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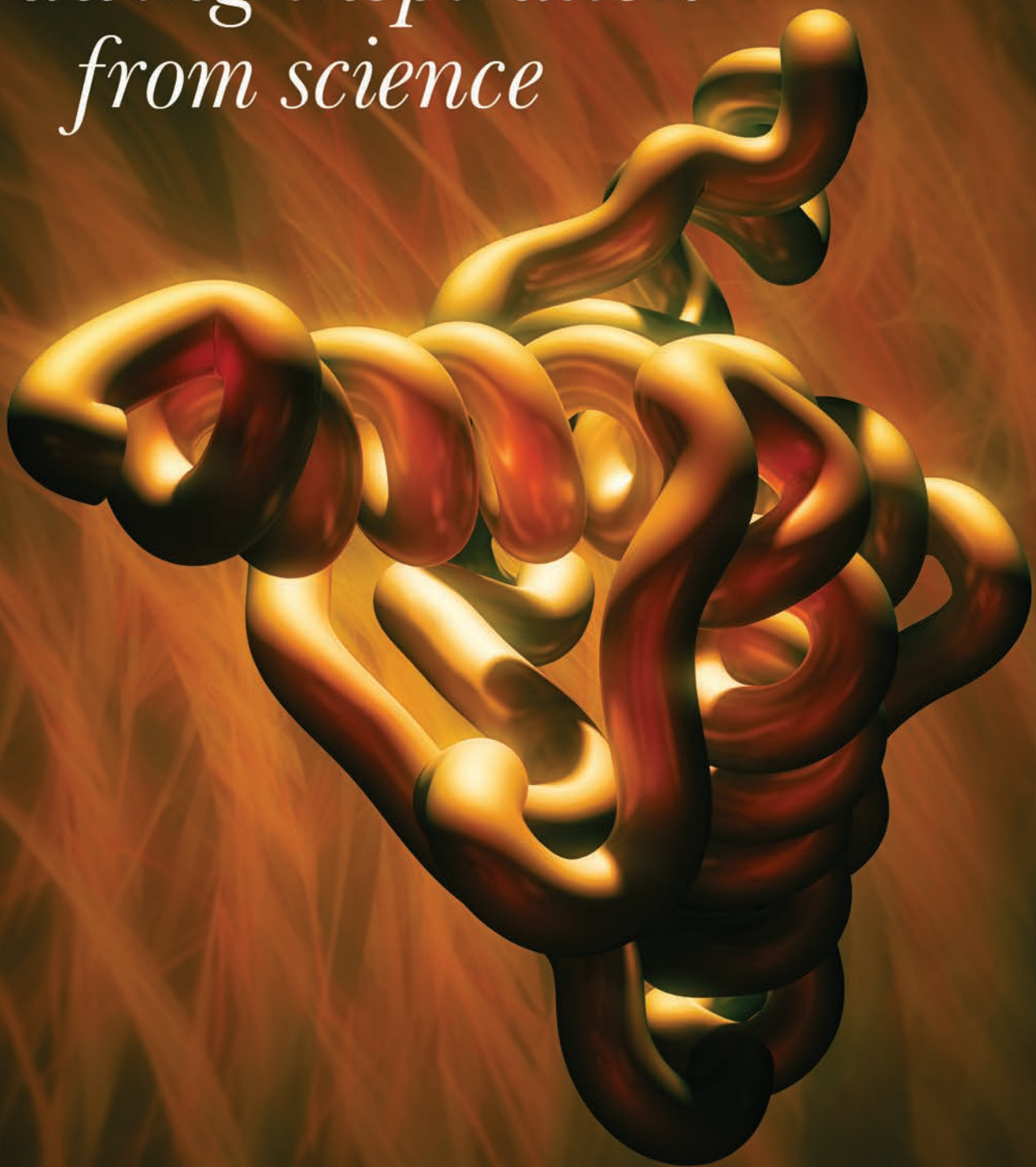
ASBMBTODAY

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

Drawing inspiration from science



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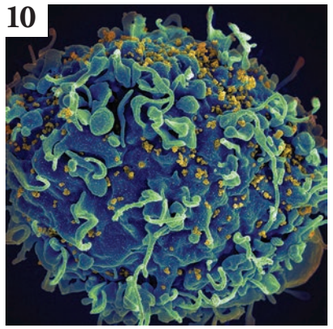

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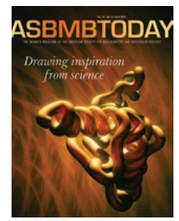
Biochemist Vikram Mulligan finds his artistic muse in structural biology.

Image courtesy of Vikram Mulligan



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Funding decisions: the NIH method

By Steven McKnight

My column last month briefly described how the Howard Hughes Medical Institute appoints new investigators and reviews existing investigators. Now let's switch to the grant review system at the National Institutes of Health, the largest funding source of biomedical research worldwide.

For the purpose of simplicity, I have in two ways restricted my analysis of the NIH grant review system. First, I've limited it to R01 grants and R37 grants (also known as MERIT awards). Second, I've limited my analysis to the 177 study sections chartered by the Center for Scientific Review. These 177 study sections assist in the disbursement of roughly $10 billion annually in the form of R01 and R37 awards.

Each NIH grant application is evaluated first by three or four members of a study section and then scored by the study section as a whole, which is composed of 20 to 30 scientists. Reviewers judge the application using five criteria: significance, investigator, innovation, approach and environment. Although study sections may weigh the importance of these criteria to differing degrees, it seems to me that feasibility of success of the proposed research plan (approach) tends to dominate. I will endeavor to provide a quantitative assessment of this in next month's essay. Unlike at the HHMI, NIH reviewers do not interview applicants in person, and past performance is not of enhanced significance.

As reported last month, 72 percent of reviewers serving the HHMI are members of the National Academy of Sciences. How do things compare at the NIH? Data kindly provided by the CSR indicate that there were 7,886 reviewers on its standing study sections in 2014. Evaluation of these data reveals the following:

1) 48 out of 324 HHMI investigators (15 percent) participated in at least one study section meeting.

2) 47 out of 488 NIH-funded NAS members (10 percent) participated in at least one study section meeting.

3) 11 of these reviewers are both funded by HHMI and NAS members.

These 84 scientists constituted roughly 1.1 percent of the reviewer cadre utilized by the CSR.

Where do these HHMI investigators and NIH-funded NAS members serve? As shown in Table 1, eight study sections enjoyed the participation of three or more HHMI and/or NAS members during 2014. All eight of these study sections can readily be categorized as being focused on basic biomedical research. As such, it is clear that when they participate in the CSR review process, HHMI investigators and NAS members gravitate toward study sections charged with the review of basic research to a far greater extent than clinical research.

Herein I compare the means by which two organizations operate in the important task of scientific review. I summarize several differences in the manner of review employed by the HHMI compared with the NIH.

1) The HHMI reviews applicants in person; the NIH does not.

2) The HHMI employs a smaller review team to disburse its funds ($20 million disbursed per reviewer); the NIH employs a much larger team ($1.3 million disbursed per reviewer).

3) The HHMI pays attention to the track record of a scientist; the NIH seems to pay more attention to the details of the proposed research plan.

4) The HHMI relies heavily on highly accomplished scientists to conduct its reviews (72 percent of HHMI reviewers are NAS members); the NIH does not (less than 2 percent of NIH study section reviewers are HHMI investigators, NAS members or both).

I close with several comments based on these differences.

First, I emphasize that there are many, many highly accomplished scientists who are not HHMI investigators or NAS members, and it is imperative that these scientists participate in the review of NIH grant applications. I have focused on the HHMI investigators and NAS members because it is straightforward to identify them and quantify their participation in the review process. It is my belief that HHMI investigators and NIH-funded members of the NAS are substantively accomplished. I readily admit that scientific accomplishment does not necessarily equate to effective capacity to review. I do, however, believe that a reasonable correlation exists between past scientific accomplishment and capacity to choose effectively between good and poor bets. This contention is open for debate and is — to me — of significant importance.

Number of HHMI investigators and NAS members who were on certain study sections in 2014

Cell Signaling and Regulatory Systems – 3
Development 1 – 9
Genetic Variation and Evolution – 3
Immunity and Host Defense – 3
Macromolecular Structure and Function C – 4
Molecular Genetics A – 3
Prokaryotic Cell and Molecular Biology – 3
Vector Biology – 3

Second, even if all HHMI investigators and NIH-funded NAS members were to participate in NIH study sections, they would constitute only 9 percent of the full roster (707 out of 7,886). The only way to change this percentage would be to reduce substantively the total number of reviewers. I will address this concept in next month's essay.

Third, it is clear that HHMI investigators and NIH-funded members of the NAS participate in study sections charged with the review of basic research to a far greater extent than clinical research. It is my belief that study sections involving HHMI investigators and NAS members benefit from the involvement of highly accomplished scientists. If that is correct, the quality of certain basic science study sections may be high.

I assume that it is a common desire of our biomedical community that all sources of funding, be they private or public, find their way to the support of our most qualified scientists — irrespective of age, gender, ethnicity, geographical location or any other variable. In subsequent essays, I will offer ideas as to how the NIH system of grant award distribution might be altered to meet this goal.

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

Upcoming ASBMB events and deadlines

MAY 30 – JUNE 2: American Society for Microbiology meeting, New Orleans, JBC booth 119

MAY 30: ASBMB workshop: Designing Scientific Teaching Tools For Underlying Concepts and Skills for BMB Education, University of Michigan–Deaborn

JUNE 25 – 28: ASBMB Special Symposium: Evolution and Core Processes in Gene Regulation, St. Louis

JULY 30 – AUG. 2: ASBMB Special Symposium: Transforming Undergraduate Education in Molecular Life Sciences, Saint Joseph, Mo.

SEPT. 17 – 20: ASBMB Special Symposium: Membrane-Anchored Serine Proteases, Potomac, Md.

DEC. 5 – 8: ASBMB Special Symposium: Kinases and Pseudokinases: Spines, Scaffolds and Molecular Switches, San Diego

The blessing and curse of legislating science

By Chris Pickett

Legislation that affects scientific research is often met with a great deal of anxiety from the scientific community. Surely the research enterprise has problems, and new legislation may be the best way to fix some of those problems. But legislative changes that alter how science-funding agencies operate can have far-reaching consequences for researchers, and the changes can be quite difficult to undo. Add in many scientists' distrust of legislators, and you can see why scientists are leery of any attempt by Congress to fix the problems of the enterprise.

Nevertheless, the 21st Century Cures initiative, launched by Reps. Fred Upton, R-Mich., and Diana DeGette, D-Colo., of the U.S. House Energy and Commerce Committee in 2014, appealed to many scientists who felt the careful approach would produce a bill beneficial to the enterprise. With the goal of identifying legislative means to accelerate discovery, development and delivery of lifesaving cures to the American public, the committee held many hearings and roundtable discussions, and it invited the community to comment on several white papers published by the committee. This work culminated in the release of a 21st Century Cures Act discussion draft in January. This draft legislation would make significant changes to clinical trials, the Food and Drug Administration, and the National Institutes of Health.

Unfortunately, this draft only confirmed scientists' long-held concerns about legislation and science. The draft legislation contains several sections of concern for basic scientists, but arguably the most troubling section attempts to address accountability and transparency at the NIH. This section states that the directors of all NIH institutes and centers must review and approve all grant awards. Furthermore, the directors must ensure that all funded grants are of "a national priority and have public support," that they are not duplicative of other research, and that the investment in the grant is commensurate with the projected benefits.

These changes would not improve accountability at the NIH. Rather, requiring institute and center directors to approve funding for every grant would increase the bureaucratic burden of grant funding and slow the pace of research. In addition, institute and center directors cannot possibly know whether specific grants have public support; nor can they know the results of the proposed research or if the investment matches the outcome. Finally, science is duplicative by nature, with many researchers pursuing very similar paths to achieve the same goals. Such broad language could cause significant damage to the research enterprise.

These directives are reminiscent of the Frontiers in Innovation, Research, Science and Technology Act introduced in Congress in 2013. This legislation would have placed many of the same restrictions on the National Science Foundation. The scientific community was unanimously opposed to the FIRST Act for this and other parts of the legislation. Similarly, should the final version of the 21st Century Cures Act still contain these directives, the American Society for Biochemistry and Molecular Biology will oppose the legislation.

That said, the draft legislation does have some positive aspects to it. Requiring the NIH to report on aging trends in the enterprise as well as the agency's efforts to eliminate waste and fraud will shine light on how the agency operates. Furthermore, the draft legislation would establish a working group charged with finding ways to alleviate burdensome NIH regulations.

The ASBMB submitted formal comments to the House Energy and Commerce Committee on the draft 21st Century Cures Act at the beginning of February. As the committee works toward a final version, the ASBMB will continue to engage with members of Congress to get the highest quality bill possible.

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

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Mecham wins Marfan Foundation award

MECHAM

The Marfan Foundation named Robert Mecham the first winner of its Distinguished Research Award. Mecham, a faculty member at the Washington University School of Medicine, was honored at the foundation's gala in March. Now in its seventh year, the fundraising gala honors those "who are so deserving for their commitment to the Marfan syndrome and related disorders community," said Alan Braverman, director of the Marfan Syndrome Clinic at Washington University, co-host of the gala and the son, brother and uncle of Marfan syndrome patients. He noted that Mecham "is a national leader in research of elastic tissue function whose work has contributed to understanding the structure and function of fibrillin, the abnormal protein in Marfan syndrome."

