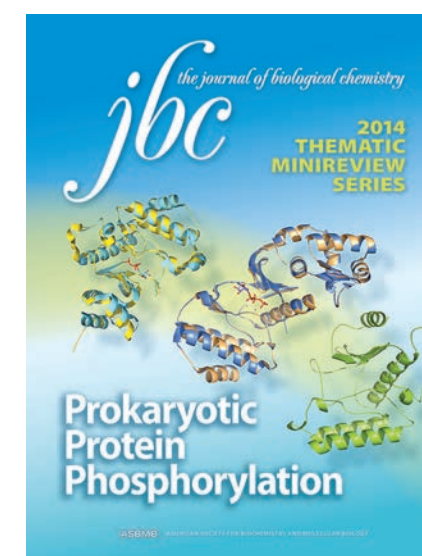
the eukaryotic-like signaling systems in bacterial pathogens. Some of the well-studied bacterial protein kinases are essential virulence factors and modify global host responses during infection. The prokaryotic protein kinases in human pathogens — such as *Streptococcus*, *Mycobacteria*, *Yersinia* and *Listeria* — are ideal candidates for drug development, because the bacterial kinases are proving to be molecular switches that play key roles in host-pathogen interactions.

In the third minireview, Peter Kennelly at Virginia Polytechnic Institute and State University focuses on phosphorylation of proteins in the domain Archaea. While prokaryotic in morphology, the Archaea share closer evolutionary ties to eukaryotic cells. The protein kinases in the Archaea are structurally related and resemble both eukaryotic Ser/Thr and Tyr kinases. Much less is known about phosphorylation in the Archaea, and much of what we currently know is from *S. solfataricus*. Kennelly nicely sum-

maries the protein phosphorylation networks in members of Archaea, and he reveals some of the intriguing questions that remain in the field.

Finally, Nicole LaRonde at the University of Maryland, College Park, reviews microbial RIO, or right-open reading-frame, kinases. The RIO kinases may be the most ancient, as they have been around since before the divergence of Archaea and eubacteria. While it is well established that RIO kinases are essential for the synthesis of new ribosomes in eukaryotes, the role in prokaryotes is unknown. By describing the structures of RIO kinases of Archaea, the search for RIO kinase substrates, the known functions of the RIO kinases and the development of inhibitors using microbial RIO kinases, LaRonde provides support for the probability that archaeal RIO kinases perform similar biological roles to those observed in eukaryotes.

The four minireviews in this series help to broaden our thinking about protein phosphorylation. In an editorial commentary, John Kyriakis, the JBC associate editor overseeing the series, concludes that we need to consider novel, noneukaryotic cell mechanisms when learning about phosphorylation in prokaryotes. While less is known about prokaryotic protein kinases, this is a new and exciting field.



Jenna Hendershot (hendeje@umich.edu) earned a B.S. in cellular and molecular biology from Grand Valley State University and is completing her Ph.D. in biological chemistry at the University of Michigan.

The dual roles of metabolic hydrogen peroxide

By Donna Kridelbaugh

In his recent **Journal of Biological Chemistry** minireview, Helmut Sies of the Heinrich Heine University Düsseldorf in Germany provides a comprehensive review on the dual roles of metabolic hydrogen peroxide production in animal physiology. As the originator of the concept “oxidative stress” and a pioneer in this field, Sies provides an expert account with a focus on the methods used to measure intracellular concentrations of hydrogen peroxide (he was the first to demonstrate H_2O_2 as a normal metabolite in mammalian tissue); the primary biological modes by which it is produced or neutralized; and its significance in both redox signaling and oxidative stress pathways.

The toxic effects of hydrogen peroxide – a reactive oxygen species produced during cellular processes, such as aerobic respiration in mitochondria, or as a defense mechanism

within phagocytes – long have been associated with a plethora of biological processes and disorders including aging, cancer, diabetes and inflammation. Research now indicates that hydrogen peroxide also serves as an important redox-signaling compound to indicate oxidative stress (i.e., an imbalance in the ratio of oxidants to antioxidants), thus posing as a transcription-independent second messenger in a number of pathways including insulin signaling and ROS-defense mechanisms.

The redox-signaling function likely results from the direct oxidation of reactive protein thiols, causing post-translational modifications that affect a large number of proteins within the redox proteome. One major unanswered question that remains is the concentration at which hydrogen peroxide is a) a useful redox signal to keep cells in a ready state to respond

to oxidative stress or b) a toxic substance that causes detrimental molecular damage. Sies advocates for the advancement of noninvasive cell biology methods toward quantitative, real-time analyses to address this issue of “redox optimization” in future research. However, he concludes, “The threshold from signaling to excessive toxic levels will be challenging to further identify. The precise transition points for these cellular responses may vary due to cell type and metabolic conditions.”



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

Glucose homeostasis

From the gut to the brain via the vagus nerve

By Joseph P. Tiano

The world is getting fatter and more diabetic. Close to 80 percent of those with type 2 diabetes are overweight or obese — leading to an increase in complications such as kidney and eye disease, peripheral artery disease and nerve damage. A recent minireview in the **Journal of Biological Chemistry** highlights the crucial role of the gastrointestinal tract in whole-body glucose homeostasis and suggests that it be given more attention.

The reemergence of the gastrointestinal tract as a primary regulator of

insulin secretion and glucose homeostasis after a meal has led to a recent increase in the repertoire of available drugs for treating type 2 diabetes. However, only two drugs, exenatide and liraglutide, have received approval from the Food and Drug Administration for the treatment of type 2 diabetes, and both are based on the same gastrointestinal-tract-derived incretin.

GI-tract-derived incretins are hormones secreted from the stomach or small intestine after a meal. They

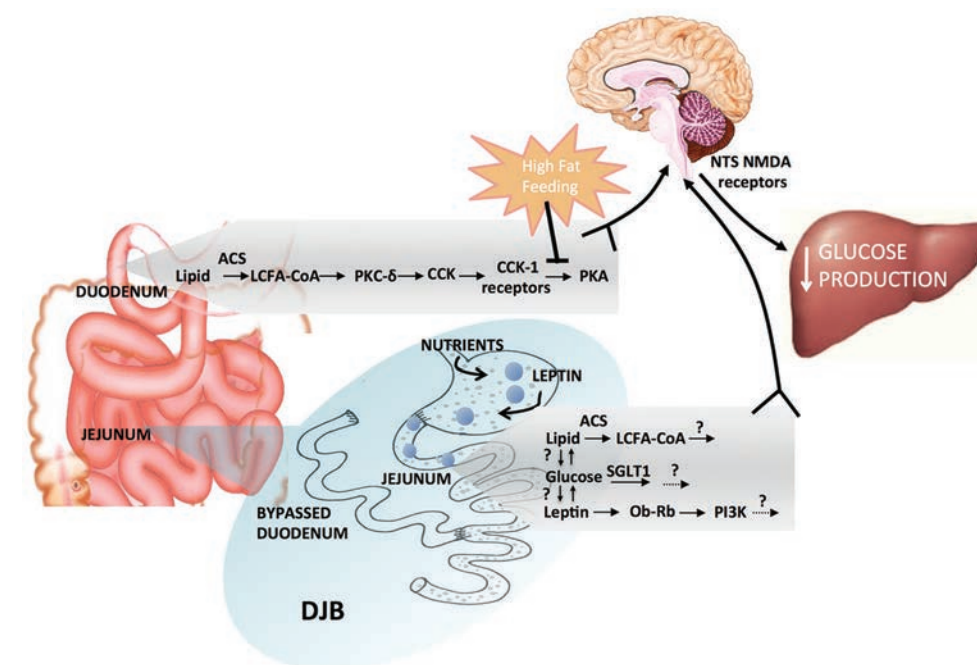
decrease blood glucose by increasing glucose's effect on pancreatic β -cells to increase insulin release and by suppressing liver glucose production. They also act in the brain to adjust food intake and energy expenditure to maintain whole-body energy homeostasis. There are at least eight gut-derived hormones, and a better understanding of how they work should lead to more effective diabetes therapies.

In their recent minireview, Tony Lam and colleagues at the University

of Toronto Faculty of Medicine, Toronto General Research Institute, have proposed a working hypothesis that nutrient-induced, GI-tract-derived hormones act locally on their surrounding intestinal cells and signal via nerves to the brain to regulate glucose homeostasis.

