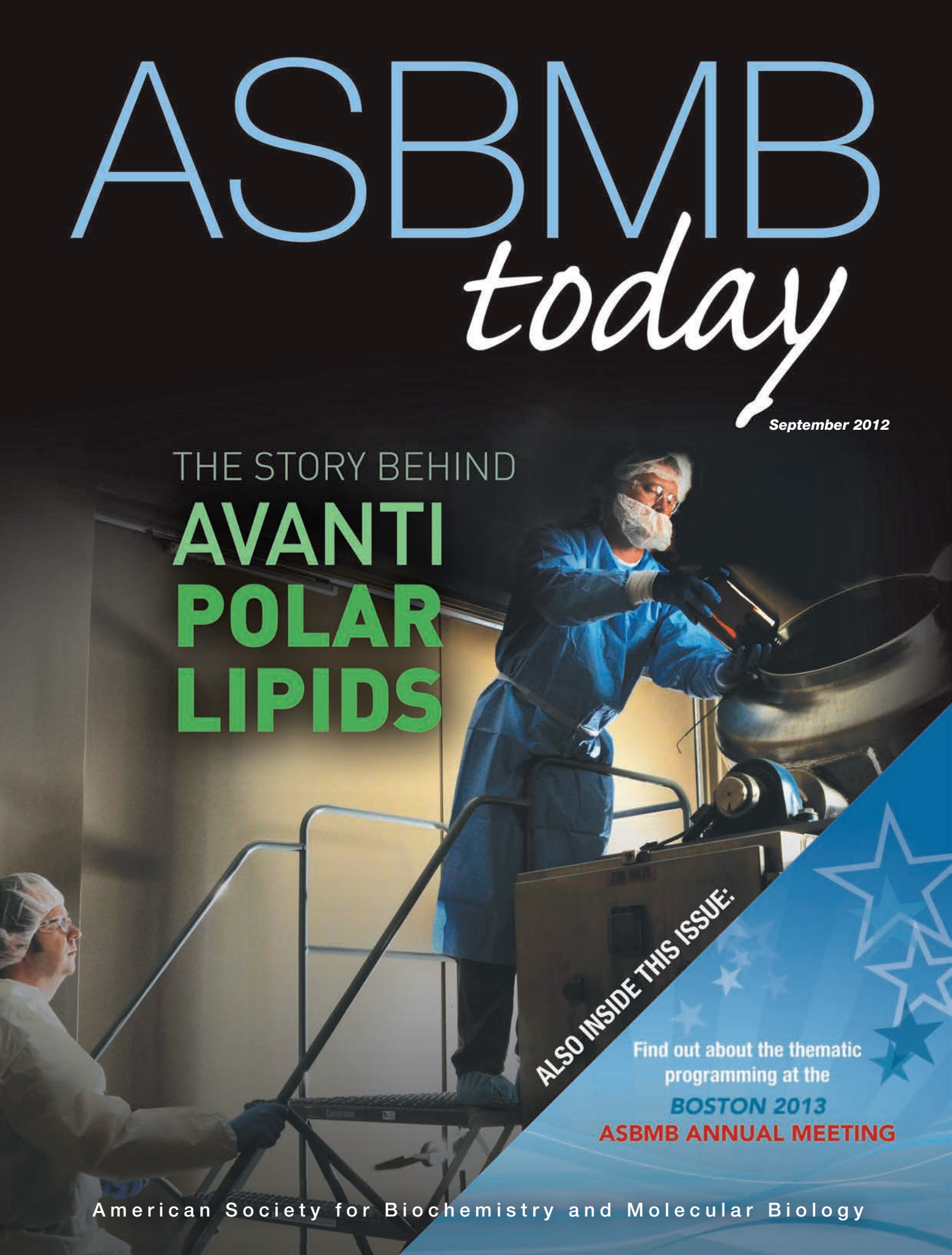
# ASBMB today

September 2012



## THE STORY BEHIND AVANTI POLAR LIPIDS

ALSO INSIDE THIS ISSUE:

Find out about the thematic programming at the

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ASBMB ANNUAL MEETING

American Society for Biochemistry and Molecular Biology

# 2014

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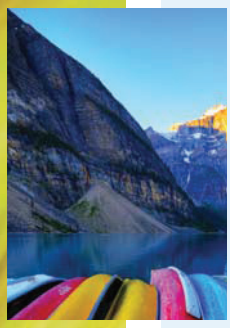

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*SEPTEMBER 2012*

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*survey*

Help ASBMB better serve your needs by taking our annual graduation survey. Find out more about it on Page 11.