Mecham with his lab. IMAGE COURTESY OF TIM JOYCE/THE MARFAN FOUNDATION

Protein Society recognizes Sidhu and Yan

SIDHU

YAN

Two American Society for Biochemistry and Molecular Biology members won awards from the Protein Society. Sachdev Sidhu of the University of Toronto won the Christian B. Anfinsen Award, and Nieng Yan of Tsinghua University won the Protein Science Young Investigator Award. In a statement, the society noted that Sidhu "has advanced the field of protein engineering through pioneering advancement of phage display technology, creation and deployment of highly designed synthetic human antibody libraries, engineering ubiquitin to create tools for studying and manipulating the ubiquitin system, and a number of other groundbreaking approaches." Meanwhile, the society pointed to Yan's crystal structures of transporters, including human GLUT1. It said: "Her work is characterized not only by the pursuit of targets that can be described as 'high hanging fruit,' but also by being thoroughly anchored by focusing on how protein structural information can be employed to illuminate protein function and related biology." Sidhu and Yan will receive their awards at the society's annual meeting in July in Barcelona.

Traktman named dean at Medical University of South Carolina

TRAKTMAN

Paula Traktman is set to become dean of the College of Graduate Studies at the Medical University of South Carolina in July. Traktman has been a professor and head of the microbiology and molecular genetics department at the Medical College of Wisconsin since 1997. Before that, she held positions at the Massachusetts Institute of Technology, Harvard Medical School and Cornell University. Mark Sothmann, the provost at MUSC, said Traktman "brings an excellent combination of research, teaching and administrative skills to lead the continued growth and development of the College of Graduate Studies." Her appointment is contingent upon the board of regents' approval.

Hilton wins scholarship, industry mentorship

HILTON

Edward Hilton, an undergraduate at Duquesne University, won a $10,000 scholarship from Clarkston Consulting. Hilton, a biochemistry major who works in the lab of Benedict Kolber, was honored by the company in March. In addition to the scholarship money, Hilton will receive mentoring from employees of Clarkston Consulting and will participate in the Pennsylvania Bio events over the next two years. "I am extremely grateful for this honor," Hilton said. "The scholarship funds will help offset the cost of my current education and allow me to focus on my professional development. I believe that the mentoring aspect of the Clarkston Scholars Program will afford a wonderful opportunity to gain further insight into this industry."

Spreading aggressive traits between cancer cells

By Edyta Zielinska

Until recently, researchers thought that cell division was the only way for an aggressive cancer cell to pass its traits along. New evidence is showing that cancers can become more dangerous by exporting aggressive traits to neighboring cells via exosomes. These small packages — bubbles — of membrane released into the extracellular environment hold pieces of host RNA, DNA and proteins. Now, a new study has shown that exosomes also can hold and transfer integrin molecules known to promote metastasis in several cancers.

"This is an important addition to the research showing that tumors have novel ways of spreading aggressive traits," says senior author Lucia Languino, a researcher at the Sidney Kimmel Cancer Center at Thomas Jefferson University.

Integrins are transmembrane molecules that tether cells to one another and to the extracellular matrix that surrounds them. They often are altered during a cell's progression into a cancerous state, allowing the cell to detach from its surroundings and become more mobile and likely to enter the bloodstream and metastasize to distant sites in the body. They also act as receptors, relaying signals that alter the gene expression involved in cell survival and division.

Earlier research showed that the integrin αvβ6 is abundant in prostate cancer cells but not normal prostate cells. It appears to promote proliferation and migration by activating intracellular signaling molecules and may be involved in promoting metastasis to the bone. It also may activate the production of cytokines that promote metastasis.

Because of its role in prostate cancer, Languino, first author Carmine Fedele and colleagues investigated whether this integrin might be transferred between cells via exosomes. In a study reported recently in the **Journal of Biological Chemistry**, the researchers examined the exosomes released from prostate cancer cell lines known to express the αvβ6 integrin and found that the exosomes were enriched with this integrin. The research also was supported by the work of Amrita Singh, a graduate student in Languino's lab, and the collaboration of professor Renato Iozzo.

To determine whether neighboring cells took up the αvβ6 exosomes, the researchers used a cell line that lacked the ability to produce its own αvβ6 integrin. They incubated αvβ6-lacking cells with PKH26 Red-labeled αvβ6 exosomes and showed that the cells efficiently internalized the exosomes. They also determined by FACS analysis that the cells expressed the integrin molecule on their surface.

Finally, to test whether these newly αvβ6 integrin-expressing cells gained new, more metastatic-like functions, Languino and colleagues plated the cells on a surface containing αvβ6 ligands. The team noted that cells incubated with αvβ6 exosomes were able to adhere to the surface and migrate in a dose-dependent fashion, whereas cells incubated with exosomes expressing the β6 subunit alone did not adhere and migrate efficiently.

"The research suggests that the αvβ6 integrin can transfer between prostate cancer cells," says Languino. "In theory, inhibiting the αvβ6 integrin could reduce the chances of prostate cancer metastasis, and targeting exosomes could be an important part of achieving that goal."

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Cell biology of GPCR signaling

By Caitlin Hanlon

G-protein coupled receptors, known for short as GPCRs, are the main conduit for cells to interact with their environments. The **Journal of Biological Chemistry** recently published a collection of minireviews examining the current state of GPCR research. These reviews cover new technology for studying GPCR activation and novel signaling methods that call into question conventional GPCR wisdom.

All GPCRs share the same basic architecture: an extracellular N-terminus, seven transmembrane spanning segments and an intracellular C-terminus. More than 1,000 genes encode GPCRs in the human genome. This large family is responsible for detecting an enormous range of extracellular stimuli, from photons to hormones to peptides.

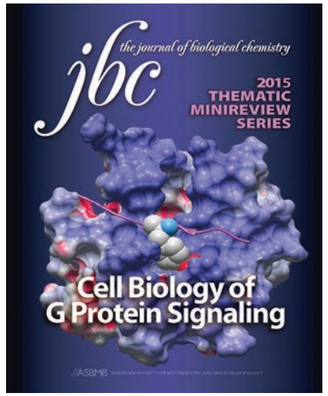
Once a ligand becomes bound by a GPCR, the receptor undergoes a conformational change and activates the heterotrimeric G-proteins (α, β and γ.) The G-proteins then activate downstream pathways corresponding to the initial stimuli. Signaling is attenuated through proteins that promote reassociation of the heterotrimeric G-proteins or through endocytosis of an activated receptor. The entire G-protein cycle occurs on a millisecond timescale and is consequently an efficient way to translate environmental information to an appropriate cellular response.

Henrik G. Dohlman of the University of North Carolina at Chapel Hill, a JBC associate editor, organized the recent JBC series. "G proteins are extremely important in pharmacology and physiology and are among the best-studied proteins in the cell," says Dohlman. "Even after nearly half a century of investigation, they continue to be a source of new knowledge and more than a few surprises."

The first JBC review, by Terri Clister, Sohum Mehta and Jin Zhang of Johns Hopkins University School of Medicine, is titled "Single-cell analysis of G-protein signal transduction." The authors discuss the use of FRET in probing GPCR activation. FRET pairs can be attached to a receptor to gauge the conformational changes or to the heterotrimeric proteins to assess receptor and G-protein interactions. The group also introduces optogenetics, which uses modified GPCRs that can be activated by a specific wavelength of light, leading to both spatial and temporal regulation of GPCR signaling.

In the second review, "GPCR signaling via heterotrimeric G proteins from endosomes," Nikoleta G. Tsvetanova at University of California, San Fransisco, and others detail how GPCRs are able to signal after endocytosis. GPCRs originally were believed to signal exclusively from the plasma membrane; upon receptor endocytosis, the signaling ceased. However, recent biochemical studies and live-imaging have shown that receptors continue to activate Gα following internalization. While it is unclear if GPCR signaling in the endosome occurs in vivo, this phenomenon represents a new compartmental component to GPCR signaling.

The final review, written by Mikel Garcia-Marcos at Boston University School of Medicine and others, is entitled "GIV/Girdin transmits signals from multiple receptors by triggering trimeric G protein activation." GIV is a unique protein that acts as a platform between GPCR signaling and other signaling cascades. Following an interaction with an activated receptor tyrosine kinase, GIV is able to act as a GEF for Gα. Consequently, G-protein activation occurs in the absence of an activated GPCR. This mechanism of G-protein activation has important implications for understanding hyperactive G-protein signaling.



Caitlin Hanlon (chanlon3@jhmi.edu) earned a B.S. from Ursinus College and is pursuing a Ph.D. in the cell biology department at the Johns Hopkins School of Medicine.

Stem cells and early-stage placental development

By Matt Shipman

There's a lot we still don't know about the early stages of placental development in humans — in part because there are practical, ethical and legal constraints that make it difficult to obtain relevant placental samples. But researchers may be closing in on a solution.

One way to address this dilemma is to use human embryonic stem cells to develop trophoblasts, the precursors to placental cells. But there's been intense debate about whether trophoblasts obtained from hESCs have the same features as "true" trophoblasts. A recent paper in the **Journal of Biological Chemistry** opens a new chapter in the debate, lending credence to the notion that bona fide trophoblasts can be obtained from hESCs.

One of the key arguments against hESC-derived trophoblasts has been that the promoter region of the ELF5-2b gene in these cells is methylated, whereas it is not methylated in trophoblasts in vivo. A second argument has been that hESC-derived trophoblasts show expression of HLA class I antigens — unlike trophoblasts in vivo.

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Those arguments have now been disproven.

"We've shown that you can form trophoblasts from hESCs that are both demethylated in the ELF5-2b promoter region and that show down-regulated expression of HLA class I antigens," said Balaji Rao, a biological engineering researcher at North Carolina State University and corresponding author of the JBC paper.

"Our work supports the claim that hESCs can be used to create models for understanding trophoblast differentiation and early placental development," Rao added.

In addition, the Rao paper identifies conditions that allow researchers to target the derivation of the two major types of trophoblasts: syncytiotrophoblasts and extravillous trophoblasts. Syncytiotrophoblasts are multinucleate, hormone-producing cells. Extravillous trophoblasts are a class of cells that perform various functions, including anchoring the placenta to the uterine wall and remodeling the mother's arteries to establish blood flow to the placenta.

The researchers found that if signaling by Activin/Nodal proteins is blocked, hESC-derived progenitor trophoblasts differentiate into extravillous trophoblasts. But if Activin/Nodal signaling is present, the progenitor cells differentiate into syncytiotrophoblasts.

"There is still an enormous amount of work to be done in this field – this is only the beginning," Rao said. "But hopefully our recent work will move the research community one step closer to developing a model system that can capture and explain the dynamic nature of trophoblasts in vivo over the course of gestation. It is a huge challenge."

Rao's research was funded by the National Science Foundation. The lead author of the JBC paper is his former Ph.D. student, Prasenjit Sarkar, who is now a biochemistry postdoctoral fellow in Boston University's School of Medicine.

Matt Shipman (matt_shipman@ncsu.edu) is a public information officer at North Carolina State University and a freelance science writer. He also writes the Communication Breakdown blog for Nature's SciLogs blog network. Read it at www.scilogs.com/communication_breakdown.

Boar semen biomarkers predict litter size

By Rajendrani Mukhopadhyay

Pig business is big business. In 2012 alone, China, the world's largest producer of pork, produced 50 million tons of the meat. Getting pigs to produce large litters reliably is of great economic importance in places like China, the United States and the European Union. In a recent study published in **Molecular & Cellular Proteomics**, researchers describe biomarkers on boar sperm that can predict the animal's fertility.

Myung-Geol Pang at Chung-Ang University in South Korea led the MCP study. He says one challenge the pork industry faces is the reliance on "inefficient methods to evaluate semen quality that could directly affect litter size." Pang explains that current semen analyses look at some quantitative aspects of the sperm, "but the sensitivity of such analyses remains a subject of debate."

So Pang and his colleagues wanted to come up with a different way to determine boar semen quality. In particular, because Pang and colleagues wanted to find protein biomarkers that would predict litter size, the investigators undertook a proteomic analysis of boar semen. They collected semen from 18 stud boars at a Korean pig farm. Using methods like gel electrophoresis and mass spectrometry, Pang and colleagues analyzed all the proteins in the samples. They then matched their data to the number of pups sired by each stud boar.

Based on that information, the investigators grouped biomarkers that predicted whether a boar would sire a large number of pups (about 12) or a small number (10 or fewer). L-amino-acid oxidase, mitochondrial malate dehydrogenase 2 and calmodulin were among the proteins notably expressed in semen that gave large litters. Proteins such as Ras-related protein Rab-2A, spermadhesin AQN-3 and NADH dehydrogenase were abundant in semen that produced small litters. In total, the investigators found 11 protein biomarkers that predicted litter size. "These biomarkers may be particularly important in the animal industry for the prediction and selection of better litter sizes," says Pang.

Pang says to improve their analyses, they now need to do large-scale mining of the mRNA markers to make sure that the mRNA expression levels correlate with the expression levels of the protein biomarkers they found. He says, "We believe that this next study will provide valuable biomarkers of male fertility and contraception" that accurately predict fertility.

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Using hamsters to study hemorrhagic fever

By Mollie Rappe

In light of the 2014 Ebola virus disease outbreak, viral hemorrhagic fevers have garnered much public interest. But not much is known about the molecular mechanisms underlying infection and progression of these diseases, so there are very few treatments and no vaccines.

The hemorrhagic fever viruses are a genetically diverse group and include Ebola, Marburg, Lassa, Hantavirus and others. They all have the same gross, even horrifying, symptoms — most notably, blood vessel damage leading to bleeding in internal organs and, in some cases, out of orifices. An article recently published in the journal **Molecular & Cellular Proteomics** reports molecular events throughout the course of infection in a model of hemorrhagic fever virus infection in hamsters. Understanding how cell-signaling networks change over the course of infection in this rodent virus, says Jason Kindrachuk, a staff scientist at the National Institutes of Health and corresponding author of the study, says could be a vital first step in the development of therapies for related viruses.