Cholecystokinin, or CCK, is a gut-derived incretin secreted from the upper intestine primarily in response to fatty acids that induces satiety and suppresses glucose production in the liver. Studies have indicated that CCK mediates its effects via local vagal signaling rather than classical endocrine signaling. The ability of CCK to suppress liver glucose production is dependent on intracellular conversion of fatty acids to triglycerides within intestinal cells and on protein kinase C- δ signaling, which happens primarily in the upper intestine.

Glucagon-like peptide-1, or GLP-1, is another gut-derived incretin, and it is secreted from the middle intestine in response to both fatty acids and glucose and acts on pancreatic β - and α -cells to increase insulin release and inhibit glucagon release, respectively. These effects initially were thought to be accomplished solely by GLP-1 binding its receptor on the outer membrane of β - and α -cells. However, GLP-1 is degraded in the blood within minutes, resulting in less than 10 percent reaching the circulation around β - and α -cells — suggesting that GLP-1 also may act in the intestine to mediate its effects via vagal signaling to the brain. Findings in rodents, in which inhibiting nerve



Gut nutrient-sensing mechanisms and subsequent peptide hormone release in normal and duodenal-jejunal bypass surgery settings. Nutrient influx in both the duodenum and jejunum triggers hormonal release and downstream signaling to lower glucose production through a neuronal network. In the duodenum, these mechanisms are disrupted upon high fat feeding. Duodenal-jejunal bypass surgery results in the influx of nutrients and hormones, such as leptin, directly into the jejunum to suppress glucose production through downstream mechanisms.


signals from the brain to the intestine blocks GLP-1-induced insulin release, lend support to this new notion of GLP-1 signaling via a gut-brain-pancreas axis.

Bariatric surgery, a now-common treatment for the morbidly obese, bypasses the upper small intestine and has serendipitously led to the discovery of novel and exciting mechanisms of glucose regulation by the gut, known as gut-nutrient sensing. Type 2 diabetics who undergo bariatric surgery very often are cured of hyperglycemia prior to significant weight loss, suggesting that gut-nutrient sensing is a crucial aspect of glucose homeostasis.

Research from Lam and colleagues shows, in rodents, that administration of glucose and lipids directly into the middle small intestine, similar to the way nutrients are sensed in the gut after bariatric surgery, suppresses liver glucose production by a gut-brain-liver axis that is independent

of insulin and dependent on leptin. Leptin administered directly into the middle small intestine suppresses liver glucose production in wild-type mice but not in mice without the leptin receptor or in wild-type mice to which leptin is co-administered with a phosphatidylinositol-4,5-bisphosphate 3-kinase, or PI3K, inhibitor.

Furthermore, blockade of vagal signaling from the middle small intestine to the brain eliminates the ability of leptin to suppress liver glucose production. These results demonstrate that middle intestine nutrient sensing is dependent on gastric leptin acting through an intestinal PI3K-brain-liver axis.



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

Finding what makes biofilms hard to defeat in lung infections

By Rajendrani Mukhopadhyay

Cystic fibrosis patients often combat lung infections. At the late stage of the infections, a bacterium called *Pseudomonas aeruginosa* becomes the persistent menace, forming a structure known as a biofilm. Bacterial biofilms are stubborn, tough structures that resist antibiotics and other means of removal. These structures also afflict AIDS and burn patients. In a paper recently published in **Molecular & Cellular Proteomics**, researchers have examined the entire protein content of *P. aeruginosa* biofilms. Their aim is to identify the molecular pathways that are critical to biofilm formation and maintenance, processes that are not well understood.

Cezar Khursigara at the University of Guelph in Canada, who spearheaded the work, says that he and one of his postdoctoral fellows, Amber Park, “wanted to examine the pro-

teome dynamics of *P. aeruginosa* cells as they transitioned from a planktonic, free-living state to a biofilm lifestyle. This transition is thought to be similar to the one *P. aeruginosa* makes in the lungs of patients with (cystic fibrosis), when pulmonary infections eventually move from an acute to chronic phase.”

The investigators compared the different protein expressions over time in *P. aeruginosa* cells as they developed through the two different lifestyles. They discovered that there were significant shifts in protein expression as the bacteria switched from the planktonic state to the biofilm state. In particular, they saw differences in expression of proteins involved in iron acquisition and a downregulation of key antimicrobial targets.

“Most surprisingly, however, was the dramatic increase in cellular adhesins that were identified only in

the later time points and were completely absent in the earlier planktonic samples,” says Khursigara. “We feel these may play a role in shaping biofilm architecture and, as a result, may contribute to the resilience of these communities.”

The investigators now are working on *P. aeruginosa* isolated from patients and developing experimental conditions that better mimic those in the lung. They are also plunging deeper into the pathways they have identified to see if they can pinpoint particular proteins that may be suitable as drug targets. Khursigara notes, “With the number of proteins identified, we will be busy for a while.”



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Breast cancer gene involved in skeletal muscle energy metabolism

By Rajendrani Mukhopadhyay

The BRCA1 gene, which is officially known as the breast cancer 1, early onset, gene, is well-known to be expressed in breast tissue. People who have particular mutations in this tumor-suppressor gene are at increased risk of developing certain types of breast cancer. But in work just published in the **Journal of Lipid Research**, investigators demonstrated the BRCA1 gene also is expressed in skeletal muscle. Espen Spangenburg at the University of Maryland, the senior author on the paper, says that the work indicates that BRCA1’s influence “extends beyond just breast cells.”

Using cells taken from mice and humans, Spangenburg’s team demonstrated that there were multiple isoforms of BRCA1 in skeletal muscle. They then showed that when mice underwent bouts of intense exercise, there were more interactions

between BRCA1 and the phosphorylated form of acetyl CoA carboxylase, a critical regulator of lipid metabolism.

When the investigators reduced the BRCA1 content in human skeletal muscle cells in culture, the mitochondria consumed less oxygen. There was also more lipid stored inside cells, and the amount of insulin signaling dropped.

Taken together, the data suggest that BRCA1 is important in regulating energy metabolism in skeletal muscle. Furthermore, the work highlights that this gene plays a role in tissues beyond those involved in reproduction. Spangenburg says, “This is particularly important when



one considers the number of known genetic mutations that develop in the BRCA1 gene. We need to consider how these mutations may affect skeletal muscle function.”



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

Thematic Series

Lysophospholipids AND THEIR RECEPTORS

Journal of LIPID RESEARCH

An introduction to the JLR thematic series on lysophospholipids
Jerold Chun

Diversity and function of membrane glycerophospholipids generated by the remodeling pathway in mammalian cells
Daisuke Hishikawa, Tomomi Hashidate, Takao Shimizu and Hideo Shindou

Autotaxin: structure-function and signaling
Anastassis Perrakis and Wouter H. Moolenaar

LPA receptor signaling: pharmacology, physiology and pathophysiology
Yun C. Yung, Nicole C. Stoddard and Jerold Chun

An update on the biology of sphingosine 1-phosphate receptors
Victoria A. Blaho and Timothy Hla

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For more information, please visit www.asbmb.org/awards/2015.