ASBMB today

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## Research Spotlight

Education and Professional Development Manager Weiyi Zhao features Stephani Page, a Ph.D. candidate at the University of North Carolina at Chapel Hill who is studying a family of microbial signal-transduction proteins called response regulators.

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# The best-laid plans: It's time to move forward

BY JEREMY BERG

In 1997, the U.S. Senate passed a resolution 98–0 stating that the budget of the National Institutes of Health should be doubled over five years. Through the leadership of Sen. Tom Harkin, D-Iowa; then-Sen. Arlen Specter, then-R-Pa.; and then-Rep. John Porter, R-Ill., this doubling became a reality. From fiscal 1999 through fiscal 2003, the NIH appropriation was increased to $27.2 billion from $13.7 billion. The goal of this dramatic growth in federal support for biomedical research was to increase the scale of the enterprise to facilitate further discoveries, to capitalize on the great scientific opportunities made possible by previous discoveries and to translate these advances, where possible, directly to affect human health.

In 2003, as the time for the doubling to end was drawing near, policy leaders from the academic community published a Science Policy Forum article entitled "The NIH Budget in the 'Postdoubling' Era" (1). The authors analyzed some of the challenges of transitioning from annual budget increases of about 15 percent to more modest increases, including maintaining progress into new research areas, incorporating the impact of ongoing commitments of previously funded grants, and sustaining support for new investigators and trainees. They developed models to estimate the effects of different rates of increase in the NIH budget from 4 percent to 10 percent per year. Their analyses revealed that annual increases below 6 percent were likely to lead to tough compromises for the NIH and the research community. They concluded that "policy-makers may feel that the federal government has done its part for NIH-funded research and that the agency can be allowed to coast … at static levels of funding. To the contrary, we emphasize that levels of growth below 6 to 8% will negate many of the advantages achieved by the doubling … They will also severely strain the relationship of trust between NIH and its awardees on which our nation's successes in biomedical research rest."

Unfortunately, this effort at thoughtful analysis did not yield the desired implementation. Since fiscal 2004, NIH budget increments have ranged from -1 percent to 3.2 percent, with an average of 1.4 percent. This is substantially below the rate of inflation for biomedical research, resulting in a loss of more than 20 percent in purchasing power over this eight-year period. The NIH did, indeed, have to make many of the tough choices that were foreshadowed in the article to prevent success rates for new and competing grants from falling dramatically.

A substantial amount of the stress on the system arose from events set in motion by the budget doubling. In anticipation of and in response to the doubling, many institutions grew by hiring additional faculty members and constructing new research spaces. However, both faculty hiring and, particularly, building construction take time, so many new faculty members did not come on line until near the end of or after the doubling period. This led to a significant increase in the number of investigators and associated grant applications competing for the available resources from the NIH and other funding sources. Furthermore, institutions had become accustomed to the relatively high success rates (approximately 25 percent for R01 applications) that occurred during the doubling period, so many institutions expected investigators to raise a larger fraction of their salaries from NIH grants or other sources than they had previously. While creating more faculty positions was beneficial to the enterprise and to the researchers who filled these positions, these and other positions became, on average, more dependent on external funding with a lower level of institutional commitment.