But, you might be wondering, what do hamsters have to do with Ebola and other hemorrhagic fever viruses? Pichinde virus is endemic to Colombian rice rats and causes viral hemorrhagic fever in laboratory rodents. The basic pathology of the Pichinde virus in hamsters is quite similar to that of Lassa virus in humans, and it is closely related, so it should to be a good model for recapitulating the molecular events of viral-host interactions. Plus, Pichinde virus doesn't infect primates or require many of the safety precautions other more dangerous hemorrhagic fever viruses require, making it a good model for labs without high-containment facilities.

IMAGE COURTESY OF SREEJITHK2000, A WIKIMEDIA COMMONS USER

Kindrachuk's team developed a novel hamster-specific kinome array to look at pathogenesis of Pichinde, trying to figure out what is actually going on at a molecular level. The kinome array detects changes in cell signaling networks at the level of kinase-mediated phosphorylation events. The team found that, while predictable immune-response signals were turned on during early infection and predictable cell-death and cell-survival signals were turned on late in the infection, the signals related to the formation of new blood vessels were turned on throughout the whole course of infection. Specifically, cellular responses related to vascular endothelial growth factor-mediated phosphorylation – which is a signal for blood vessel formation and widening of blood vessels – were upregulated one, three, five, and seven days after infection.

In addition, other signaling pathways related to blood-vessel formation, including those mediated by the angiopoietin receptor Tie2 and cell-motility regulator Rac1, were upregulated five and seven days after infection. These findings suggest that VEGF-mediated signaling plays a central role in host response to Pichinde viral infection and may contribute to the blood vessel leakiness seen in hemorrhagic fevers.

The team also found that the amount of proteins involved in binding cells together changed drastically over the course of the infection and corresponded to peak vascular leakage – that is, bleeding from everywhere. Two proteins, Claudin-1 and VE-cadherin, decreased as the infection progressed, while two others, intracellular adhesion molecule 1 and vascular cell adhesion molecule 1, increased. Most interestingly, this dysregulation of proteins involved in holding blood vessels together has been seen before in Hantavirus, another rodent-carried hemorrhagic fever virus.

Kindrachuk said he finds the unexpected similarity of molecular responses of infection between Pichinde viral infection and Hantavirus quite encouraging. If there is a conserved molecular hallmark among the genetically diverse hemorrhagic fever viruses, that opens up the possibility of a more general therapeutic approach. "If we could find therapeutics that are a little bit more broadly applicable and seem to attack some sort of conserved pathology within the infected individual, it gives us a better approach to dealing with these (outbreaks) as they come up in the future," he said.

The next step for Kindrachuk's team is to see how Ribavirin, an antiviral drug used to treat Lassa virus infections, or additional antiviral therapeutics, work at the molecular level. Kindrachuk says he would like to "try and pick apart the molecular mechanism for how that therapeutic is working." Another possible future direction, he said, is to exploit this new knowledge about kinases important in Pichinde viral infection and try to repurpose known kinase inhibitors as novel antiviral drugs.

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HIV: Early diagnosis saves lives

By Indumathi Sridharan

Every year, 50,000 new HIV infections occur in the U.S. (1). Thirty percent of those infections are caused by HIV-positive people who are unaware of their condition (2). As part of April's focus on sexually transmitted diseases, the Centers for Disease Control and Prevention are raising awareness on early detection and prevention of HIV. Since HIV is highly contagious in the initial stages, getting tested and treated early can reduce unintended transmission, which is an important step toward eradication.

What are the stages of HIV infection?

Initial stages of HIV infection cause severe flulike symptoms followed by an asymptomatic period that can last up to 10 years (3). The last stage is the acquired immunodeficiency syndrome, a condition where the immune system is weak enough for opportunistic infections and tumors to occur. Antiretroviral therapy can help manage symptoms and delay the onset of AIDS to prolong life expectancy.

How does HIV affect the immune system?

The virus targets CD4 T cells, which are white blood cells that mount an immune response against pathogens. Once infected with HIV, these cells self-destruct via caspase-1-mediated cell death called pyroptosis (4). Proinflammatory cytokines, like IL-1β, produced during pyroptosis recruit more CD4 T cells. The ensuing vicious cycle of infection, death and inflammation severely depletes CD4 T cells. When the CD4 T cell count drops below 200 cells/μL, it leads to AIDS (3).

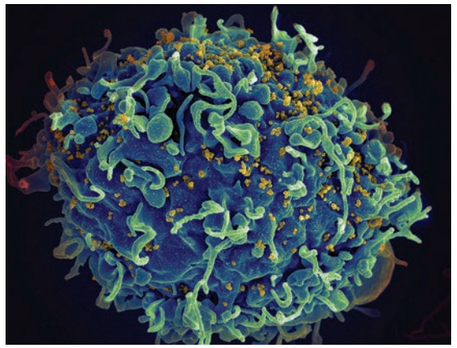

IMAGE COURTESY OF SETH PINCUS, ELIZABETH FISCHER AND AUSTIN ATHMAN, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES, NATIONAL INSTITUTES OF HEALTH

What are the recent advances in HIV diagnostics?

Latest technologies, such as a microfluidic device powered by a smartphone (5) and a nanopore-based molecular sensor (6), are geared toward rapid, portable and inexpensive point-of-care diagnostics. Paul LaBarre and colleagues at PATH, a Seattle-based nonprofit organization, developed an electricity-free heater that enables HIV diagnosis in resource-limited countries. The technology, called non-instrumented nucleic acid amplification, or NINA, uses the constant heat generated from an exothermic reaction between an alloy of magnesium and iron and a saline solution to power the conversion of the viral RNA into DNA and then the amplification of the DNA (7). Subsequent detection is based on the nucleic acid lateral flow technique. The technique, which is similar to a home pregnancy test in principle, relies on the capillary flow of the analyte in a dipstick and uses a visible color change to indicate the presence of the analyte. The technology allows early diagnosis, because it detects viral RNA rather than anti-HIV antibodies that are produced later in response to the infection. The team has developed a prototype based on field tests conducted in remote areas in Zambia, India and Kenya.

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Insights from recent plant studies

Triacylglycerol metabolism, fatty acid β-oxidation and lipid homeostasis

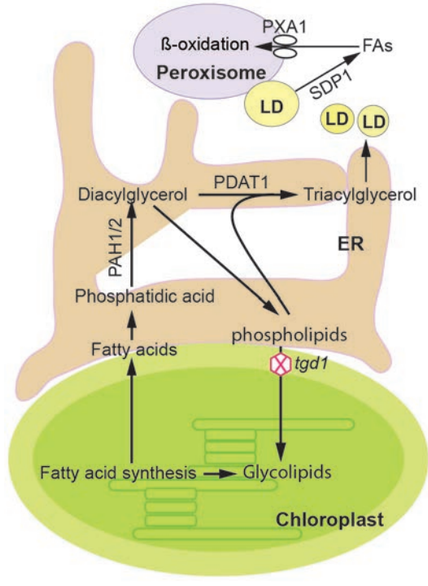
By Changcheng Xu and John Shanklin

The neutral lipids referred to as triacylglycerols, or TAGs, are ubiquitous storage forms of reduced carbon and energy in eukaryotes and some bacteria. Seeds are recognized as the primary organs for TAG storage in plants. It is interesting, however, that another structure often found in mammalian cells, lipid droplets composed of neutral lipids, are present in most plant cell types, including those in vegetative tissues, such as leaves (1). Besides its role in fueling postgerminative growth of oilseed plants, recent studies have shown that triacylglycerol represents the source of fatty acids oxidized in peroxisomes, and this metabolism is a key aspect of lipid homeostasis important for plant growth and development.

The importance of triacylglycerol metabolism in maintaining lipid homeostasis in plants is perhaps best illustrated by the trigalactosyldiacylglycerol 1 mutant, known as tgd1 (2 – 4). In this mutant, a defect in membrane lipid synthesis leads to increased accumulation of triacylglycerol and a marked increase in both the synthesis and turnover of fatty acids. Disruption of tgd1 does not affect overall vegetative and reproductive growth, but tgd1 plus inhibition of triacylglycerol biosynthesis via disruption of phospholipid:diacylglycerol acyltransferase 1 (also known as PDAT1) leads to severe growth retardation, gametophytic defects and necrotic lesions in growing leaves. This appears to be due to the accumulation of cytotoxic free fatty acids and possibly other lipid intermediates.

The deficiency in triacylglycerol synthesis also results in increased membrane phospholipid levels, which sequesters a fraction of the toxic fatty acids. Apparently, this response is insufficient to compensate fully for the buffering function conferred by triacylglycerol synthesis and turnover as evidenced by the necrosis described above.

Further evidence supporting the notion that triacylglycerol metabolism is important for maintaining lipid homeostasis in plants derives from studies in which sugar-dependent triacylglycerol lipase, known as SDP1, or peroxisomal transporter 1, known as PXA1, are disrupted.



A simplified scheme showing the role of triacylglycerol metabolism in fatty acid β-oxidation and membrane lipid homeostasis in plants

In vegetative tissues of plants, fatty acids are synthesized almost exclusively in the double-membraned plant organelles called chloroplasts. During rapid cell growth, the vast majority of de novo-synthesized fatty acids are incorporated into membrane lipids, and despite high triacylglycerol synthesis rates, triacylglycerol does not accumulate to significant levels (5).

However, when either SDP1 or PXA1 are disrupted, leaf triacylglycerol levels increase by approximately 150-fold relative to wild-type plants (4, 6), confirming that triacylglycerol is turned over rapidly during vegetative growth.

Membrane phospholipid levels increase in either tgd1sdp1 or tgd1pxa1 double mutants as they did in the tgd1pdat1 double mutant described above. These data provide compelling support for a triacylglycerol metabolism role in membrane lipid homeostasis in plants.

CONTINUED ON PAGE 13

Special symposium: evolution and core processes in gene regulation

Join us at this small, focused meeting in June in St. Louis

By Justin Fay, David Arnosti and Julia Zeitlinger

"Nothing in biology makes sense except in the light of evolution"
– THEODOSIUS DOBZHANSKY

The American Society for Biochemistry and Molecular Biology will host a special symposium this summer exploring the gap between evolutionary biology and mechanistic gene-expression studies.

The ability to survive and reproduce exerts considerable evolutionary pressure on diverse biological processes, perhaps none more than gene expression, a central hub of life. Many molecular studies have illustrated ways alterations in cis-regulatory elements play key roles in evolutionary innovations. Such changes are expected to have fewer pleiotropic effects than alterations in transcription factors or even the core transcriptional machinery.

However, the core machinery of gene expression is also subject to evolutionary selection, but less is known about how selection sculpts these complexes. The advent of new technologies has made it increasingly possible, and indeed necessary, to investigate how the central components, including the complex transcriptional, RNA processing and translational machines, experience evolutionary pressure to drive diverse outcomes on population- and species-specific levels.

The symposium seeks to foster cross-fertilization between the disciplines. By bringing together diverse international researchers in a small setting, this focused, four-day meeting will allow extensive informal interactions between participants, help them gain a better understanding of key challenges in the respective areas of study and provoke collaborations.

Speakers will include renowned scientists who have bridged the gap between hard-core mechanistic and evolutionary studies. Other outstanding invited scientists study gene regulation from standpoints of evo-devo, mechanism and genomics, including Trisha Wittkopp, Tracy Johnson and Alex Stark. In all, we will have 27 top speakers from North America and Europe who will present a rich offering of views from gene-expression research at many scales.

Justin Fay (jfay@genetics.wustl.edu) studies evolution of gene regulation at Washington University in St. Louis. David Arnosti (arnosti@msu.edu) studies transcriptional regulation in the context of Drosophila development, and leads the Gene Expression in Development and Disease group at Michigan State University. Julia Zeitlinger (jbz@stowers.org) is an associate investigator at the Stowers Insitute for Medical Research.

ABOUT THE MEETING

WHEN: June 25 – June 28

WHERE: St. Louis, Mo.

SAMPLING OF SPEAKERS:

• Robert Tjian, a pioneer in biochemical studies of transcription factors and the core transcription machinery, discovered that general transcription factors may not be always general but may function in a tissue-specific fashion and thus may have created tissue diversity in evolution. In addition to biochemistry, he currently is using genomics and imaging approaches to study transcription in stem cells and in differentiating cells.

• Mike Levine always has operated at the interface of transcription, development and evolution. Using Drosophila as a model system, his work has been pivotal in understanding the mechanisms by which enhancers control the spatio-temporal expression of genes. He also has established the model organism Ciona intestinalis to study the evolutionary origin of body plans.

• Robb Krumlauf, a long-standing investigator of Hox genes, has made key contributions to understanding segmental identity and body plan organization in development and evolution. His laboratory's recent genomic analysis of Hox genes has revealed complex specificity of regulation by Hox transcription factors.

• Rachel Green has provided key insights into the workings of that most ancient RNA enzyme, the ribosome, following early in vitro evolutionary work on self-copying ribozymes with Jack Szostak. Her own laboratory has identified key molecular mechanisms affecting ribosome processivity and control.