2014 ASBMB ANNUAL MEETING

Travel Award Winners

Undergraduate Student Competitive Travel Award Recipients

- Jennifer Arbella, *Juniata College*
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- Anthony Brandt, *University of Wisconsin-La Crosse*
- David Calianese, *Providence College*
- Christine Dang, *University of Delaware*
- Guillermo Flores, *Hope College*
- Bobby Geiger, *Otterbein University*
- Pablo Gonzalez, *University of Puerto Rico-Rio Piedras*
- Jeffrey Hall, *Texas State University*
- Kristin Harrington, *University of Wisconsin-Madison*
- Christy Heidema, *Dordt College*
- Nnejiuwa Ibe, *California State University, Long Beach*
- Linda Jimenez, *Colorado College*
- Kyle Kaster, *University of Wisconsin-La Crosse*
- Mohammed Mosaheb, *Tufts University*
- Dustin Mueller, *North Dakota State University*
- Miles Paszek, *Gettysburg College*
- Katherine Seehusen, *Winona State University*
- Sophia Stone, *Mary Baldwin College*
- Chanel Venkataraman, *Cornell University*

Undergraduate Faculty Travel Award Recipients

- Victoria Del Gaizo Moore, *Elon University*
- Dipak Banerjee, *University of Puerto Rico*

- Dale Cameron, *Ursinus College*
- L. Michael Carastro, *University of Tampa*
- Sarah Connolly, *DePaul University*
- Maria Craig, *Mary Baldwin College*
- Artem Domashevskiy, *City University of New York*
- James Dyer, *Montclair State University*
- Austin Gehret, *National Technical Institute for the Deaf*
- Dan Grilley, *University of Wisconsin-La Crosse*
- David Hall, *Lawrence University*
- Chanaka Mendis, *University of Wisconsin-Platteville*
- Patrick Murphy, *Seattle University*
- Odutayo Odunuga, *Stephen F. Austin State University*
- Yinsheng Wan, *Providence College*
- Chin-Chuan Wei, *Southern Illinois University-Edwardsville*

NSF Student Research Travel Award Recipients

- T. Reid Alderson, *University of Wisconsin-Madison*
- Beatriz Camacho, *San Jose State University*
- Rachel Knox, *Seattle University*
- Nicole Ladd, *Hope College*
- MarkVic Naniong, *Northeastern University*
- Kevin Qian, *Yale University*
- Cassandra Rickertsen, *St. Olaf College*
- Aislinn Rowan, *Lehigh University*
- Clara Schreimer, *Hope College*
- Matthew Urban, *University of Delaware*

- Jessica Waninger-Saroni, *St. Mary's University*

NSF Undergraduate Faculty Travel Award Recipients

- Andrew Bonham, *Metropolitan State University of Denver*
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- Kenneth Mills, *Holy Cross*
- Niroshika Keppetipola, *California State University, Fullerton*

UAN Travel Award Recipients

- Nana Agyepong, *Otterbein University*
- Jasmine Allen, *Virginia Commonwealth University*
- Ryan Augustin, *St. Thomas University*
- David Barnard, *Rochester Institute of Technology*
- Nick Berthelsen, *Minnesota State University*
- Amanda Biederman, *Salisbury University*
- Ernest Bile, *Virginia Union University*
- Amanda Bolles, *Kalamazoo College*
- Christian Brutofsky, *Montclair State University*
- Wesley Cai, *University of Arizona*
- Demetrius Carey, *University of Tampa*
- Kevin Carlson, *University of Arizona*
- Yelena Chekayev, *Medgar Evers College*
- Allison Chirigos, *Washington & Lee University*
- Derek Deshaies, *Juniata College*
- Selma Elsarrag, *Mary Baldwin College*

- Shea Feeny, *San Francisco State University*
- Charlotte Flatebo, *St. John's University*
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- Jin Lee, *Juniata College*
- Anthony Lentscher, *Tennessee Tech University*
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- Stacy Thomas, *Providence College*
- Alice Trye, *Marymount Manhattan College*
- Tsz Ming Jeremy Tsang, *Brigham Young University-Hawaii*
- Rachael Valdez, *San Jose State University*
- James Waldschmidt, *University of Wisconsin-Platteville*
- Jonathan Yamaguchi, *University of Arizona*

2014 Chi Omega Lambda Inductees

- Christopher Adams, *St. Mary's College of Maryland*
- Nana Agyepong, *Otterbein University*
- John Bettinger, *Rochester Institute of Technology*
- Kimbria Blake, *Rochester Institute of Technology*
- Adele Bubnys, *Wesleyan University*
- Wesley Cai, *University of Arizona*
- Tessa DiDonato, *Rochester Institute of Technology*
- Shea Feeny, *San Francisco State University*

- David Freeman, *Missouri Western State University*
- Catherine Gaissert, *Marymount Manhattan College*
- Bobby Geiger, *Otterbein University*
- Ryan Graff, *Wesleyan University*
- Jakob Hebert, *Siena College*
- Samuel Knecht, *St. Mary's College of Maryland*
- Allison Liberato, *William Paterson University*
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- Sai Phyo, *St. John's University*
- Ekaterina Protsenko, *Providence College*
- Alyssa Savarino, *Wesleyan University*
- Naomi Schwartz, *Yeshiva University*
- Nickie Seto, *University of Arizona*
- Commodore St. Germain, *San Francisco State University*
- Sophia Stone, *Mary Baldwin College*
- Ryan Tantone, *Siena College*
- Stacy Thomas, *Providence College*
- Alice Trye, *Marymount Manhattan College*
- Lisle Winston, *Wesleyan University*
- Kaleb Wolfe, *Hendrix College*
- Glenna Wong, *St. Mary's College of Maryland*
- Chelsea Woods, *Hendrix College*

Propagating possibilities

RESEARCHER TINKERS WITH TREE GENETICS, HOPING TO CULTIVATE VALUABLE COMMODITIES

By Rajendrani Mukhopadhyay



Norman Lewis at Washington State University began his scientific career as a natural product chemist. But his interests soon turned toward the biochemistry of plants.

These days, Lewis is focused on generating transgenic trees that are designed to make high-value products needed in the flavor and fragrance industries. The American Society for Biochemistry and Molecular Biology's science writer, Rajendrani Mukhopadhyay, spoke with Lewis about his work. The interview has been edited for length and clarity.

How did you become interested in creating transgenic trees?

Plants produce a wonderful array of medicinals and aromatics. I've been very interested in many of the plant biochemical pathways for medicinals as well as flavors and fragrances. We've looked at a number of biochemical pathways of compounds that are used widely in cancer treatment. All of the molecules that we look at are derived from an amino acid that humans don't make, which is phenylalanine. Phenylalanine can be converted into other molecules – for example, phenylethanol, which is the rose oil odor – as well as into a structural material called lignin, which is the reason plants can stand upright.

We wanted to be able to use fast-growing plants, like poplar or maybe even red alder, for producing

molecules that you would get from someplace else, like rose oil or the oil of cloves, which you get from places like Zanzibar (in east Africa) ... The molecule phenylethanol is widely used in the cosmetic and food industry in all sorts of things. We view this as a way to begin to produce high-value chemicals.

How do you choose which compounds to go after?

We look at molecules where we think we can manipulate the pathways in relatively small steps. For example, much of what we know about taxol, the anticancer drug, is that it's a very lengthy pathway. It's still, to this day, not completely understood. That would be a kind of molecule you would like to be able to produce, but you've still got a lot to learn about the

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genetic information. The phenylethanol one was chosen simply because it has a relatively short pathway from phenylalanine. It has only a couple of steps. It's our intent now to start thinking about how we can use synthetic biology to perhaps circumvent steps, perhaps enable some enzymes to become catalytically more active.

Plants differ from most other life forms in that many of their specialized cell types accumulate molecules. For example, in the Far East, where cedar is used extensively for building temples, the cedars pump (and store) their chemicals, which help protect against fungi and bacteria. Those structures stand up for thousands of years. Plants evolved a way of storing things. So what we're trying to look at are ways to not just put a pathway into poplar but also begin to ramp the levels up much higher. We began a company we call Eelasid Inc. We're moving forward with the processes of commercializing our technologies.

What concerns do you have to address with genetically engineered plants?

There are many aspects to that question. One is that when we do our field trials we have to go through a process of working with (the U.S. Department of Agriculture's Animal and Plant Health Inspection Service). We indicate where we are going to set these things up. They give us a set of conditions that we've got to very closely follow.

We are not allowed to – and we don't plan to and we don't want to – let (the trees) get to the point where they can flower. We're looking at doing a thing called coppicing. Basically, coppicing means you harvest the stem materials and they pop back up again. We don't have to replant them. We can do that once or twice a year for about four or five years before it's

time to renew the plant material. That way, (the trees) never pollinate, so they can't mix with other species.

I would say that these (transgenic trees) are still new technologies. They are still certainly worthy of discussion. Yet it's not really different from genetically modified corn and things like that. If one is going to be able to sustainably feed, clothe and shelter our burgeoning population, it really looks as if the only solution, at least that I can see, is being able to get these increases in productivity, even through genetic-engineering means. I think now folks at least have gotten the acceptance that (GMOs) are now in the marketplace.