In addition, as detailed in the recent Biomedical Research Workforce Working Group report from the Advisory Committee to the NIH Director (2), among other sources, the number of biomedical Ph.D.s awarded remained almost constant at 5,400 per year during the doubling period. However, this number grew linearly to 7,700 by 2009. Given an average of five to six years for Ph.D. training, the post-doubling increase in Ph.D.s reflects growth in the size of Ph.D. programs during the doubling period; that is, most of the students

who graduated through 2009 started their graduate training during the doubling period, before the NIH budget had flattened out. This growth was not based on any attempt to increase the number of trainees, but rather it was due to the fact that Ph.D. production is quite strongly coupled to research activity: When more research funds were available, institutions responded by increasing the sizes of their graduate programs.

Thus, many of the factors that are placing the biomedical research enterprise under stress were set in motion by the NIH budget doubling followed by stagnant NIH appropriations after the doubling. Of course, further stress has been imposed by the worldwide economic downturn, which has had substantial effects on federal and state budgets, institutional endowments, and the availability of capital. The support for the NIH and the National Science Foundation in the American Recovery and Reinvestment Act postponed the full brunt of these factors, but we now have reached a critical time.

What can we forecast from the facts at hand? First, it is unlikely that substantial increases in federal support for science will be forthcoming until a more robust economic recovery is under way (although we still must make the case that such investments are important in driving a recovery and that every dollar counts in minimizing the damage that is done in the meantime). Second, the current state of affairs is unlikely to be sustainable. Few laboratories can be confident of sustained support given present and projected success rates. Review groups tend to become quite conservative when success rates are so low, to the detriment of scientific progress. Third, many young scientists have been (and are still being) trained and are ready to move on to different stages of their careers.

Given these realities, what can be done to build a more sustainable future? The Biomedical Research Workforce Working Group report touches on a number of important issues relevant to this question. Some recommendations relate to graduate students and postdoctoral fellows, including those directed toward shortening the training period. The lengthening of this period has been primarily a symptom of some of the factors discussed above, namely the strong coupling of training to research activity and the growth in the number of trainees competing for available positions. Taking steps to shorten the training period is important, but these steps are not likely to be very effective without tackling some of the bigger issues raised in the report. Another key aspect of graduate and postdoctoral training is driven by the appreciation that individuals with Ph.D.s in biomedical sciences go on to pursue a wide range of academic and nonacademic careers. A key question is how training programs need to adjust to accommodate this reality; effective answers to this are likely to come only by energetic engagement with those from nonacademic sectors.

Two of the remaining topics covered by the report reflect fundamental changes in the biomedical work force and the relationship between academic institutions and the NIH. The first of these involves staff scientists. The report notes the important roles that staff scientists can play in supporting the research enterprise. The development of a more robust staff scientist career path has the potential to provide career opportunities for individuals and to provide an avenue for conducting research that is substantially less coupled to training than is the current system. In my opinion, the working group's recommendations that "NIH study sections … be receptive to grant applications that include staff scientists" and that "institutions … create position categories that reflect the value and stature of these researchers" are not bold enough. The academic community should work with the NIH to explore creative ways to make such positions sufficiently stable so that they become attractive options for individuals interested in long-term careers in research. The second involves the balance of faculty salary support provided by institutions and the NIH. As the report notes, more data are needed, and the diversity of practices at different institutions makes this a challenging policy area, but this issue has so many implications that it must not be ignored and bold options must be explored.

These issues must be addressed by the academic community, government and others working together — and now is the time. Doing so will require careful analysis of desired and potential unintended consequences and creativity to find reasonable policies that balance often-conflicting needs; the future of the biomedical research enterprise in the United States depends on it.

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1. *Science* **296**, 1401 – 1402 (2003).
2. http://acd.od.nih.gov/Biomedical_research_wgreport.pdf

# Don't let this crisis go to waste

BY BENJAMIN CORB

Chicago Mayor (and former Democratic U.S. representative and White House chief-of-staff) Rahm Emanuel is often credited with the quote "You never want a serious crisis to go to waste." And these days, if you have been paying attention to discussions about federal funding for biomedical research, you know we are on the verge of a full-blown crisis.