DEADLINES:

- **April 15:** *Deadline to submit abstract for short talk consideration*
- **April 24:** *Deadline for discounted registration (save $100)*
- **May 13:** *Deadline to submit abstract for poster presentation*

MORE INFO: www.asbmb.org/SpecialSymposia/GeneRegulation

LIPID NEWS CONTINUED

CONTINUED FROM PAGE 11

Studies in yeast and mammals established lipins, a family of phosphatidic acid phosphatases, called PAH for short, as key players in triacylglycerol synthesis. Interestingly, Arabidopsis lipin homologs PAH1 and PAH2 are not required for triacylglycerol synthesis in developing seeds, the major lipid-storage organ of plants (7). However, disruption of lipin homologs in the tgd1 mutant causes a severe decrease in leaf triacylglycerol accumulation (4), suggesting a conserved role for lipins in triacylglycerol synthesis for yeast, mammals and plant vegetative tissues.

Recent biochemical and genetic analysis has uncovered an intricate interplay between triacylglycerol metabolism, fatty acid β-oxidation and membrane lipid homeostasis in plants. These studies highlight the similarities of the roles these metabolic events play in plants, yeast and mammalian cells. They also illuminate another potential model system for studying these relationships that may provide important insights for advances in agriculture, drug development and human health.

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Changcheng Xu (cxu@bnl.gov) and John Shanklin (shanklin@bnl.gov) are supported by the Division of Chemical Sciences, Geosciences and Biosciences, Office of Basic Energy Sciences of the U.S. Department of Energy, under Grant DOE KC0304000.

Results of the 2014 ASBMB annual graduation survey

Women and men received an equal number of baccalaureate and graduate biochemistry degrees

By Erica Siebrasse

The American Society for Biochemistry and Molecular Biology has surveyed baccalaureate and graduate programs in biochemistry and molecular biology since 1999. The 2014 graduation survey was sent to more than 800 biochemistry programs across the U.S., and 133 programs participated. The survey collected information on the institutions, the degrees they awarded and their graduates' demographics.

Most of the respondents worked at primarily undergraduate institutions. Respondents working at research-intensive institutions or medical schools comprised a much smaller percentage.

Of the 133 programs that participated, 109 submitted information on the types and number of degrees they awarded in 2014. The majority of the programs awarded degrees in biochemistry, and they were primarily baccalaureate degrees. The survey did not request information on interdisciplinary programs (e.g., biochemistry/molecular biology), which likely were lumped into biochemistry or molecular biology.

Women received slightly more biochemistry, molecular biology or chemistry (biochemistry track) master's and doctoral degrees than men in 2014. Men received slightly more baccalaureate degrees. The survey did not request data on postdoctoral fellows or tenure-track faculty members, but other surveys show that the number of women declines after graduate school (1, 2).

The survey also requested race and ethnicity data for 2014 degree recipients. Students of American Indian or Alaskan Native background received 2.3 percent of biochemistry-related degrees, although they comprised only 1.2 percent of the U.S. population, according to U.S. census data. Even when the data are broken out by degree type, a greater percentage of American Indians and Alaska Natives received biochemistry-related baccalaureate and doctoral degrees than would be expected based on the U.S. population. Data on master's degrees was too limited to draw any conclusions. This difference did not seem to be driven by geography, as only 13.6 percent of the surveys were received from states in the West, as defined by the census, which had the highest number of residents identifying as American Indian or Alaska Native (3). The data are promising, but greater participation in the survey will be necessary to confirm this statistic, as only 72 institutions provided data on students of American Indian or Alaska Native backgrounds.

No programs reported a Hispanic Ph.D. recipient in 2014. However, the ASBMB survey size was not large enough to draw any conclusions about that statistic. Out of 3,368 reported degrees awarded in biochemistry, molecular biology or chemistry (biochemistry track), only 180 were doctoral degrees. In addition, the majority of surveys came from primarily undergraduate institutions.

The ASBMB is in the process of developing the 2015 graduation survey. If you are a program director or department chair and would like to participate in the survey, please email education@asbmb.org.

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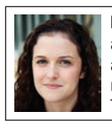

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TABLE 1

INSTITUTION TYPE	NO. RESPONDENTS
Primarily undergraduate institution	73
Research intensive institution or medical school	18

TABLE 2

	2014 ASBMB GRADUATION SURVEY	2013 U.S. CENSUS ESTIMATE
American Indian or Alaskan Native	2.3%	1.2%
Asian or Pacific Islander	18.0%	5.5%
Black, not of Hispanic origin	5.1%	13.2%
Hispanic	5.2%	17.1%
White, not of Hispanic origin	64.1%	62.6%
Unknown or other race/ethnicity	5.2%	N/A

FIGURE 1. Programs awarding biochemistry degrees in 2014

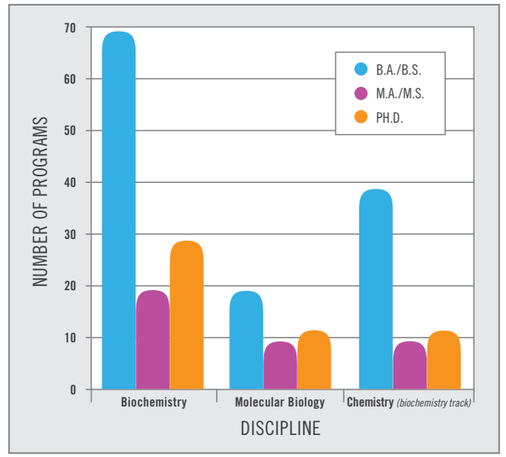


FIGURE 2. Degrees awarded by sex

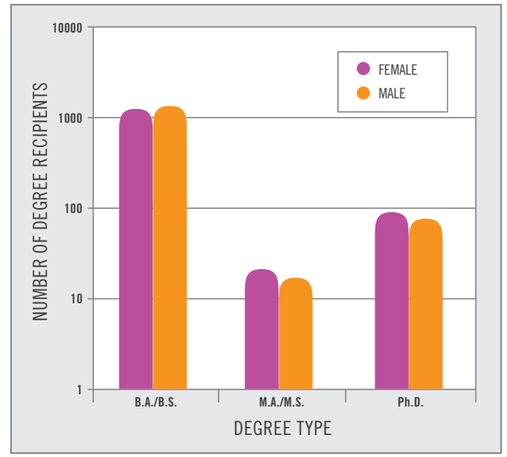
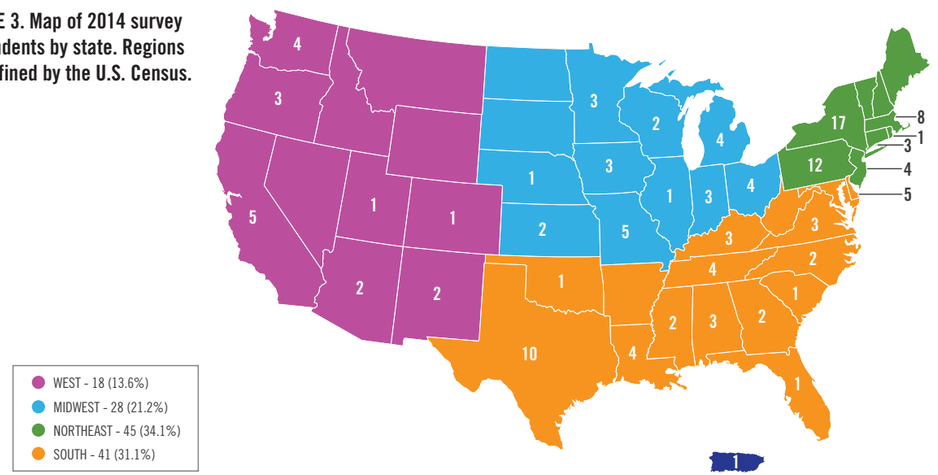


FIGURE 3. Map of 2014 survey respondents by state. Regions are defined by the U.S. Census.



DEFYING STEREOTYPES:

The other lives of cheerleaders

A select group of women with training in STEM and successful careers demonstrate that there is more to cheerleading than glitz and glamour

By Rajendrani Mukhopadhyay & Geoffrey Hunt

Simply listening to Julia, a cheerleader for the NBA's Washington Wizards, describe her weekly routine is exhausting. She rattles off a typical schedule for the team's cheer squad: "Game on Monday, practice Tuesday, game on Wednesday, practice Thursday, maybe a night off, game Saturday, practice on Sunday and another game on Monday."

IMAGE COURTESY OF WASHINGTON WIZARDS

Julia leads a cheer by the Wizards Girls during a game in 2014.

And, for Julia, this demanding schedule is merely half of her story. Like nearly all professional cheerleaders, she also has a full-time job on top of her duties on the sidelines. "I don't think people realize the double lives we lead," says Julia, who is a producer and reporter for PBS NewsHour and holds a master's degree in environmental science.

Counting nurses, accountants and lawyers among their ranks, cheerleaders like Julia and Teleza, a cheerleader for the NFL's Washington Redskins who teaches middle-school science and math, devote an equal amount of time and effort to cheering and their careers. (In keeping with team policy, neither woman can reveal her last name.) In doing so, they are able not only to fulfill their personal and professional dreams and ambitions but also to serve as role models for younger generations.

Simply by being who they are, women like Julia and Teleza represent a nontraditional type of advocacy that is critical, according to Darlene Cavalier, the founder of the STEM outreach organization Science Cheerleader. For better or for worse, cheerleaders have the aura of glamour and glitter, which "allows us to tap into audiences that are almost impossible to (otherwise) reach," says Cavalier. "There's no denying the long lines of little girls who come up to them at events who want signed autographs."

Julia concurs: "Shiny pompoms always have a way of capturing young girls' attention."

Pursuing science and dance

Teleza and Julia both say that their passion for cheerleading developed when they were little girls, brought about through an interest in dancing. Teleza remembers that when she was a child, "my mother immediately threw me into dance classes." Following a move to the Washington, D.C., area from Montreal, Canada, she trained extensively at the National Ballet Institute for the Arts and The Washington School of Ballet, and joined her high-school dance team.

Inspired by her pediatrician, Teleza also developed a strong interest in science and medicine. She was so enamored of biology in high school that she decided to major in the subject (and minor in chemistry) at Howard University with plans to attend medical school. Teleza also kept up with her dancing, joining the school's "Showtime" Marching Band, which performs dance routines at football games.

During her senior year, encouraged by former and current Redskins cheerleaders with whom she was friends, Teleza tried out for the Redskins' cheer squad. In her first tryout, she made the team, and she has been a cheerleader for the Redskins for three seasons.

Julia similarly was introduced to dancing at a young age. "The irony was when I was really little, I didn't like going to ballet classes, but I wanted to be a cheerleader," she recalls. "My mom said, 'If you want to be a cheerleader, you have to go to ballet classes.'" So Julia did ballet throughout her childhood while also developing a burgeoning interest in science, inspired by her father, a chemical engineer at Louisiana State University.

After obtaining a degree in marine biology from Duke University, Julia went on to pursue a master's degree in environment science management at the University of California, Santa Barbara, where she also ended up taking journalism classes. Deciding to pursue a journalism career after graduating, Julia arrived in Washington, D.C., in 2010 for an internship at PBS NewsHour. She ended up being hired on full time and has been there since.

For a few years, dancing and cheerleading had taken a back seat. But in 2011, Julia watched one of her former Duke cheerleading squad members, at that point a consultant at Accenture, successfully audition to be a cheerleader for the New York Knicks. "I started thinking that if she could balance both — a real stressful career and cheerleading — maybe that's something I can do," she says. Julia is now in her fourth season as a Wizards Girl and has served as one of the team captains for two years.

IMAGE COURTESY OF EMILY RAWDON

Teleza has been a cheerleader with the Washington Redskins for three seasons.

Both Julia and Teleza say that they were nervous initially about how they would be perceived in the workplace once their cheerleading personas were uncovered.

'Career suicide'

Both Julia and Teleza say that they were nervous initially about how they would be perceived in the workplace once their cheerleading personas were uncovered. Such apprehension is to be expected, says Cavalier. She points out that a generation ago, for a female scientist or engineer to admit to

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cheerleading "would absolutely have been career suicide."

However, Julia and Teleza both found that they had nothing to worry about. At first, Julia told only her boss at PBS about her cheerleading, concerned that men would behave inappropriately toward her and that women would judge her.

But as she has become more open about being a Wizards Girl, Julia has been delighted by the responses. "People are taken aback and surprised that I'm able to do almost two full-time jobs at once and that I'm talented enough to have made the team," she says.

She notes with delight that these conversations usually bring up one question: "They wonder, 'Oh, can I get tickets to the games?'" The answer is no.

Teleza has taken a different approach. At her first teaching job in a Virginia suburb of Washington, D.C., she was open about her cheerleading. But when she switched to a new teaching job in D.C., she kept it under wraps. Within a month of school starting, rumors were circulating. So Teleza took control.

In one of her classes, she confirmed for her students that, indeed, she was a Redskins cheerleader. "The reaction was hilarious," she says. One student "was taking all these deep breaths and tears started coming out of his eyes," she recalls fondly. "I asked him 'What's wrong?' He was like, 'I can't believe you're a Redskins cheerleader!'"

Fellow teachers also expressed surprise. "'If you cheer, why are you here?'" Teleza recalls being asked. "I say, 'I have to have a job too!'"

(Both Julia and Teleza make it clear that it's very hard to survive on a cheerleading paycheck.)

A life beyond pom-poms

Teleza and Julia have used their cheerleading positions to serve as ambassadors for science and reach audiences that otherwise wouldn't be exposed to science. "As someone who got teased here and there for her love of science growing up, I took pride in being a role model," Julia says of her experience working with Science Cheerleader, which has more than 300 members, during the 2012 USA Science and Engineering Festival.

Likewise, Teleza has embraced her status as a role model for her students. She constantly reminds them: "You don't have to be afraid to live outside of your box."