You've got to do all the testing and make sure that everything is playing out the way you believe it is. We fortunately are able to bring the fantastic -omics (tools), from transcriptomics to proteomics and metabolomics, to see what we're doing with these plants. I will have to say the safeguards that are placed in here are unparalleled with anything that ever has been seen before. I don't think anybody has demonstrated (any) truly negative aspect of genetically modified organisms.

How do -omics technologies help you understand that you have the safeguards in place?

You can look at what effect that new pathway has on all the gene-expression patterns in the plant. By using transcriptomics, for example, you can see if the plant is functioning the same way or in a different way. If it's functioning in a different way, what are those differences? Do these differences really matter? Similarly, when you do it from the proteomics side or the metabolomics side, you can see what influences this pathway has in there. Currently, we use a method called MALDI (matrix-assisted laser desorption ionization) metabolite imaging,

where we look at tissues and find out precisely where these molecules are accumulating in the cell types.

There's never been a more wonderful time than now to be able to not just incorporate these genes but really look at the effects it has on the entire organism.

Why use poplars?

We're looking at something that is fast growing so we can have a system where we can produce large amounts of biomass containing these chemicals. They are not as fast growing as bamboo or eucalyptus. But in much of North America, these and other plants, like red alder, which we also have a program on, are some of the most rapidly growing organisms. They are also very adaptable to marginal land – not very productive land that now can have alternate uses.

How long have these projects been going on?

We've been working on the (rose oil) pathway for several years now. We put it into *E. coli* to begin with to make sure that we had the right genes. Then we put it into poplar ... The other ones we are doing go back much longer than that, like the oil-of-clove chemicals. The oil of clove goes back to about 1999. (The trees) are in field trials as we speak. The oil of cloves is something that is still in the process of being patented.

What are the challenges of making the leap from the bench to field work?

There are a number of challenges. One is nobody wants to pay for the field work. There aren't that many opportunities for funding from the federal agency side other than doing (federal small-business innovation research, or SBIR) programs.

The USDA APHIS has very stringent requirements to ensure that



IMAGE PROVIDED BY NORMAN LEWIS.

Poplars are being engineered to produce valuable products for the flavor and fragrance industry.

things are done properly. They come and do regular inspections. There is a lot of oversight of these plants. You might think that you might be able to do all these things in a greenhouse or a growth chamber. Of course, you can certainly do this to get the first indications. But it's not until a plant is actually outside, growing out in the environment on a particular soil or in a climatic condition, that you really know how it's going to function.

What do you deem a successful transgenic plant?

If you get the effect you want, it's successful. The scientific achievement is the first place. But why are we building this company? In order to get something that might be used commercially, somebody's got to get the (intellectual property) protection and prevent anyone else from willy-nilly running off with it – getting things moving in a way that is responsible and transparent. There are very few examples of (transgenic) woody plants out there, unlike the annual crops.

But ultimately this goes beyond phenylethanol or taxol or any medicinal or any flavor and fragrance. We are developing technologies that are going to help the growing needs of the world's population. I think that's where the true success lies. One would like to hope to be a small part of that.



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Grant-writing advice

10 things to know when applying for a Ruth L. Kirschstein training grant from the NIH

By Andrew D. Hollenbach

Thousands of trainees apply annually for the National Institutes of Health's Ruth L. Kirschstein National Research Service Award training grants (F30, F31, F31 Diversity and F32). However, many of these applicants, and their mentors, have little experience with writing such training grants.

Here are 10 things to know when constructing an NRSA training grant application:

1. First impressions are important!

Many times reviewers are reading your grant after a long, tiring day. Be kind to your reader. Provide visual rest by putting spaces between paragraphs. Present your figures in a logical and orderly manner. Use a spelling and grammar checker! Typos and poor grammar are unacceptable. Failure to pay attention to these details will give a negative first impression that ultimately will reflect poorly on you.

2. Assume the reviewers know nothing about your field of research.

Reviewers may be familiar with the general topic but will not implicitly know your field of research. Therefore, be detailed and avoid jargon when writing the research plan! Be explicit when describing your data; describe exactly what you want the reviewer to see. What is obvious to you may not be obvious to others.

3. Evaluation of the "Research Plan" focuses on training potential.

A poorly laid out research plan indicates poor mentoring by the sponsor. However, the focus on training potential allows more tolerance for exploratory techniques (e.g., next-generation sequencing). These large-scale techniques provide great training opportunities. However, these fishing expeditions must be justified. You must provide feasibility for the study, and you must illustrate a solid understanding of the larger implications of the results.

4. Your educational history is just that ... history!

Be forthcoming about a less-than-perfect past! If you had poor grades, if you have a minimal publication record or if there is a gap in your training history, provide genuine reasons for this history. If you have overcome these issues, state that and have your references address why your past is not a barrier to your future training.

5. Know your future career goals and describe why your training environment will help you achieve them.

It is essential to communicate a mature and concrete view of your career goals. You must describe clearly how the training (including environ-

ment, research, sponsor, department and so forth) is perfect to help you achieve these goals.

6. Make the training plan personalized. Remember: Training is not just technical!

One of the biggest mistakes a sponsor makes is to provide a generic training plan focusing solely on technical aspects. Overall training requires experience in communication, presentation, teaching, networking, and — for postdocs — lab management and transitioning to independence. Remember that each trainee is different so each training plan must be personalized for each applicant.

7. Inclusion of a co-sponsor must be integrated fully into the training plan.

A co-sponsor can make up for perceived deficiencies of the sponsor. Therefore, the co-sponsor must be integrated fully into the training plan. The applicant needs to describe the selection of the co-sponsor and how he or she will contribute to achieving the applicant's career goals. How the co-sponsor will be involved must be described fully by the sponsor in the training plan.

8. Assume the reviewer of the resubmission has never seen your grant before.

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On hindsight and gratitude

By Philip Yeagle

Ixperienced an extraordinary privilege in the mid- to late 1970s when I became a postdoc in a vibrant, exciting, even brilliant scientific community that recently had been built at the University of Virginia. I became so immersed in and stimulated by that community that I am embarrassed to say I did not fully realize how special it was until leaving it to pursue my independent research career.

The cluster of immensely talented faculty members, most of whom were in the biochemistry department, was dedicated to understanding the structure and function of biological membranes. The prime mover behind the construction of this community was Tom Thompson, who brought with him a number of scientists from Johns Hopkins University — both established leaders in their fields as well as a number from the ranks of the most promising young scientists. This group was complemented by faculty members in other departments at UVa (including microbiology, pharmacology, physiology and chemistry) who also studied biological membranes. (One became a Nobel laureate.)

To appreciate the importance of this community fully, it helps to know that the field of membrane studies, while having some significant antecedents, nevertheless was very



The author in 1976.

young at that time: Acquisition of hard proof of the lipid bilayer as a fundamental component of membrane architecture was within the scientific memory of all these scientists. As I came to appreciate more fully later, the UVa community was one of two major epicenters of progress in the understanding of membranes, with the other being in Utrecht, Netherlands.

Therefore, it was the place in the U.S. where young scientists could learn to stand on the shoulders of their mentors and prepare to take the field of membrane studies into a new and much more expansive era. This community of scientists was notable for the so-called "smart" experiment; deeply thought-out experimental design gave substance to a clever

idea, resulting in the experiment that provided important new information, no matter the result.

While these scientists exemplified the best in the practice of science, they were not particularly aware of the significance of what they had created on the world stage. They were human beings with balanced lives that generally included families and close personal relationships with their students and postdocs. Thus, they not only crafted a powerful center of scientific excellence but at the same time built supportive terrain in which young scientists could take root and grow.

Therefore, this is an overdue letter of deepest appreciation to a remarkable community of scientists from one individual and on behalf of what became a new generation of scholars originating in Virginia and spreading out over all the scientific world.



Philip Yeagle (pyeagle@andromeda.rutgers.edu) has been with Rutgers University–Newark since 2007. From 2011 to 2013, he was interim chancellor there and, before that, dean of the Faculty of Arts and Sciences. He spent a decade as a chairman of the University of Connecticut's molecular and cell biology department and prior to that was a professor at the University of Buffalo School of Medicine and Biomedical Sciences. He has served as executive editor of the journal *Biochimica et Biophysica Acta – Biomembranes* and as an editorial board member of the *Journal of Biological Chemistry*.