Congress in late July agreed (in principle[1]) on a continuing resolution to fund the federal government through March 2013 at its current level, avoiding the kabuki dance of government shutdown threats so lawmakers can focus on more looming problems – specifically the "fiscal cliff" you may have heard about in the media. The fiscal cliff is a mountain of financial policies and decisions that are rapidly approaching and need congressional action. Expiring tax cuts, another debt-limit increase, and sequestration (mandated $1.1 trillion in spending cuts over 10 years) are the hallmarks of the fiscal cliff. The latter may affect you, your lab, your university, your students and your future more than any proposed cuts you've seen before.

The White House must lay out the spending-cut details by Sept. 6, and if Congress doesn't act each federal program on Jan. 3 will absorb a 7.8 percent cut as a result of sequestration. The National Institutes of Health, the National Science Foundation, the U.S. Department of Defense — no one is safe from the ax. Because the cuts don't take effect until the second quarter of FY13, they must be made in nine months. That means Q1 will remain untouched, but Q2 through Q4 will see 9.8 percent cuts. NIH Director Francis Collins testified to Congress that as many as 2,100 grants may be cut next year. That is nearly $3 billion of federal investment in biomedical research vanishing soon after the new year. We clearly have a crisis brewing.

Back to Emanuel. Often left off of the Emanuel quote, said at a conference of corporate chief executives put on by the Wall Street Journal in 2008, is, "And what I mean by that is an opportunity to do things you think you could not do before." In our case, this opportunity is the renewed chance to talk with your member of Congress about the important role federal investment in biomedical research plays in your lab. Concerned about the very real possibility of significant cuts to the biomedical research enterprise, scientists across the country are doing what many have been reluctant to do in the past. They are talking to — and being listened to by — politicians in their home district offices about the importance of federal funding for biomedical research. And more importantly, it's working!

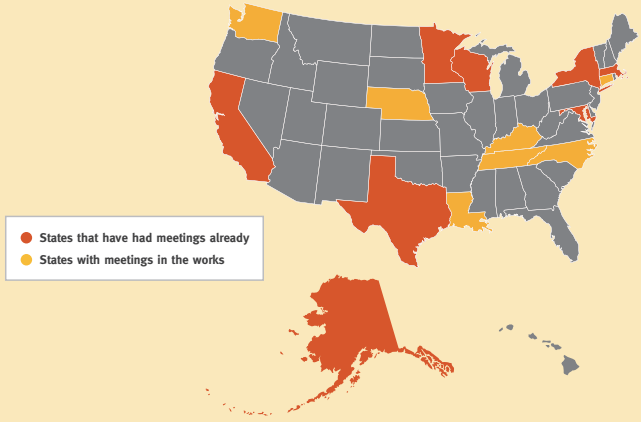
Members of Congress on both sides of the aisle today are hinting that sequestration shouldn't be a necessity. Sequestration is beginning to look like it may be avoidable. Avoidable if you continue to educate your lawmakers on the important role that federal investment plays in the research enterprise. Avoidable if you are mobilized and talking about science with policymakers. Avoidable if you show members of Congress just how much of an impact your research makes on the health of their constituents and the health of the economy.

[1] This must be passed by both houses of Congress in mid-September and signed into law by the president.

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

## THE 100–MEETINGS CHALLEGE

**Your colleagues are delivering the message. Across the country, 43 American Society for Biochemistry and Molecular Biology members conducted meetings in their districts over the summer. Find out how you can keep up the pressure this fall by emailing bcorb@asbmb.org.**



# asbmb member update

## Blumenthal to head up Down syndrome institute


BLUMENTHAL

Tom Blumenthal of the University of Colorado–Boulder was named the next executive director of the Linda Crnic Institute for Down Syndrome. Blumenthal has been associated with the institute, based at the University of Colorado School of Medicine, Anschutz Medical Campus, since its inception as a member of its advisory board and its board of directors. In a statement, Blumenthal said he intends to increase significantly the volume of research conducted at the institute, emphasizing that he believes "we are obligated to help people through scientific study." He added that, given today's technological advances, "we have a fighting chance at delivering." Upon accepting the appointment, Blumenthal stepped down from his post as the chairman of the University of Colorado–Boulder's department of molecular, cellular and developmental biology.