Both Julia and Teleza acknowledge that their days on the sidelines are numbered because of the demanding schedule and intense physical stamina required of cheerleaders. A torn meniscus forced Julia to sit out for two months during the 2014 NBA season. "I am seeing the writing on the wall," she says.

Once her cheerleading days are over, Julia hopes to have her own show on television to bring science to the masses. "I would love to see more focus on actual science and try to find ways that actually hold people's attention other than (the Discovery Channel's) Shark Week," she says.

Teleza also sees the end as near. She is taking more science classes, preparing for the MCAT, and putting together her applications. "I know once I am in medical school, I will not be able to do this," she says.

Until the day comes when they have to hang up their pom-poms, Julia and Teleza say they will continue to pursue their passions with equal vigor, because science and cheerleading are integral to their identities. As Teleza puts it, "This is who I am, and this is what I want to do."

Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the senior science writer for ASBMB. Follow her on Twitter at twitter.com/rajmukhop. Geoffrey Hunt (ghunt@asbmb.org) is the ASBMB's public outreach coordinator. Follow him on Twitter at twitter.com/thegeoffhunt. Both writers contribute equally in creating and developing the profiles for the "Defying Stereotypes" series.

Meet Hans Schöler

A new associate editor of the Journal of Biological Chemistry

By Maggie Kuo

IMAGE COURTESY OF MPI MUENSTER, SARAH EICK

Hans Schöler joined the Journal of Biological Chemistry as an associate editor in May. He is a director of the Max Planck Institute for Molecular Biomedicine in Münster, Germany. Schöler's laboratory investigates how mature body cells can be reprogrammed into pluripotent stem cells. This interview has been edited for length and clarity.

Would you briefly explain what your research group is studying?

We study how pluripotency is induced and what mechanisms drive this process. We have shown that a gene called Oct4 plays a key role. Normally, it is expressed only in gametes, two types of cells that are completely undifferentiated: embryonic stem cells and the precursors of egg and sperm cells. In contrast, in all mature cells, Oct4 persists in a Sleeping Beauty-like state and therefore must be targeted and activated if we want to transform mature cells into pluripotent ones.

Although we have several reprogramming techniques at our disposal today, none of them has proved optimal. We are striving to develop methods that enable reprogramming of Oct4, and any other required gene, in a more targeted way and with as few adverse effects as possible for the patient.

Tell us about your academic background and research training.

I studied biology at the University of Heidelberg. For my diploma thesis, I purified and studied topoisomerase I, a rather biochemically oriented topic. My Ph.D. thesis concerned studying transcriptional enhancers. At that time, those elements had just been described in mammalian cells, and I was the first to show that cellular factors have to interact with enhancers to be functionally active.

After completing my Ph.D. in molecular biology at the University of Heidelberg, I was appointed head of several research groups in Germany, namely at Boehringer Mannheim, now Roche, the Max Planck Institute for Biophysical Chemistry in Göttingen and the European Molecular Biology Laboratory in Heidelberg. In

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1999, I was offered a professorship at the University of Pennsylvania, where I served as professor of reproduction physiology at the School of Veterinary Medicine and director of the Center of Animal Transgenesis and Germ Cell Research.

In 2004, I was appointed director of the Max Planck Institute for Molecular Biomedicine in Münster and moved back to Germany. I am also a professor at the University of Münster and an adjunct professor at University of Pennsylvania; Hannover Medical School; and two South Korean universities, Ulsan National Institute of Science and Technology and Konkuk University. Actually, I visit South Korea quite often, because a number of Korean professors were trained in my department and I make a point of maintaining a close collaboration with them.

Did anything occur, in a milestone sort of way, that made you choose science as a career?

Not really. I have always been excited about biology. Even as a boy, I loved watching insects and studied their behavior. "The Dancing Bees" by Karl von Frisch was one of my favorite books at that time. I wanted to understand how insects develop and was extremely happy when I had earned enough money from my summer job to buy my first microscope. That was when I was 14. In my high-school years, I was fascinated by books like Erwin Schrödinger's "What is Life?" and Jacques Monod's "Chance and Necessity: An Essay on the Natural Philosophy of Modern Biology," to name just a couple. There were countless other books on similar topics that I found extremely stimulating to read. You could say I was a bookworm. I gradually developed into this person who wanted to understand developmental processes at the molecular level.

During grad school and/or postdoc, did something especially impress you to choose the path you've taken in research?

One paper that really struck me right between the eyes was the report on the cloning of Dolly by Ian Wilmut, Keith Campbell and co-workers published by Nature in 1997. I had an incredibly hard time believing that the transfer of a somatic cell nucleus into an enucleated unfertilized egg could actually result in a viable organism. Just imagine what it meant to repack all those chromosomes! Then Teru Wakayama, Ryuzo Yanagimachi and co-workers showed in 1998 that this was also possible in the mouse, again in Nature. I wanted to know how reprogramming works. And we've been working to break down the process since then, but still there is a lot to explore!

What does it mean to you, on a personal level, to be an associate editor for the JBC? What was your reaction when you were asked to be an associate editor?

I was surprised and also very happy. I was surprised, because so far, the JBC, albeit quite broad in scope, has not really been known as a platform for stem cell research. But quite clearly, this is what I should stand for — to encourage stem cell scientists to send their exciting work to the JBC! I was very happy, because it acknowledges that the manuscripts I have submitted are as solid as possible, even if it meant we only came in second. I am also proud and honored to take on this role for the journal, because the JBC has such an amazing tradition. The first issue was published in 1905! To be part of such a long tradition means a lot to me, and I look forward to expanding coverage of the stem cell field to the readership of the JBC.

How is the new role going so far? Have you been surprised by anything during your tenure with the JBC?

I was actually quite surprised by how much fun it is to be part of the JBC family and to take part in the associate editor meetings. So far, I've attended two. Certainly, being an associate editor comes with a lot of responsibility and work, but the meetings and discussions with the other associate editors are a real treat and a great forum where I can share in discussions and learn a lot. I am on the editorial boards of top-notch journals such as Cell, Cell Stem Cell and other stem cell journals, but with the JBC, I am really on the other side of the process. The JBC allows me to serve other scientists in the most direct way. My hope is that I will deal with their submitted work in the most respectful manner.

What do you do outside of the lab? Hobbies? Do you have any advice for balancing life in the lab with life outside of the lab?

I always tell my friends that I am paid for my hobby. Isn't it exciting to see something that nobody else has seen before? It is like being Columbus and discovering America over and over again. But of course there is more to being a scientist than just doing the science — and I guess every scientist knows what I mean — like administrative meetings. Life outside the lab is also important to me, and that means finding time to be together with my family, to meet friends and to enjoy the arts. I went to Africa last year for the first time in my life. While my friends and my wife especially enjoyed the large animals, the amazing beetles that I watched in Botswana and Namibia fascinated me.

For scientists in training, do you have any words of wisdom or a favorite motto?

Be curious and critical, but also respect the accomplishments of other scientists.

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

Drawing inspiration from science

Biochemist Vikram Mulligan finds his artistic muse in structural biology

By Indumathi Sridharan

In 1961, Irving Geis illustrated the sperm whale myoglobin molecule based on the crystal structure deduced by John Kendrew and colleagues (1). This iconic painting is touted as the first molecular illustration. While early illustrators like Geis used watercolors and ink, modern illustrators craft their designs on computers. Vikram Mulligan, a biochemist with a talent for digital art, captures the intricate structure and exquisite contours of a variety of biological systems in his illustrations.

MULLIGAN

Mulligan is currently a postdoctoral researcher at the University of Washington. His research focuses on protein folding and misfolding mechanisms and the design of artificial peptides for therapeutic purposes.

Through his art, Mulligan has depicted biological entities, such as protein cages, inhibitors against influenza hemagluttinin and prions. He also has created animations of protein folding for a lecture series on bovine spongiform encephalopathy (also known as mad cow disease) presented by science broadcaster and writer Jay Ingram. Besides scientific illustrations, Mulligan loves science fiction and often depicts spaceships and distant worlds in his art.

Designing 3-D digital illustrations is more than a hobby for Vikram Mulligan: It is a creative process that fuels his scientific thinking. In this interview, Mulligan explains how his art inspires his scientific work. The interview has been edited for length and clarity.

What is your research focus?

My doctoral work at the University of Toronto focused on the unfolding and misfolding processes of superoxide dismutase, a protein involved in amyotrophic lateral sclerosis. I also studied the general mechanisms of protein folding and misfolding.

My current work at David Baker's laboratory at the University of Washington deals with the development of new computational algorithms for the design of cross-linked peptides and artificial heteropolymers with rigid structures.

How did you get into science?

My parents were a big influence. My mother is a geneticist and my father, although not a scientist, has a deep interest in astronomy, an interest that I inherited. They instilled the value of academic excellence and a love for learning and exploring the world. I always wanted to be a scientist, but I did not know what field until I got to university. I majored in physics and biochemistry for my bachelor's degree. I decided to stick with biochemistry for my Ph.D. I think there is nothing more satisfying than exploring the world and being able to say, "Yes, I am the first person to know this new fact."

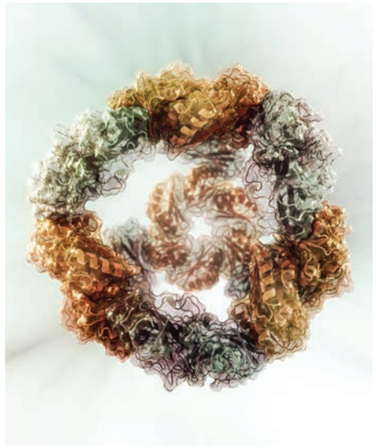
How did you get started with digital illustration?

I used to build lot of plastic models of spacecrafts when I was a kid. I always liked science-fiction movies, particularly the work of special-effect artists of the '60s and '70s. When I watched "Star Wars," part of me said, "Wow, what a great movie," and another part said, "How did they do that?"

So I read a lot about how special effects were done. I taught myself how to do 3-D computer graphics. Not only was it a fun activity and a way of distracting myself, but it turned out to be a very useful skill eventually.

How do illustrations benefit science?

Illustrations can be educational. The figures and graphs in a scientific paper are not informative to a layperson; they are too detailed and technical. But illustrations are a visually appealing means to convey the science behind a concept.



A rendering of an artificial two-component protein cage designed by David Baker's laboratory. Reference: http://www.ncbi.nlm.nih.gov/pubmed/24870237.

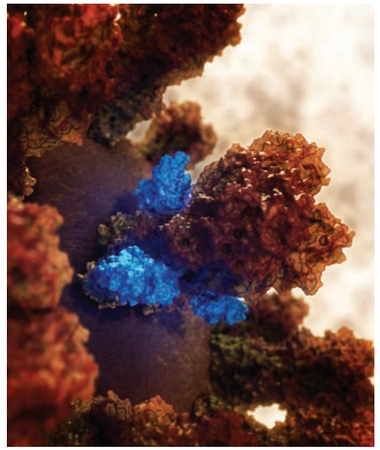


Illustration of an artificially designed protein, HB36.3 (shown in blue), binding to influenza hemagglutinin (shown in red). Reference: http://www.ncbi.nlm.nih.gov/pubmed/21566186.

IMAGES COURTESY OF VIKRAM MULLIGAN

A rendering of the prion protein, PrP.

What tools do you commonly use for your artwork?

In general, I use whatever tool does a particular part of the job well. For example, when illustrating molecules, I start with PyMol to set up the surface and cartoon geometry. Then I use Blender, a free, open-source 3-D program, to transform the crude-looking representation into a polished version. I create different versions of the molecule with little tweaks in texture, rendering or lighting and superimpose the different versions in Photoshop for final compositing.

Did your interest in digital art and illustration play any role in choosing protein design and protein folding for your research?

There is a visual component to structural biochemistry. I like that there is something concrete to look at and manipulate in 3-D. So I do believe that my interest in visual art and 3-D graphics led me to this particular field. The same skills that I use in my art also help me visualize, design and manipulate 3-D models of proteins in my work.

How does your artwork influence your scientific work?

When I am working on a (nonscientific) illustration purely for enjoyment, that is when my mind wanders and I come up with some creative ideas or solutions to problems in my research. Recently, I was trying to debug a piece of code (that I am developing for peptide design). The source of the particularly tricky bug only occurred to me while I was working on some completely unrelated artwork.

Tell us about the nonscientific themes in your art?

My father's interest in astronomy has a lot to do with my interest in science fiction and space exploration. Science fiction often gets the science wrong. But at the same time, the imaginative aspect of science-fiction movies and stories is very appealing to me. Picturing a better world made possible through science or imagining the possibilities of science is why I like science fiction so much. I explore these ideas through nonscientific illustrations, such as ones of space exploration and space ships, and not battles.

What are your plans moving forward? How will you reconcile science with art in your future endeavors?

I like academia quite a lot. I hope to find a professorship in the next few years and continue working on protein design and folding. I suspect that the artwork will serve the same two purposes it has served so far: One, a fuel for creative thought and a needed distraction from work and two, a means of conveying information about my research.

REFERENCE

1. http://shar.es/1g5ntB

Indumathi Sridharan (sridharan.indumathi@gmail.com) earned her bachelor's degree in bioinformatics in India. She holds a Ph.D. in molecular biochemistry from Illinois Institute of Technology, Chicago. She did her postdoctoral work in bionanotechnology at Northwestern University.

‘I found the notes’

By Rossie Clark-Cotton

Many years ago, when I read Mark Salzman’s novel The Soloist, about a cellist whose childhood promise overshadows his adulthood, I was introduced to the cello suites of J.S. Bach. Salzman’s protagonist is a cellist in his 30s, a former child prodigy who no longer plays in public. Determined that he will someday play again professionally, he practices the Bach cello suites every day but only for himself and his cat.