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Because service on NRSA study sections is ad hoc, the person who reviewed your grant the first time may not be on the committee overseeing the resubmission. It is also highly likely that the grant will be assigned to a different reviewer. Even if it is assigned to the same person, four to six months will have elapsed, during which time he or she will have reviewed and discussed dozens of other grants. The reviewer most likely will not remember having read your application the first time.

9. In the resubmission, address every single criticism!

How well you address previous criticisms contributes to the score of your

resubmitted application. Regardless of whether you agree or disagree, it is essential that you address every single criticism! If you feel a criticism is incorrect, state in the introduction that you respectfully disagree and provide a clear and logical explanation as to why. Reviewers are provided with the previous summary statement, so they know exactly what criticisms were raised the first time around.

10. Natural human bias affects reviewers' perceptions of strengths and weaknesses.

Although it may not seem like it, reviewers are human beings. As such, natural human bias will contribute to the review of your grant. Each reviewer will have a different opinion

on how issues such as a big-name investigator, big-name institute, quality vs. quantity of training history, and quantity vs. quality of publication history strengthen or weaken an application.

Given the natural biases and influences of human nature in the review process, there is no perfect formula for writing a fundable grant. However, these 10 simple points should make you aware of what reviewers are looking for in a top-quality application.



Andrew D. Hollenbach (aholle@lsuhsc.edu) has served on multiple NRSA study sections and has written the book "A Practical Guide to Writing a Ruth L. Kirschstein NRSA Grant," which is available through the Elsevier Store and most online book-sellers. He is also available for informational and educational seminars on this topic.

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The skills you need for a career in science policy

By Chris Pickett

Almost exactly two years ago, I sat down to write an article for ASBMB Today detailing the problems I, a classically trained bench scientist, had with constructing a curriculum vita fit for a future career in science policy. I wasn't blazing the trail from the bench to policy, so why was it so difficult to find and walk the same path as others before me? Through some hard work and a giant mound of perseverance, I found my way. Now, after a stint as a science policy fellow, I am a policy analyst for the American Society for Biochemistry and Molecular Biology.

What I didn't realize two years ago is that there is no single path from the bench to policy. Everyone starts on the path at a different place, so everyone is going to have a different experience. But what I've learned since then is that the many paths have commonalities. Here are some of the things scientists can do to blaze their own trails from the bench to careers in science policy:

Get involved

How do you even know that you like policy work? Luckily, policy is one of those things you can try without investing too much time or money. I encourage you to check out the ASBMB's and other organizations' meetings programs. Or you can pick up the phone and call your representative's or senator's office in Washington to give your two cents on specific pieces of legislation. Or you can apply to participate in a Capitol Hill day, which provides participants



with the chance to travel to Washington to meet with federal representatives. These meetings make up only a small fraction of an actual policy job, but they can serve as a crucial test to determine if science policy might be right for you.

My first experience with policy work was as a participant in a program that set up meetings between scientists and their representatives and senators during the summer congressional recess. I discussed research funding and scientific workforce issues during a pair of 30-minute meetings with the staff members of my district's representative and one of my state's senators. I was encouraged by the staff members' interest in these topics, and more importantly, I came away from those meetings excited and eager to get more involved in policy activities.

Ask questions

As a scientist, you have highly tuned critical-thinking and investigatory skills, and these should be used in your job search. First, write out your list of questions about science policy. Make the questions as basic (What exactly is science policy?) or as specific (What is your organization's position on immigration reform?) as needed. Next, seek out people who have some experience in policy work, whether these are people you know or just know of. Then, being respectful of their time and position, ask all of your questions about science policy. If you are appropriately passionate and professional, you also can build a relationship with this person to widen your network while learning valuable information about your new career

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Give credit where it is due

Thoughts on the ‘competition’ between senior and young investigators

By *Eleftherios P. Diamandis*

Nowadays, science rarely is performed by a single person or a few individuals. Modern science frequently is done by multiple collaborating groups or consortia. This sometimes creates confusion as to who did what and how credit should be given when authors are considered for promotions, grants, patents and awards, including the highest ones, such as Nobel Prizes. Shared first or last authorship is a new invention meant to accommodate these new realities.

The position of young investigators (usually postdocs, graduate students or visiting fellows) on who should receive more credit is straightforward and might go something like this:

- “If I did the critical experiments, made the discovery and showed its value, I should be credited.”

- “Without my hard work, endless nights in the lab, countless lost weekends (I have not seen a movie for three years), and not spending much time with my family (when I leave or go home my kids are asleep), this discovery would have not been made. Not to mention that I do not see my supervisor more than once every six months, and I take full initiative in designing and executing more and more experiments.”

- “I wrote the first draft of the paper, I prepared all the figures, I presented the data at international meetings, and I won poster and oral presentation awards in numerous conferences.”

- “Since I was the first author in the Nature paper, everybody knows that I was the major player in the discovery. How could I have been

neglected by the Nobel committee?” (For example, Dominique Stéhelin wrote an open letter to the Nobel committee of physiology and medicine expressing displeasure that the 1989 award went to Michael J. Bishop and Harold E. Varmus but not to him.)

The lab director’s view may be slightly different. Postdocs and graduate students working in the lab may not immediately recognize that a line of experimentation likely was ongoing for many years and that their projects have been built by tens, if not hundreds, of previously serving associates.

Modern science requires appropriate space, sophisticated instrumentation (sometimes costing millions of dollars) and expert technicians

to operate them, at the cost of the principal investigator. The PI needs to spend considerable time to identify financial resources to keep the lab going. Moving fast with the research project requires buying expensive reagents, participating in conferences, bringing in other scientists for discussions and consultations, and securing clinical material, including human tissues and fluids, as well maintaining animals, sometimes counted in the hundreds.

Students sometimes forget that even a rare meeting with the supervisor can generate ideas about how to perform experiments better or smarter. In general, bench researchers sometimes underestimate the collective contributions of the principal

WHAT ABOUT ME?

Controversies for credit are numerous for the Nobel Prizes and other high-profile awards.

For example, one of the most controversial Nobel Prizes was the 1923 prize for physiology or medicine for the discovery of insulin, awarded to Canadians Frederick Banting and John Macleod. While Banting clearly deserved the prize, Macleod’s contribution was controversial.

Banting complained that Macleod’s contribution was providing space at the University of Toronto and that Macleod was on vacation when the discovery was made.

But Macleod also loaned Charles Best, a lab assistant, and 10 dogs for experimentation. He also reviewed some early and rather unsuccessful experiments, provided advice and suggested more experiments. He also later provided better lab equipment, more dogs and better lab space. He also began paying Banting.

Subsequent experiments were a success. Around the same time, other scientists contributed significantly to the project with insulin purification. The Nobel committee considered that Macleod’s grant to finance the project was a major factor for awarding him half of the prize.

For more Nobel controversies see http://en.wikipedia.org/wiki/Nobel_Prize_controversies.

investigator.

Should financial and other background support be enough to supersede ingenuity and technical competence in credit allocation? There is no simple answer to this, but in order for a discovery to reach fruition, a number of elements need to come together, and ingenuity alone likely will not make it. There are countless examples of collaborations between senior and young investigators that led to great success.

A superhorse may not win the

Kentucky Derby without a skilled jockey, and a fast car may not win the Indianapolis 500 without a top-notch driver. A team of highly talented basketball players will likely not win an NBA title unless they have excellent coaching staff.

An interesting observation (that I and others have made) is that most young scientists tend to overrate their contributions in comparison to their mentors, but when they become established investigators themselves they change their minds. It seems

appropriate to conclude that in science, best results can be achieved by a combination of the creative mind and energy of the youth and the resources and wise advice of his or her mature mentor.



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PROFESSIONAL DEVELOPMENT CONTINUED

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path.

When I started building my policy CV, I didn’t know anyone involved in policy. So my asking-questions process started with a number of cold calls and emails to people who I hoped could help me refine my policy interests. My experience reaching out like this ran the gamut: One person flat-out told me I was wasting her time, whereas another was so helpful and supportive that I asked her to write recommendation letters for me. Finding out what policy is and how it works from those who have been involved in it for years was the most important thing I did in my entire job search.