When I finished the novel, I wondered what sort of pieces could hold that kind of allure — to warrant revisiting each day? Was it their technical difficulty? Their emotional richness? Alluring melodies? I went out and bought a CD of the pieces. I’d never really heard much string playing, but I’d assumed I’d only hear a melody, a single voice carrying a tune. But Bach had embedded harmonies in the melodic line of a single instrumentalist. The sound was dark, rich and complex. It suited the instrument on the cover of Salzman’s novel. I loved the cello suites. From then on, in my fantasy life, I was a cellist.

Years later, I lived in a city with several well-regarded music schools and a dearth of jobs for the professionals who were trained there. Opportunities to take music lessons were all over, including at the music school a brief walk from my apartment. I wanted to learn to play the cello, but I had no car and would struggle with it on public transportation. A friend played the viola, and she taught me all of its virtues: less flashy, less shrill and richer in sound than the violin; smaller, more manageable and cheaper than the cello. It is hard to hear the viola line in a string quartet, but you’d miss it if it wasn’t there. “The inner voice of the strings,” she said, “the alto.” I sang alto in choirs, and I loved low notes. Alto strings would suit me. I could rent a viola from a local instrument store.

I mentioned my idea to a few musician friends. “Learning the viola is hard,” I was told. “It’s really easy to pick up the guitar, but you have to learn the viola when you’re young, or you won’t be any good.”

“But I can sing,” I objected. “I have a pretty good ear. I sing on pitch. I can read music decently.”

“It takes so much practice,” I heard. “Do you have time for that?”

This was a good point. I had a full-time job. I sang in a chorus and took voice lessons. I was thinking about going back to school for a Ph.D., so I took a biology class most semesters. No, I probably didn’t have time to learn to play the viola. But it was summer. My chorus was on hiatus, and I wasn’t taking a class. My work schedule had become a little lighter. The local music school offered trial lessons — as many or as few as you wanted — over the summer. No, I probably didn’t have time, but I was curious: Could I do it, or was it too late? I would only know if I tried. So I went to the instrument shop, picked out a rental viola and signed up for a handful of summer lessons.

Rossie Clark-Cotton is a Ph.D. student at Duke University.

The first surprise: For reasons I still don’t quite understand, the viola has its own clef. As a choral singer, I can read the treble clef, and in a pinch, I can summon some mnemonics from childhood and muddle through the bass clef. But a C on the alto clef is just half a line below its position on the treble clef. So I was constantly looking at a note and thinking, “OK, that looks like a G, so that means it’s an A. I think that’s a D, so it’s really an E.” To play the viola, I would have to learn to read the alto clef, a skill that would serve me no other purpose unless I also decided to take up conducting.

But there were interesting things about the viola. My teacher started me with exercises to learn to hold the bow — how to pivot my wrist, the proper angle and height for my elbow. He showed me how the quality of the sound changed when I used different parts of the bow and when I placed it on different parts of the bridge. I found that applying resin to the bow allowed me to produce a lovely sound with less effort. I listened as the tone changed throughout a bow stroke, and I tried to make a consistent sound throughout the note. I discovered how responsive the instrument was to subtle changes in my bowing. I started to recognize the clashing vibrations that signaled that the strings were out of tune relative to each other. I began to play scales that didn’t make me cringe and learned some simple tunes. I signed up for more lessons during the fall and eventually bought the viola. But I didn’t practice enough, and progress beyond first position was slow.

I recently moved to start a Ph.D. program, and as I sorted things from my closet, I found the viola case, where it had been resting for two years. I opened the case and recognized it all: the dark, polished wood; the smell of the resin; the bow not quite taut. I tightened the bow and played a few strokes. It sounded out of tune, so I took a few moments with the metronome and then tried again, playing a scale. My fingering was off, but with a few attempts, I found the notes. But it was time to pack and move and set up my apartment and then to meet classmates, navigate a new campus, start classes, begin lab rotations and apply for fellowships.

But it turns out that my new home also has a music school just down the street. Someday.

Rossie Clark-Cotton (mrc47@duke.edu) has degrees in biology and linguistics and is currently a Ph.D. student in Cell and Molecular Biology at Duke University. She was a 2013 winner of the Just-Garcia-Hill science blogging contest, a 2014 American Academy for the Advancement of Science Mass Media Fellowship semifinalist and a participant in the ComSciCon 2015 science communications workshop. She enjoys reading, singing and learning about the history of rural Mississippi, where her family has lived for more than 130 years. This semester, she is satisfying her love of J.S. Bach by singing the St. Matthew Passion as a member of the Duke Chapel Choir.

‘There is a lot of work to do’

By Christopher W. Williams

I am often told that I do not fit the stereotypical profile of a scientist. Is it because I am a tall, former collegiate swimmer and extremely extroverted? Or is it because I grew up in Baltimore City and posed for pictures at my Ph.D. graduation ceremony with dreadlocks under my cap? As you may have guessed, I am a young African-American male scientist. I am not the first, but I am still a rarity in the life sciences. My atypical look provides an opportunity to engage with others to deconstruct the stereotype and actively diversify the profile of scientists.

Although I am passionate about science, I realize that I could be the last scientist in my family. I accept that my future children may not be interested in following in my footsteps. However, I do not accept that a child, especially one who looks like me, may never have the opportunity to become a scientist and contribute to groundbreaking research, discovery and innovation.

My strategy to address this is to start the recruiting process early for the next generation of African-American scientists through effective science education and outreach initiatives.

My recruiting tactic is simple: I show up. I consistently give my time and energy to disprove misconceptions about who scientists are, what they look like and how they can impact the world. The students do the rest of the work. They are challenged and encouraged with science lessons and, as a result, demonstrate improved reading, analytical, math and interpersonal communication skills.

Christopher W. Williams

My goal is not to turn anyone into a scientist but rather to improve scientific literacy and allow future scientists to reveal themselves. Ultimately, I want the students that I interact with to become more focused and confident individuals.

With that said, I must get going. There is a lot of work to do.

Christopher W. Williams (Christoph.W.Williams@gmail.com) is a postdoctoral fellow studying genetics at the National Institutes of Health. He grew up in Baltimore City, Md., where he attended public grade school. As a child, he was fascinated by living things. He took that passion for biology to Frostburg State University. He earned his Ph.D. from Georgetown University in 2012. Contact him for STEM-related educational and outreach opportunities.

The reality that dare not speak its name

By Andrew D. Hollenbach

I walked into an empty lab. I looked at the bare desks and benches, and I was overcome by emotions too strong to contain. It was the day after my lab manager left, forced to find a new job by a vicious funding environment that took a trusted employee and friend from me and shut down my research program.

I spent 20 years studying the mechanisms underlying a childhood muscle tumor. I published more than 20 articles with a lab of no more than three people at one time, intentionally kept small so I could focus on mentoring. I established a new paradigm in my field, identified viable therapeutic targets and trained five students (three of whom went to Harvard University for postdocs). I am recognized worldwide for my research.

You would think that all of that would be enough to bring in money and continue my research. But it's not.

With only one out of 20 researchers getting funded by a seriously flawed reviewing system and with careers being validated not by the quality of work but by the flashiness of the work, my life is the harsh reality of what is happening to research in this country. Good people are leaving academic science, forced out by a lack of money, inequity in decision making, and hypocrisy in career recognition and advancement. Many are tired of playing a game whose rules change before you even know what the rules are. The job Sisyphus had looks easy in comparison — and it was probably more rewarding!

Some may say that I did not do enough. Maybe I didn't. I could have been a slave-driving mentor to get more publications in journals with higher impact factors. I could have worked 80-hour weeks, ignoring my family and friends. I could have given in to unfettered ambition, rolling over anyone who got in my way.

However, that is not who I am. Ultimately, I must be true to who I am and not what the system requires me to be. By staying true to myself, I produced good science, established myself as a person of integrity who can be trusted to do a job well and became known as an engaging, demanding, yet caring teacher with the best interests of his students in mind.

In the long run, that is not enough to secure money to continue my research. My career was decided by others: a government that does not value research, a review system so flawed that a fair review is not possible, and academic committees that focus on one aspect of a person's career to determine their advancement. Because of these factors, I stand in an empty lab with no money, no workers, no ability to do research — yet needing to do the research to bring in the money. This is the horrible catch-22, a vicious circle, a no-win situation.

In the early 1900s, when on trial for gross indecency to mankind, Oscar Wilde called same-sex love "the love that dare not speak its name." Everyone knew it existed, but nobody wanted to speak its name. Today, I am the face of reality in academic science, the reality that dare not speak its name.

Look at my picture, and you will not see a failure. You will see someone who worked hard, excelled at what he did, held true to himself and maintained his integrity. However, you also will see someone whose work was brought to a halt by an unfair system.

Life has come full circle. I started this phase of my career standing in an empty lab, arriving there through hard work and drive. I now stand in an empty lab at the end of this phase of my career, an end brought about by a system that has changed such that I no longer recognize it.

In essence, this is the beginning of a new phase of my professional life, and honestly it is very exciting. It's a chance find out what else I love to do and a chance to find a way to do what I love without having to be evaluated by the system. At this juncture, I feel two very different, yet very powerful, emotions: sadness and hope. I know I am not alone in feeling these conflicting emotions; I just have the strength to talk about it. So take a good look at my face, and pay close attention to my words. I am the face and voice of the reality of academic science in the 21st century.

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

So you want to be a graduate student?

A commencement speech

By David B. Iaea and Natalya Gertsik

Each year, we have the opportunity to meet the incoming class of graduate students and witness their optimism and ambition. By the time we cross paths again, many of them are looking for jobs outside academia or considering dropping out to work on Wall Street. The long hours, interminable troubleshooting and low pay of our industry contribute to the general disillusionment, but a kind of naive obliviousness is equally to blame: Many people simply do not come prepared.

So, to those serious students who crave to know what it is they are entering into, who are mentally and spiritually ready, willing and able — those who have a visceral need to know and understand — we say this: Welcome to our world! We offer the below advice, gathered over a perilous half-decade spent pursuing Ph.D.s in the biomedical field, to prepare you for the journey to come.

Be dedicated

Don't be a fence sitter or a flip-flopper. If you are going to be a scientist, be sure about it. Be single-minded in your determination to achieve the goal you have set. If the idea of standing in the cold room all day purifying a protein makes you want to curl up in a blanket and cry, or if squinting at a confusing Western blot wondering if the band is real or the result of spilled coffee leads you to doubt the wisdom of your decision, you will be a liability not only to yourself but to others.

Biomedical research is a certain path to uncertain data, and you must be OK with the ambiguity as part of your daily routine.

Be prompt

Keep reasonable hours in the lab and arrive at classes and meetings on time. Despite the inherent flexibility of your work schedule, do not let yourself slide into an overly relaxed routine just because no one is punching you in and out of the office. Scientists generally roll into work at a pleasant 10 a.m., so go ahead and sleep in a little, but remember that you will probably get a lot more done if you show up in the morning, not the afternoon. Similarly, arriving late to meetings reflects poorly not only on you but also on those you represent. In the best case, your lateness simply will be noted. In the worst, you will have missed your own presentation, and the seminar will go on without you. Also, do not make it a habit to call in sick. Unless you are bleeding from the eyes, have lost a limb or there was a death of an immediate family member, you can tough it out and make it into lab.

Never make excuses or blame others

This is most tempting when your experiments are not working and you discover cathartic release in scapegoating a colleague or junior student. It is easy to blame the technician for making a faulty buffer, the lab manager for ordering the wrong item or the rotation student for contaminating the samples, but as a graduate student, you must recognize that you are the one who planned, executed and screwed up the experiment. Figure out what went wrong, own up to it and don't do it again. Ever. You are going to make mistakes; at least keep things interesting by making different ones.

Be prepared to witness every form of human folly and injustice

Science is no different from other industries when it comes to potentially strained employer-employee relations, unfair credit and compensation, and workplace strife. What may be different is your unrealistic expectation that biomedical research is invariably just while banking is fundamentally vile. The truth is that you will have to endure or confront the contradictions, double standards and inequities of this and any other work environment. Do not let petty squabbles drive you to tears or depression, but do chime in, for example, if

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your contribution to the manuscript is being overlooked.

Stay motivated even when there is little hope for immediate gratification

The first year of graduate school consists of classes and rotations, both of which have strict deadlines similar to those of a curriculum at an undergraduate institution. However, the next five to six years are an amorphous amalgam of not-really-required requirements.

For example, you can apply for a fellowship, but you do not really have to. You can present at the Gordon conference, but chances are no one will notice if you don't. Additionally, with the exception of grants, there are few strict deadlines. You can choose to write your manuscript this month or next month. You can schedule your committee meeting anytime between April and September. You can pick up that new project today or forget about it entirely.

The freedom can be liberating and inspirational, but it also can cause a kind of dejected impotence, crippling your ability to be timely and productive.

Do not covet thy neighbor's project or Nature paper

Your neighbor's project may be flourishing while yours is floundering in a sea of 5 percent blocking milk, but remember that what matters most in these five to six years are your personal accomplishments (not how many papers your lab mate has published). After classes are over, you are not in direct competition with any of your colleagues. Focus on your science — not theirs.

Do not lie

Small lies have a way of building on one another until the line between omission and fabrication is blurred entirely, as evidenced by the many horror stories of prominent scientists' falls from grace. Reputation is everything. Keep yours unscathed.

Choose an adviser who is a good mentor

Your adviser and, to a lesser extent, committee are going to be your guides through graduate school. Besides making the choice to attend graduate school, choosing the right adviser is the most important decision of your academic career. No pressure!

Read, read, read!

This is one of most important habits of a blooming scientist. Keep a constant and vigilant eye on the literature for your area of interest, development of new techniques and, most importantly, your competition. This will help prevent you from spending several years working on a project only to realize that your competition already published the same data. While you may find that there is an overwhelming amount of literature on any given subject, learning how to sort through a sea of esoteric information is part of your graduate training, so jump right in.

Have a sense of humor about things

You are going to need it.

On the bright side

The above list, by attempting to prepare incoming students for the more challenging aspects of graduate school, attests to the difficulty, laboriousness and confusion of pursuing a biomedical Ph.D. without giving equal voice to the advantages of spending six years in an intellectual alcove teeming with brilliance and inspiration. In the spirit of fairness and balance, here we offer a few words on why attending graduate school is, contrary to popular belief, one of the most worthwhile endeavors you will undertake.

First, you will make friends — the kind who witness the roller coaster of your graduate-school career and empathize every step of the way; the kind who drink with you at happy hour to mourn the day your paper is rejected by one top journal and to celebrate the day it is accepted by another; the kind who critically read your fellowships and manuscripts for nothing more than a brief acknowledgment at the bottom and a hope that you will do the same; and the kind who come into work on a Saturday morning to read your plate because you are feeling particularly hungover and incompetent that day.

You will learn to ask great questions, make astute suggestions, troubleshoot complex problems, respond prudently under rapid fire and store beer in the cold room in a way that makes it impossible for anyone but you to find it.

You will become an expert in your field and give back to the scientific community. You will inform your colleagues about the new trick you discovered for setting up a more reliable assay, you will teach the rotation student how to run a Western blot and you will mold the college junior into an up-and-coming scientist. You will enlighten your committee members and your boss, people who invested a great deal of time in your education so that you could return the favor.

So go to graduate school, because while there will be no grades, dean's lists or guidance counselors to gratify your ego-driven need for commendation, there will be a self-propagated collection of opportunities and achievements that are more intimately yours than any A+ we can deign to award you.


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For technicians only

By David B. Iaea

For the laboratory technicians who are in the trenches and considering going to graduate school, I have some advice too. As an ex-technician myself, I may be able to offer relevant insights.

So you really, really want to be a scientist? You want to go to graduate school and earn those three little letters (Ph.D.) after your name?

First, let's back up: You have become familiar with this business, accustomed to working eight- or nine-hour days, with weekends, evenings and holidays off. You went home for your father's 60th birthday, picked up guitar lessons two nights a week and still managed to get your name on a paper or two. You enjoyed a structured work schedule and were treated with a modicum of dignity by your colleagues and employers.

You think graduate school will be a prolonged extension of this condition? Then perhaps you should reconsider.

The first year of graduate school is a confounding and arduous combination of difficult courses and disorienting rotations, juggled until you drop the ball, become a master multitasker or sign up for psychotherapy sessions because they are free with the school's insurance.

You will have little to no time for hobbies, trips or a significant other, and good luck explaining to your grandmother the concept of not having vacation time when she calls biweekly for four years straight to ask if you are coming to visit for the holidays.

You may be more overwhelmed within the first month of graduate school than at any other point in your life. However, don't let that stop you.

Graduate school will give you the opportunity to own your projects, first author your papers and control the direction of your experiments. It will be a chance to birth and raise your own thought babies, not just babysit someone else's.

It may be one of the most rewarding experiences of your career, and it will allow you to put the manual skills you already have to the critical-thinking skills you crave to nourish.

Rooting student assessment in the literature

A proposal for a Web-based resource using current research papers

By Henry Jakubowski

Imagine if biochemistry and molecular biology instructors could go to the cloud and download high-quality assessment questions based on current research published in journals, such as the Journal of Biological Chemistry, for undergraduate classes. Key to such a collection would be the quality of the assessment questions. They should probe students' ability not just to remember and to understand but also to apply, analyze and synthesize information and concepts. These skills correspond to higher level cognitive learning objectives articulated by Bloom's Taxonomy (modernized in figure 1). I would like to propose a model for such a Web collection to meet this need. By sharing this vision, I hope to generate interest and foster collaboration with the larger community of educators to develop such a resource.

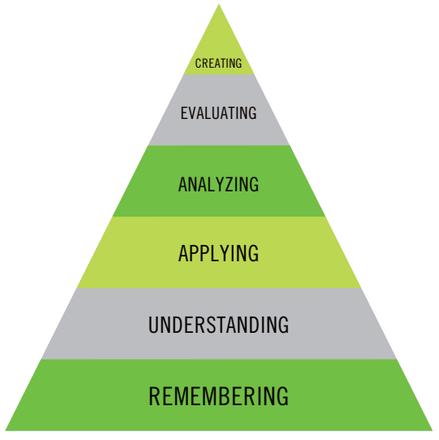

FIGURE 1. Bloom's Taxonomy

Over the past 27 years of teaching, I have discovered that exams based on recent research publications readily target those higher level Bloom's Taxonomy skills. It has become increasingly apparent to me that it is more important that students develop scientific reasoning and inquiry skills and an understanding of how our knowledge developed than that they memorize a canon of structures and pathways.

Existing resources

In line with these ideas, new initiatives by the American Society for Biochemistry and Molecular Biology and the Association of American Medical Colleges endorse and assess learning competencies and defined learning goals and objectives (instead of proscribing a list of courses) for students studying biochemistry and molecular biology and taking the new MCAT15 exam.

The new MCAT, offered for the first time this spring, has an explicit section on biochemistry, as input from targeted cohorts showed it as important for academic success in medical school. The exam also puts greater emphasis on scientific reasoning and inquiry skills. Anyone familiar with the ASBMB core concepts and associated learning objectives can see immediate congruence with the MCAT goals (figure 2).

Over the past three years, the AAMC developed the Pre-health Collection of the iCollaborative (1). This Web repository of resources is for faculty members and students (especially those at under-resourced institutions) as they teach and prepare for all areas represented in the new MCAT. All material is searchable by, and tied explicitly to, biochemistry foundational concepts and associated content categories. As an editor for biochemistry submissions, I have seen the potential this site offers. The value of an even more expansive collection based on the research literature and covering a wider range of biochemistry and molecular biology topics becomes apparent.

In a parallel fashion, the ASBMB division dedicated to education has developed an institutional accreditation process for biochemistry and molecular biology degree programs and a way to certify graduates of those programs (2). For accreditation, institutions must have a curriculum focused on critical-reasoning skills, laboratory experience, and the development of students' scientific communication skills.

For certification, students must pass an exam in their junior or senior years. Efforts also are continuing

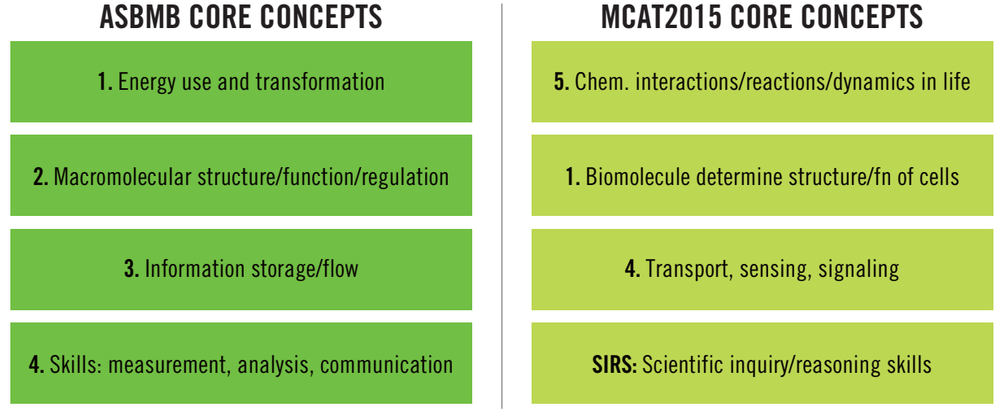

FIGURE 2. How ASBMB's core concepts relate to new MCAT core concepts

to develop summative assessment questions for that exam. Although the ASBMB efforts are not targeted toward formative assessment per se, the Education and Professional Development Committee also initiated a broad effort to build Web resources that will help move faculty members toward "concept-driven teaching strategies" (3). Specially, the committee seeks to build a collection of tools to assess key concepts and student skills.

A proposal

An easier and more robust process to create formative assessments is still lacking and needed. I propose that the community of biochemistry educators build, contribute to, review and curate a Web-based collection of assessments based on research literature. This initiative very clearly would complement the AAMC and ASBMB initiatives. If a database of such open-ended, literature-based questions were available, it greatly would help faculty move toward a more progressive approach for assessment of student learning.

To offer an example of what the collection could look like, I developed a prototype collection containing four literature learning and assessment modules (called LLAMs for short) that target the four ASBMB core concepts and associated learning objectives and that broadly overlap MCAT2015 biochemistry foundational concepts and associated content categories (4). The chosen articles and questions are typical of what a broad group of educators might use as the basis of an assessment in a biochemistry class. The richness of experimental techniques used to develop assessment questions for one of the LLAMs should be obvious immediately from the collage of figures taken from one JBC paper used for that purpose (see figure 3) (5).

I chose to use open-ended assessment questions in the LLAMs because they take less time and are easier to write (though not grade) than credible and valid multiple-choice questions. That's also what I have used in my classroom.

In my prototype, faculty members can use a Web version, a downloadable version that they can adapt easily and a key. I also included a student version with the full assessment, a question-by-question version with links to an answer after each question, and a full key.

Each assessment begins with the relevant JBC reference, use guidelines, and tables that show the ASBMB and MCAT foundational concepts addressed by the questions. The main assessment consists of background from the paper followed by questions based on figures, data, graphs, images and legends. The format is obviously only one of many possible ones.

An established collection of resources theoretically could be available to both faculty (as a teaching resource) and students (as a learning resource, as is presently the case for the AAMC Pre-health Collection. If it were available to students, it could enhance their development of the scientific inquiry and reasoning skills needed for their majors, future education and careers. It also would help students prepare for summative exams including the ASBMB certification and MCAT exams. However, student access might dissuade faculty from contributing and using the resource. Until a sufficient number of resources is available, it would be best to limit access to faculty.

Participation needed

How can we move from this simple prototype to a structured, sustainable and utilized Web resource? Darrell Porcello and Sherry His at the University of California, Berkeley, recently described ideal characteristics

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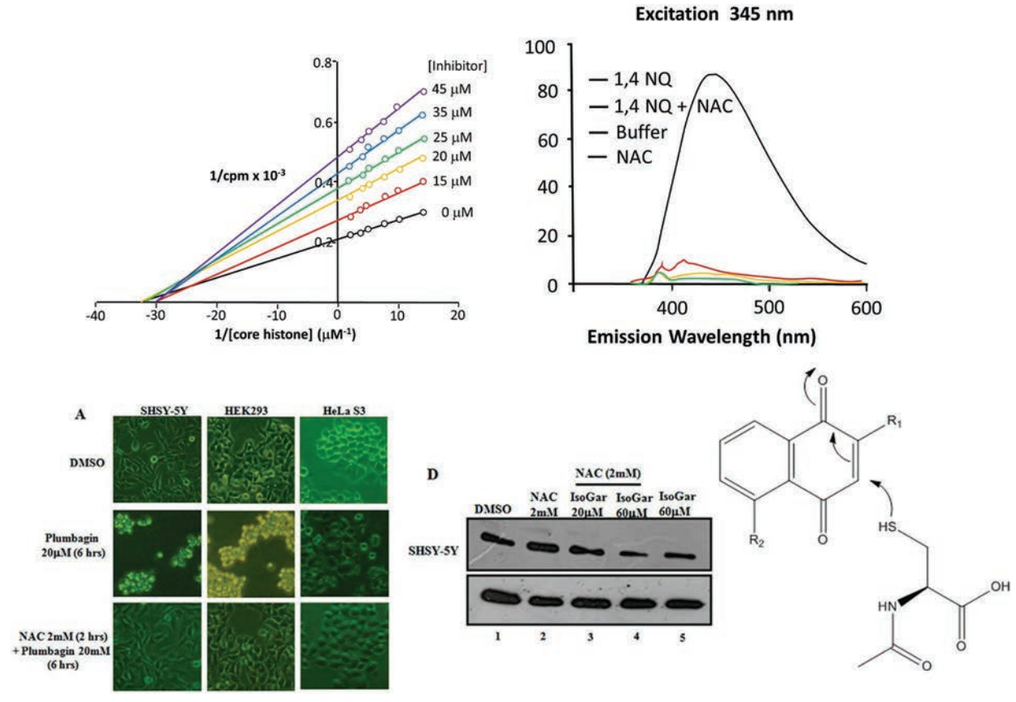

FIGURE 3. Sample JBC figures from http://www.jbc.org/content/289/11/7702

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of online educational resources for use in online courses (6). Of course, they must be high quality and user-friendly to promote use, sustainability and learning. They should contain metadata for content tagging; use both expert and community definitions of quality to provide a curated collection of resources; and request input from both submitters and users, whose comments can evolve the quality of the collection.

What's required is a structure and process to organize the community. As faculty members would be both users and contributors, the database would require crowdsourcing for both contributions and improvements. Jay Pedersen and co-authors at the University of Nebraska, Omaha, developed a conceptual model for crowdsourcing (7) (see figure 4).

In crowdsourcing, a problem (in this case the development of a trusted and used Web collection) is addressed using a process (a step-by-step action plan), a governance structure sufficient to guide the contributors' efforts, participants (owners, contributors and improvers with defined roles and obligations who trust the process), and technology that enables the enterprise.