Pay attention

How do you make sure you don’t get scooped in science? Read the relevant literature. How do you make sure you’re speaking intelligently on science-policy topics? Pay attention to the news. Science funding, minority affairs, immigration reform and many other science policy matters are discussed in top-tier scientific journals and the mainstream media. Read these stories! You also should search for blogs and other publications that discuss policy topics. No one expects

you to be an expert on all the issues, but knowing a little about a lot of issues will allow you to converse intelligently with others in the field.

When I was investigating science-policy jobs, I came across a notice that the National Institutes of Health had released a request for information pertaining to the future of the biomedical workforce. Workforce issues are a passion of mine, and I saw this call for input as an opportunity to practice researching and writing about science policy. Of course, this had to be done after my daily lab work was complete, but I was excited about this chance to gain policy experience on a topic I cared about. Simply paying attention to what was going on provided a great opportunity to learn more about science policy while making my voice heard in the process.

Write — a lot

The vast majority of policy work is writing. Policy writing requires the precision of science writing while weaving a narrative together with enough data to make a compelling point. This is true whether you’re writing blog posts, op-eds, position statements or news releases. The only way you can develop your policy-writing skills is to practice. What you

write is up to you, but the goal is to become proficient at conveying a single, cogent message about science and science policy for a variety of audiences. Search out opportunities, and start writing! (ASBMB Today always welcomes contributions. Contact Editor Angela Hopp at ahopp@asbmb.org to find out more.)

I also wrote several letters to the editor of my local newspaper. None of them was published, but I still found the exercise of writing about policy issues an important step in my growth into science policy. My most extensive experience with policy writing was when I was crafting policy fellowship applications. While the string of initial rejections was disheartening, when I was finally offered a fellowship position, it signaled that my writing skills had matured to a point that was appropriate for a policy position.

To transition from the bench to science policy, you have to be passionate about science as well as interested in how government operations affect the course of research. These interests, as well as working on the skills listed here, will help you blaze your own path from the bench to science policy.

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

Reimagining the undergraduate science course

By Brent R. Stockwell and Michael Cennamo

The “Biochemistry: Structure and Metabolism” course at Columbia University had a lot going for it: It had high enrollment numbers, with upward of 180 students, and it received high ratings in student evaluations. But like a lot of courses, there was still room for improvement.

First, many students came to class without completing the required reading, which made it difficult to build upon that material during class. Second, a large fraction of students skipped class, likely because the lecture notes were posted online. And third, some students just didn’t master the material, particularly those from disadvantaged backgrounds.

So we made a decision that might seem radical to some readers, but it’s one that is being adopted across disciplines: We flipped the classroom.

What does it mean to flip the classroom?

When we say we flipped the classroom, we mean that we had students watch recorded videos before class, freeing classroom time for discussion, group work and solving problems. But this is not something you can do overnight.

We took time to define our goals: Obviously, we wanted the students to be better prepared for each class, allowing them to engage more fully in class discussion. But we also wanted to have students put lecture material into action by tackling practical biochemistry problems.

Last summer, we had a number of meetings to design a new course that

not only would get students thinking and problem solving in a new way but would provide instant feedback on how well they understood the material.

Here is a step-by-step description of the course redesign and our experience.

Step 1: Record lecture videos

Two technologies were used to construct low-cost video lectures: the slide-design software PowerPoint and the video-recording application ScreenFlow. Weekly slide presentations were first built with PowerPoint. Then we simulated a presentation while recording a voiceover using ScreenFlow.

The finished video was uploaded to YouTube. Once on YouTube, the video was embedded into the syllabus section of the online learning-management system. Students simply had to go to the course’s syllabus page and watch the weekly video. The students really liked the videos and asked for even more of them (see table).

Step 2: Create quizzes

Once we had digitized some of the traditional lecture material, we had to make sure that the students would watch the video lectures prior to class. That led to what we call the lecture quiz (see example question).

We created a series of short quizzes directly related to the video material and made them count as part of the course grade. A link to the quizzes

was placed underneath the video player on the syllabus page – adopting an effective tactic from Columbia Center for New Media Teaching and Learning’s MOOCs (massive open online courses). The quizzes ensured that most of the students would be prepared for the next day’s class.

Step 3A: Rethink the face-to-face lecture

With a majority of students now prepped for class, we were able to go deeper and in new directions with the face-to-face content. Most teachers wish that they had more time to explain their content and thoughtfully and critically discuss why it is so important. Strict time constraints, however, often make that difficult. By digitizing much of the fundamental lecture content for viewing outside of the classroom, we were able to delve into topics in more detail than in the traditional, lecture-only format.

We also incorporated a wide array of research articles, again taking advantage of the additional time. This allowed students to understand how science actually is performed in the lab.

Step 3B: Poll the class

During live lectures, we incorporated a polling service called Socrative that uses mobile devices, which most students bring to class anyway. We also had iPads on hand in case students needed devices. We prepared a series of questions that we posed to the class and received anonymous responses in

real time, which were displayed in the front of the class as a graph or chart.

This anonymous polling strategy allowed students to answer questions without the fear of being wrong in front of peers. The responses cued the next step in the live lecture. For example, we would revisit a difficult topic or speed up if everyone understood. Polling became an engagement tool: Discussions were livelier, and students asked more questions. Asking questions in class was simple and broke up the lecture, making it more interactive, which also gave the instructor time to organize his thoughts.

Step 4A: Create student groups

Class discussions were only a part of the plan for establishing community and collaboration.

We wanted to use group work, which had a powerful effect on us during our college years.

The class of 180 students was divided into groups of five. Because the redesign was implemented at the start of the semester, it was difficult to group students by their knowledge of the material, so we let students form groups on their own. If a student could not find a group, only then did we intercede and place him or her in an established group.

We were surprised by how much we learned about the students’ thinking by listening to them work on group problems together. The same questions would come up in different groups, and we would realize how we should phrase the question differently in the future or how some students think about a problem in different ways that lead them to different answers. This helped us develop better explanations for these concepts.

Step 4B: Problem-based learning

Once the groups were established,

Top Videos

Lecture	Number of views	Estimated minutes watched
Biochemistry class 5	456	5,634
Biochemistry class 7	401	5,745
Daphne Koller Lecture	397	3,330
Biochemistry class 4	240	2,707
Biochemistry class 12	208	2,362
Mediathread lecture	143	196

Example Quiz Question

Please watch this video: <http://youtu.be/eXQPXazUddY> and then take the rest of the quiz.

I certify that I completed watching the video

True False

Example Quiz Question

What is the product of the deamination of alanine?

A. Glycine B. Pyruvate C. Acetyl CoA D. Glutamate E. Aspartate

Example Of A Group Problem

If glucose labeled with ^{14}C at C-1 were the starting material for amino acid biosynthesis, the product(s) that would be readily formed is/are:

A. Serine labeled at alpha carbon B. None of these C. All of these
D. Serine labeled at the carboxyl carbon E. Serine labeled at the R-group carbon

they were given practical biochemistry problems to discuss and solve. The old view of learning was that the teacher filled an empty vessel: The teacher needed only to tell the student the facts and the answers, and he or she would learn them. The newer view of learning is that students need to construct new knowledge on top of their existing knowledge: To teach something new, you need to know their current knowledge.

In addition, you want to provide the intellectual scaffolding for them but also let them come to the answers on their own. Problems allow students to do that, hopefully in real-world situations that motivate them to struggle through to the answer (see example group problem).

For the last part of class, we frequently would have the students divide into their groups and work

on a problem or set of problems, such as predicting how specific fatty acids would be labeled if you began with a starting material with a label in a particular place, or predicting the mechanism of action of a drug based on the results of an experiment. These problems required students to synthesize and apply the information from the textbook, videos and class discussion.

Step 5: Student feedback and evaluation

We elicited feedback and evaluation in a number of ways. We analyzed poll data after each session, learning how best to structure upcoming lectures. We closely monitored students as they worked in groups, coming to understand their thought processes

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and problem-solving strategies. We interviewed students and teaching assistants, inquiring as to how things were working. And finally we sent out a summary evaluation at the end of the semester, looking for ways to improve the course for next fall.

The students seemed to enjoy the new aspects of the course, but some of them seemed nervous about trying a different style of learning, and many seemed concerned about whether they would be prepared for the exams. Many students requested more practice problems so that they would feel better prepared.

One student wrote:

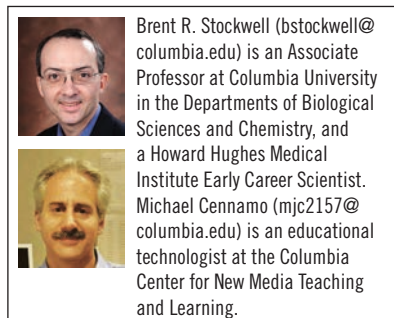
“The group problems were an interactive and creative way to

strengthen my understanding of the material with the help of my classmates. I also really enjoyed reading the assigned research articles, not only because they demonstrated interesting research methods but also because they helped me think more critically about the topics we learned in class.”

We also found that the group work created a sense of community and collaboration. Other students said that they originally feared that a biochemistry class would be competitive and scary because of all the premedical students, but with this format, they didn't find that to be the case. In fact, the group problems made it a more collaborative and friendlier environment than they had expected and compared with other courses.

Next steps

We were pleased with the results of this experiment: Attendance increased considerably, and anecdotally, students had a better grasp of the material. Our biggest problem now is that we don't have enough complex, high-level problems to provide to students. That is our challenge for next year.



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‘Creativity is in all – not a possession of only a certain few’

By Nestor Concha

This fall's cohort of kindergartners will graduate from high school in 2026. With the pace of technological change in our society faster than ever before, we have no idea how the world and the workplace will look then, what tools they will need to be agents in the transformation of their world or what they will need to be successful. We do know, however, that to prepare the class of 2026 and beyond, our educational system requires diversity, inclusiveness and open-mindedness.

We often hear the drumbeat for improved and expanded education in the fields of science, technology, engineering and math, and the reasons are fairly obvious. A U.S. Department of Commerce study in 2012 titled “The Competitiveness and Innovative Capacity of the United States” indicated that innovation is “the key driver of competitiveness, wage and job growth, and long-term economic growth” (1). The report went on to say that innovation “requires basic research, education and state-of-the-art infrastructure. In this context, making college more affordable, spurring classroom innovation at all levels, expanding the size and quality of the STEM teacher ranks, and encouraging and facilitating students’

and workers’ continued STEM education are critical. Education is the centerpiece of the advancement of industrial and technological competitiveness.”

Indeed, sometimes it is difficult to restrain the excitement imagining what lies ahead, and few would argue against the importance of STEM education and training. But we should be clear that we don't have to make a choice between STEM and such things as art programs. Rather, we should choose to nurture everyone's talents in the classroom.

Education needs a transformation, to borrow the words of Ken Robinson, an author and expert on creativity. Education needs a transformation where testing is a diagnostic tool and not necessarily an end in itself; where strong STEM, arts and social-sciences programs are integrated into multidisciplinary themes as opposed to the traditional isolated subjects; where the overarching goal is discovering and developing the talent in all; and where learning by doing and learning by using all human abilities, mental and physical, are valued. This is a transformation that recognizes intelligence not as a quantity measured by a score but as an individual quality that is tremendously dynamic. It is

a transformation that conceives that creativity is in all — not a possession of only a certain few. By developing everyone's talents, we are sure to spur and foster innovation in all fields of human curiosity.

In the workplace, the principle of diversity is reflected in the interplay among different fields of endeavor and human activity. This includes a consideration of different points of view; the active engagement of different peoples; collaboration among disparate academic departments (anthropologists and computer scientists, psychologists and economists); and the thoughtful organization of scientific meetings where the sessions are pointed toward broad problems and are tackled by multidisciplinary approaches.

That inclusiveness and diversity work is exemplified by a study published in February that found diversity in the composition of the authors contributing to scientific papers leads to significant and important scientific contributions (2).

By adopting the value of diversity as a guiding principle, we will all, young and adult, be better off.



Nestor Concha (Nestor.O.Concha@gsk.com) is a senior scientific investigator at GlaxoSmithKline.

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1. <http://1.usa.gov/1mUttbM>
2. <http://www.nber.org/papers/w19905>



The University of Vermont

The University of Vermont has openings for both Ph.D. and postdoctoral training positions in fields related to blood coagulation research, encompassing vascular biology, hemostasis, hemorrhagic diseases and thrombosis. Programs extend over a broad range of basic, translational and population science. Graduate students and M.D. and Ph.D. fellows are invited to apply for positions in this NIH-sponsored training program leading to either the Ph.D. degree or to postdoctoral studies. Past fellows have been from the fields of Biochemistry, Cell Biology, Hematology, Cardiology, Surgery, and Pathology. For fellows pursuing hematology-oncology training, integration with clinical training is offered. Specific areas of interest include:

- Blood coagulation reaction mechanisms
- Biochemical/biophysical/X-ray structural characterizations of protein-protein, protein-metal ion, and protein-membrane interactions
- Dynamics and proteomics of the blood coagulation/fibrinolytic systems
- Platelet/megakaryocyte biology
- Epidemiology
- Treatment of hemophilia and venous thrombosis, and thrombosis prevention

Participating mentors are in the fields of Biochemistry, Pathology, Cardiology, Hematology, Epidemiology, Surgery, Genetics, Vascular Biology and Cell Biology.

Applicants must be citizens, noncitizen nationals or permanent residents of the U.S. Additional information can be found on our websites: <http://biochem.uvm.edu> www.med.uvm.edu/lcbr www.med.uvm.edu/pathology www.fletcherallen.org/services/heart_health/specialties/cardiology www.uvm.edu www.fletcherallen.org

Minorities and women are encouraged to apply. Send inquiries to: Dr. Kenneth G. Mann, University of Vermont College of Medicine, Department of Biochemistry, 208 South Park Dr. Rm 235, Colchester, VT 05446 or email Kenneth.Mann@uvm.edu.

Yale Science Diplomats: DIY science outreach

By Bryan Leland

Science outreach efforts often are run by a few passionate individuals who possess ample dedication but lack experience running an organization. Yale Science Diplomats is a great example of a graduate student-run outreach group that started small but has developed into a successful, sustainable program. By sharing our experiences and the knowledge that we have gained in the process, we hope to inspire other graduate students at institutions around the country to follow in our footsteps.



Now in its sixth year, YSD has about 25 graduate students and postdocs. The group runs events, workshops and other programs at the interface of science and policy. For example, in our annual Science in the News series, graduate students and postdocs explain the actual research behind hot-button issues like climate change and genetically modified organisms to the greater New Haven community. YSD also organizes seminars and workshops for scientists, such as a policy-writing workshop, a

mock policy debate about dual-use research and a seminar on communicating science to the public.

Groups like YSD are proliferating across the country, but if you can't find the right group for you at your own institution, why not start your own? Here are some tips for starting and running your own student outreach group:

Pick something you're passionate about

YSD was founded by a group of graduate students inspired by a presentation about scientists pursuing policy careers at the "What can you be with a PhD?" event in New York City. Griselda Zuccarino-Catania, one of YSD's founding members, said that she and her colleagues already were "interested in scientists being better communicators and interacting with the community." After the presentation on policy careers, she says, "we thought it was a cool idea to have scientists more involved in politics ... We were excited to bring this to Yale, so we decided to form the group and spread the word to see who else might be interested."

Find other like-minded colleagues and work together

Doing something meaningful outside of the lab will require a team of like-minded people. Jessica McDonald, another founding member of YSD, emphasizes the importance of building a strong team. "I think one of the

secrets behind our success was that early on, our group was small and made of friends," she says, "[so] there was a genuine bond and a sense of responsibility to each other."

Come up with a mission statement and start with small, defined goals

According to McDonald, "many of our initial ideas were too nebulous, and people wanted to help, but it wasn't clear to them how they could do so." Former YSD President Elizabeth Stulberg suggests: "Start by drafting a mission statement. Figure out exactly what you want to do and what your group can contribute." YSD's mission is to foster a scientifically informed electorate. This mission statement is broad enough to encompass the range of different workshops and outreach activities that YSD runs but still narrow enough to keep the group focused.