Evidence shows that high-quality contributions arise from users who are engaged in the process and who have a personal interest in the outcome and "that a positive user experience is a strong predictor of continued involvement for both problem owners and the crowd members" (7).

Both the educational wing of the ASBMB and the editorial staff of the journal Biochemistry and Molecular Biology Education would be logical stakeholders in the design, creation, review and curation of the suggested portal. The ASBMB is wrestling with similar issues as it develops assessment tools for certification. I would like to see the ASBMB either house the collection or facilitate submissions from individuals who house the files on their host institutions' sites. Another possible host/portal site is the Pre-health Collection of the iCollaborative.

The JBC and other journals provide downloadable PowerPoints for educational use. To jump-start the proposed web collection, the JBC could encourage authors to include assessment questions targeted to undergraduates when they submit their manuscripts for review. This would provide a great experience for graduate students and postdoctoral researchers who are thinking about

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How the National Alliance for Broader Impacts can help you

By Susan D. Renoe, Sara Vassmer and Kaye Storm

If you have submitted a proposal for funding to the National Science Foundation, you are familiar with the term "broader impacts." Broader impacts are the societal benefits of the research. They also can be viewed as the return on the taxpayers' investment in research. A requirement to explain the significance or impact of the research is found across all federal funding agencies including the NSF, the National Institutes of Health and the U.S. Department of Agriculture. However, detailed guidance in formulating broader impacts statements and programming is missing.

With this deficit in mind, the National Alliance for Broader Impacts (1) emerged in 2014 with support from the NSF (2) to develop institutional capacity and engagement in broader impacts activity. A national network of universities, professional societies and informal science organizations, the NABI is a community of practice focused on the development, implementation and evaluation of science communication and public engagement programming — generally designed to meet the NSF's broader-impacts criterion. Today, there are 240 individual members of the NABI from more than 100 institutions.

All are welcome to join the NABI free of charge. We currently are offering only individual memberships so that members retain their memberships even if they change institutions. A benefit of NABI membership is the sharing of resources and knowledge. The increased emphasis on the broader-impacts criterion has led to the creation of campus-wide offices, such as the Broader Impacts Network at the University of Missouri (3). Broader impacts offices aid researchers in the design, implementation and evaluation of their broader-impacts activities. While not all institutions have broader-impacts offices, NABI resources are available to anyone who needs them — regardless of affiliation. Sharing resources and experience across the network allows for effective use of time and resources, both of which are in high demand.

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The 2014 Broader Impacts Summit featured participants from universities, federal agencies, local organizations and professional societies.

The NABI also provides periodic, in-depth training for anyone interested in broader impacts in theory and in practice — including students, faculty members, staff members, administrators, and nonacademic professionals and organizations. For instance, the University of Missouri hosted a Broader Impacts Intensive Training in the fall that included information on the criterion and how to address it, information on evaluation and assessment of broader impacts plans, and breakout sessions on specific topics, such as using the Web effectively in your strategy and working with primary- and secondary-school teachers.

NABI activities contribute directly to the national discussion on the future of broader impacts. The annual Broader Impacts Summit organized by the NABI, for example, provides professional-development opportunities for professionals who support broader-impacts initiatives and fosters discussion of issues related to broader

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impacts. The 2014 summit (4) hosted France Córdova's first public talk after she was confirmed as the NSF director. She stressed the need for researchers to stay relevant to the American taxpayers who fund them. The NSF Perspectives on Broader Impacts publication (5) featured the summit.

Members of the American Society for Biochemistry and Molecular Biology are invited to the next summit, which will be held April 29 through May 1 at the University of Wisconsin–Madison (6).

In addition to keynote speeches by Wanda Ward (head of the NSF's Office of International and Integrative Activities), Pramod Khargonekar (head of the NSF Engineering Directorate) and Bob Mathieu (Vilas distinguished professor of astronomy at the University of Wisconsin–Madison; director of the Wisconsin Center for Education Research; and director of the Center for the Integration of Research, Teaching and Learning), there will be many professional-development opportunities and workshops for attendees. Participation also will afford attendees the opportunity to contribute to the national dialogue about broader impacts.

The NABI has many plans:

1) To continue to facilitate communication between researchers and federal funding agencies about the realities of implementing the broader-impacts criterion,

2) To grow the support community for broader impacts by encouraging graduate students to consider it as a profession, and

3) To provide training and resources for researchers so they can better understand the criterion and how to address it.

Our end goal is to move from an NSF-funded network to a self-sustaining professional organization.

For more information, to join the NABI or to register for the summit, visit www.broaderimpacts.net. You also can follow us on Twitter at www.twitter.com/NA4BI.

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pursuing academic positions.

I believe that other biochemistry and molecular biology educators would find the benefit of such a collection compelling enough to motivate their participation as designers, contributors, users and reviewers. A critical mass is necessary to proceed. I would like this article to lead to further dialogue and potential development of this resource. I invite you to visit the following Web site if you are interested in contributing to the development and/or use of this proposed collection: http://bit.ly/1CcYdxu.

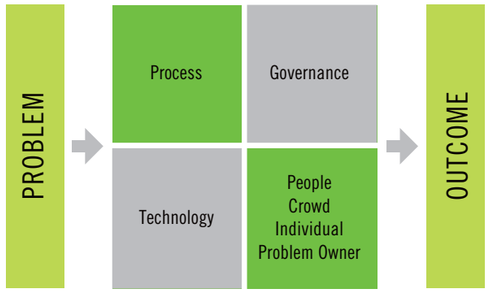

FIGURE 4. Conceptual model for crowdsourcing by Jay Pederson et al.

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What can you do for science?

Outreach seed grant recipient runs a science night for a Texas town

By Maggie Kuo

"What was the first thing that got you interested in science?" Teresa Evans asked the volunteers who joined her science outreach program at the University of Texas Health Science Center at San Antonio. "Every single person would have some very vivid memory of what it was," she says, and they all wanted "to give that experience to another generation."

EVANS

Evans, who directs the Office of Career Development in the Graduate School of Biomedical Science at UTHSCSA, established Teen Meetings Outside the Box to provide graduate students and postdoctoral fellows the opportunity to engage underserved students. With funds from the ASBMB's Outreach Seed Grant program, TeenMOB held its first outreach event, a science night for Natalia, a rural town 45 minutes outside of San Antonio, in October.

The group set up eight booths at Natalia High School. Each booth focused on a specific area of the health sciences and an age range — elementary, middle or high school. UTHSCSA trainees, professors and local K–12 teachers staffed the booths.

"We were asked to put the booths and the science content in a way that could be absorbed by all of the community," says Evans. "So we brought things like organs from the pathology department. They got to see diseased and healthy organs. We had pathologists, graduate students, postdoctoral fellows, nursing students talking about what that means and why healthy living is important to prevent these kinds of disease. Then we had more interactive booths where they did worksheets and problem solving, learning about how biology and chemistry affect the human body and our health."

The event was a huge success,

Evans says. All told, 180 people came out: students, their parents and local residents. They ate dinner and participated in prize raffles.

To plan the event, Evans had partnered with teachers from the Voelcker Biosciences Teacher Academy, a program at UTHSCSA that offers curriculum resources and professional development to science, technology, engineering and math teachers in the San Antonio area. She also worked closely with a science teacher and VBTA member from Natalia High School, Anjali Dandona. For 2015, Evans plans to build more of these relationships with teachers in the San Antonio area through her collaborations with the VBTA and run outreach events at their schools.

Evans is a fervent believer in outreach. "I came from a rural community," she says. "And I went to a great school, but the exposure to the diversity of what science has to offer wasn't there. I often think about my hometown and my community, and I see it increasingly important as a scientist myself to share my knowledge and to share my journey with the generations after me."

While a graduate student, Evans participated in science outreach and communication programs and joined the ASBMB's public outreach committee. She then applied for and won the outreach seed grant to start TeenMOB.

We talked more about how she got the science night running and what made it work. Our conversation has been edited for length and clarity.

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Where did you get this idea to do a science night outreach?

It stemmed from my collaboration with the teacher in Natalia. I realized that in order to pull off a program like this, where you're interfacing with a K–12 school, you really need to have somebody on the ground, at the school, who's passionate about this.

When I met Anjali, I could tell she would go above and beyond her classroom — she's done so in the past — so I asked her how we could help. I told her about the funding I had received from the ASBMB and said that the funding was to do outreach for K–12 schools with our graduate students and postdoctoral fellows.

We started out with the idea of doing a teen science café, which is more of a journal-club setting, but based on what Anjali was telling me, that wouldn't fit so well because of where her school is located, so far outside the city, and the actual travel for her students. She suggested having a science night, because she had wanted to do something like that for many years but didn't have the resources to do so.

We brainstormed and came up with this model, brought in as many people and experts as we could, and made the program around what Anjali was looking for. And that's the plan moving forward — to maintain that relationship with the teacher and to build the program around what the school is looking for.

Do you feel like the students were responsive to these booths?

Absolutely! We really tried to have the booths be focused at different age groups. The five-year-old students loved making the brain cap. You colored this brain, and you created a

cap that you wore on your head that showed you where all the different parts of the brain were, and they loved those. There were all these little kids running around wearing these brain caps.

But then the high-school students enjoyed having a longer conversation at the table with the organs or, for example, another table that talked about blood pressure and how blood pressure is tested, what that means and the implications. I was actually quite surprised with the parents. The parents were very eager to have their blood pressure taken and to have a conversation about the things a physician might talk to you about during a visit.

Also, it was informative to have the Voelker Bioscience Teacher's Academy right there with us graduate-level trainees. So for myself, I've been a student for many years but never a teacher in a classroom at this level. Hearing a teacher say, 'OK, this is more for elementary students, and you need to do this to hit your high school students,' I think, was what made it such a great success. And it was great to see our graduate students and postdocs learning from the teachers about how you need to communicate your science differently to each one of these populations.

When reaching out to elementary-school students and high-school students, what concepts do you focus on?

For the elementary-school students, we try to do things that are very hands-on and tactile — a lot of coloring and a lot more animated. The people at that booth were getting down on their knees and showing them images and being visual, remembering that they needed to stay at the 50,000-foot view and not get down into the weeds.

With the high-school students, the communications were more specific, but also we coached our trainees to talk to the high-school students about careers in science. Do you want to go into a career in science, what kind, have you thought about college — trying to really let them know that the people in the room are from a diverse scientific career background and science doesn't just mean you will be a medical doctor. There are many options.

What about middle school?

So for the middle-school students, we tried to choose activities that had a little more mass in them and a little more of a game component. We would talk a little bit about careers but in a broader sense, getting them to think about how there are more opportunities out there than just being a doctor but not so much what college they wanted to go to.

It was fascinating. In the community, for them, San Antonio is very far away. When you say, "Do you want to move?" they're like, "Oh, I don't know." So we wanted to help them see what's out there for them.

What do you think the grad students and postdocs got from this experience?

So the idea was that, first, they have the experience of communicating varying types of science, not just their background, to a broad audience. Second, our institution is a medical institution; we don't have undergraduates here. This opportunity provides them with the experience of teaching to see if that's something they're interested in. It also gets them plugged into the K–12 community through the networking we did in Natalia and our VBTA teachers.

I was also surprised to see that many of our graduate students and

postdoctoral fellows were really doing this to give back. It was giving them that opportunity to spark scientific interest in students, in parents, in the community, in a way that was provided to them when they were young.

So your initial idea was to do an outreach event, and after you got the seed grant, it started evolving and you reached out to the teaching academy?

Right. And honestly, as a graduate student, one of the most influential things that I did was join the ASBMB Public Outreach Committee. The individuals on that committee are so diverse and so enthusiastic about science outreach in many different avenues and genres. I would sit at this table with leaders in science outreach, and they introduced me to the outreach seed grant program. And I was like, "This is something that we got to do. It needs to be brought to San Antonio." And so that was really the catalyst.

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

You went to your first meeting, but now what?

By Vivian Tang

While there are many tips online for how first-time conference attendees can make the most of the experience, suggestions of post-conference moves are rare. While preconference planning is essential, post-conference moves also may help you realize the benefits of a meeting. Here, I've pulled together a few recommendations.

Establish new contacts

This applies to authorities in your research area or areas of interest whom you did not have a chance to approach during the conference. Explain why you didn't see them during the meeting and why you have decided to contact them after the conference. If you have gotten very familiar with the research projects in their labs and are equipped with relevant skills, doing this may be helpful, as some postdoc positions are not advertised, and, even if there aren't any positions waiting to be filled in their labs, they might pass on your CV to other faculty members.

Request feedback on your presentation

The feedback and advice from those you get to talk to during the conference is valuable, but you never know how the feedback from those you communicate with via email after the conference can further benefit you.

Keep track of their latest publications

Whether you are a trainee planning to do postdoctoral work or are just generally seeking to become a better scientist, keeping track of the latest published work of leaders in your research area is important. Read their latest papers and keep in touch.

Follow up

Following up with your peers is just as important as following up with leaders in your research area. When you go for interviews or explore opportunities for collaboration, you never know who you are going to encounter. Even if immediate collaborations are not possible, follow-up emails or any other means to keep in touch may turn out to have long-term benefits.

I recently learned that a friend of a friend had just started postdoctoral training. This fellow's postdoc position was in the laboratory of an investigator who was an ex-colleague of a contact he established after a conference he attended over two years ago. They kept in touch and the contact got him connected with his ex-colleague, who happened to be looking for a postdoc. The rest was history. This is a good reminder that the opportunities and benefits of post-conference follow-up can come in an indirect way.

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