Define a leadership structure and divide responsibility

There are many different leadership structures, so experiment to find the right one. For example, YSD has several committees, each focusing on a specific event or type of project, such as the Science in the News committee. The key to organizing Science in the News and our other events has been breaking them into small, manageable tasks like finding speakers, booking locations and advertising.



Back row (left to right): Danielle Larese, Kimberly Barrett, Michael Manas, Brandon Nam, Chris Mckitterick, Evan Pease, Bryan Leland, Richard Sarro. Second row from the back: Chad Miller, Shannon Stewart, April Rose, Jen Gillies, Lily Guillot, Allison Gilder, Jessica Miles (trip co-organizer). First row: William Gray, Nathalie Celcis, Irene Tebbs, Rebecca Brown, Nina Brahme (trip co-organizer), Elizabeth Turner, Olivia Kelada, Jedidah Isler, Sarah Schreiner, Vincent Yip. Seated: Lu Jin, Ruiqi Mao.

Pool resources and collaborate

At a large university, it can be challenging to identify existing resources. Seek out university offices or other campus groups that have people, ideas, money or other resources you need. Many large schools have offices dedicated to teaching, career services, community outreach, and press or communications – these all may be good places to start. If something similar to what you want to do exists already, collaborate! YSD co-organized a career trek with Graduate Career Services. Graduate students interested in policy careers went to Washington for two days to network with scientists at various government agencies. Combining YSD's resources with Graduate Career Services was critical to the trip's success.

Raise money and apply for funding

While there are many simple events

and initiatives that do not require funding, eventually you may want to raise money for more ambitious efforts. Find funding opportunities at your university such as a student-activities or career-services fund. Look for community-development grants in your city or county. Many scientific societies also have grants available for outreach activities. For example, the American Society for Biochemistry and Molecular Biology funds seed grants to help outreach programs get started.

Recruit new members

Make your group sustainable by actively recruiting participants, especially first-year graduate students. For example, bring fliers or a poster to department orientations and other events. Social activities are another great way to spread the word about your group. YSD runs a "Welcome BBQ" during orientation to tell incoming graduate students about our group and how they can get involved.

Don't stop when you graduate!

The leadership and communication skills you gain from a student outreach group are useful for virtually any career path. After graduating, several YSD members have continued to pursue their interests in science communication and policy. McDonald is a health reporter for WHYY in Philadelphia and the Web intern at Science Friday. Stulberg is an American Society for Microbiology Science and Technology fellow in the office of U.S. Rep. Louise Slaughter, D-N.Y.

Leading your own outreach group will not only allow you to share your knowledge and passion for science with the public. It will give you valuable skills that translate to nearly any career.



Bryan Leland (bryan.leland@yale.edu) is the co-president of the Yale Science Diplomats.

Desperately seeking Sputnik for fundamental science

It is clear that researchers and the public need something around which they can rally, but what should it be?

By Daniel M. Raben and Joseph J. Baldassare

We have been pondering an important question: Do we need a Sputnik for fundamental science? We have become convinced that we do, which leads us to another question: What might our Sputnik be?

The need for increased funding for research and training became a national priority 55 years ago after the launch of the first artificial satellite, Sputnik 1, by the former Soviet Union. Sputnik inspired President Kennedy in 1961 to challenge NASA to put a man on the moon and return him to Earth before the close of that decade.

This challenge reawakened a national interest in science and support for funding of both applied and fundamental research. These investments paid off in many ways. The 1960s spawned a number of scientific discoveries – the first laser, the first kidney transplant, the first commercial communication satellite, the first human heart transplant and the first handheld calculator. NASA directed a successful round-trip manned flight to the moon in 1969. In addition, advances in our understanding of

basic biomedical science, physics and astrophysics led to technological advances that today are part of everyday life.

But now the nation appears to have lost sight of the role of science and the need to maintain funding for science. What do we need to do to spur enthusiasm in lawmakers and the general public for fundamental research similar to the enthusiasm that was present after Sputnik?

First, let's look at why the launch of Sputnik was so effective. One obvious and important reason is national pride: The Russians were beating us! But today, because of rapid communication and other factors, the scientific community is global. Appealing to national pride alone is not only short-sighted but counterproductive. Clearly, global scientific collaboration is necessary. Focusing on national competition could damage collaborations important for future advances and discoveries.

Today, when we do engage in public discourse about science, we often hear the refrain, "We put a man on the moon in 10 years, so why can't we cure cancer?" What people fail

to realize, and what scientists fail to communicate effectively, is that we understood the laws of physics and essential aspects of cosmology necessary to put someone on the moon and return them to Earth. But we don't understand all the rules of cancer and a variety of other diseases and destructive natural phenomena. That's why we need to support fundamental research!

Clearly, it's a major challenge to convince the general public once again of the vital role of science, especially fundamental research, to maintain and improve our lifestyles and lives. So we are putting the question to you: How can we inspire widespread support for advances in fundamental research that provide the foundations on which practical discoveries and applications depend? Which mission or cause do you think could be the Sputnik of fundamental science?

Daniel M. Raben (draben@jhmi.edu) is a professor of biological chemistry at The Johns Hopkins University School of Medicine. Joseph J. Baldassare (baldasjj@slu.edu) is a professor of pharmacological and physiological science at the St. Louis University School of Medicine.

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Reader comments

Re: "Petsko on the Ph.D. pipeline" April issue

As usual, Greg (Petsko) has written another thought-provoking article. Again, I find myself in complete agreement, but there is one issue I'd like to highlight/clarify. The emphasis during students' graduate education should be on training them as scientists. While it is certainly our responsibility to provide them with the tools they need to pursue a variety of career options, preparation for various careers should not interfere with their education and training as scientists. So the question may not rest on whether we should or shouldn't provide these opportunities, but rather when students should pursue the exploration of various career options. For academic careers, this isn't an issue. But for nonacademic careers, it may be more complicated, and the timing may be graduate-program-dependent. Just some thoughts.

– DANIEL RABEN

Re: "The impact of the sequester: 1,000 fewer funded investigators" President's Message, March issue

The study is incredible, and I look forward to more analyses over the coming years. I have become weary of (National Institutes of Health) reports, which present descriptive data of limited scope. The NIH has data on every applicant, and it only seems fair to release more information about the population of applicants and not only the "winners." I have wondered if the NIH would release more applicant data — after all, researchers (funded or not) are taxpayers, too.

– LEO

I recently had a conversation about this. One theme of the discussion was who comes through this crucible? As a result of terrible funding rates, what kinds of researchers are we losing,

and is there a trend of who makes it through this horrible gantlet? Do we lose good mentors? Risk takers? Are we only keeping the best minds or those who can put aside all other issues to focus on their projects? Who wants to join in this madness? Ask a postdoc right now how they feel. I hope that the dam breaks soon, or we will lose good people, and I wonder what our new generation of research scientists will look like.

– JP

Thanks for this excellent analysis. Hope someone at NIH is listening. The R00 is becoming a liability in study sections. Pink sheets from '12 and '13 are expecting full productivity of an established investigator from an (early stage investigator) who had an R00. But without R00, probably wouldn't be an ESI. The funding angst is really propelling the avalanche of inefficiencies in extramural research that are burying us ESIs and juniors.

– formerESI

The American Society for Biochemistry and Molecular Biology is accepting applications for the 2014 Hands-on Opportunities to Promote Engagement in Sciences (HOPES) seed grants.

The goal of the HOPES seed grants is to incentivize and support the development of outreach programs and partnerships by teachers and researchers. Each grant is worth up to \$2,000 and will be awarded to teams consisting of one or more junior high/high school teacher(s) (or another K-12 educator) and one or more university, college or institutional (e.g., NIH, NSF, USDA) research scientist.

All applications from interested teachers and research scientists will be considered. **All applications are due June 27.**

For application instructions, go to www.asbmb.org/hopesgrant.



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Lunteren, The Netherlands



Transcriptional Regulation: Chromatin and RNA Polymerase II

October 2-6, 2014
Snowbird Resort
Snowbird, UT



Post Translational Modifications: Detection and Physiological Role

October 16-19, 2014
Granlibakken Conference Center & Lodge
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