## Mizzou bestows its annual President's Award on Sun


SUN

Grace Y. Sun of the University of Missouri won her institution's President's Award for Sustained Excellence, given to a faculty member "who demonstrates and sustains a record of distinguished scholarship, research or creativity," according to the university. Sun, who studies the malfunctioning of central nervous system signaling pathways associated with neurodegenerative diseases, was lauded for her use of new technologies to study Alzheimer's disease and for excellence in research. Sun, a professor of biochemistry, has served on numerous editorial boards and organizing committees and has been recognized with many awards over the past decade.

## Varshavsky wins two international awards


VARSHAVSKY

Alexander Varshavsky of the California Institute of Technology won the 2012 King Faisal International Prize for Science and the 2011 BBVA Award in Biomedical Sciences. Both were issued in recognition of numerous achievements by Varshavsky and his research team over the years, including the discovery of the first biological functions of the ubiquitin system and regulated protein degradation, the discovery of the first degradation signals in short-lived proteins, the discovery of the first ubiquitin-conjugating enzymes with defined physiological functions, and the identification and cloning of the first ubiquitin ligase. Collectively, this and other pioneering work by Varshavsky and his lab in the 1980s laid the foundation for the field of ubiquitin biology. Upon receiving the second award in Madrid, Varshavsky said he felt "privileged having been able to contribute to the birth of this field and to partake in its later development." He added, "This arena grew rapidly in the 1990s and has become, by now, an immense and profoundly important biomedical realm."

## Barton, Blackburn to serve jointly as deans

The University of Texas Graduate School of Biomedical Sciences at Houston, a partnership between the University of Texas Health Science Center at Houston (known as UT-Health) and the University of Texas MD Anderson Cancer Center, chose Michelle Barton and Michael Blackburn to serve jointly as deans of the institution. A professor in the graduate school's department of biochemistry and molecular biology, Barton joined MD Anderson in 2000 and studies chromatin function and tumor suppressor gene p53. Blackburn, vice-chairman in the department of biochemistry and molecular biology at UT-Health's medical school, joined that institution in 1997 and studies chronic lung disorders. Barton and Blackburn replace George Stancel, who ended his 13-year stint as dean to become the executive vice president for academic and research affairs at UT-Health.


STANCEL


**Michelle Barton and Michael Blackburn**

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# The expanding multiverse of the scientific community: new media for communication

BY BIOCHEM BELLE


## ABOUT THE AUTHOR

Biochem Belle (biochem.belle@gmail.com) is a postdoctoral fellow in a biomedical research hub in New England and a member of the ASBMB. She holds a B.S. in biochemistry from a Southern U.S. state university and a Ph.D. in chemistry from another Southern university. Her doctoral studies focused on enzyme substrates and inhibitors. She is now exploring how protein organization and interactions affect their functions in cells. Follow her on Twitter at www.twitter.com/biochembelle.


Sometime during the upstart days of social Web, blogs earned a reputation in some circles for being places where people posted pictures of their cats or inventories of what they ate for breakfast. The stigma carried over to other social media platforms, from the microblogging site Twitter to the search giant's Internet playground, Google+. Although you certainly will find no shortage of pet videos and meal updates on the Internet, the web has much more to offer scientists than cat photos and muffin recipes – and much to gain from our presence and interactions.

### More than muffins

The way scientists are sharing via social media is not so different from what scientists have been doing for centuries. In a lecture on improving science communication on the Web at the University of Rhode Island Metcalf Institute in late July, the editor of Scientific American's blog network, Bora Zivkovic, likened blog posts to the earliest forms of scientific communication, such as the letters and journals of Newton and Darwin, which were written as very personal accounts of their observations that were later published to disseminate information.

Although peer review has changed how we communicate original research findings, science bloggers provide the same types of content that journals, symposia and society newsletters have been cranking out for decades. Commentaries on science in policymaking, science education and training, the power and pitfalls of peer review, and much more appear in numerous social media postings – and in editorials and letters in the most prestigious journals.

Research blogging gives brief synopses of new research papers and in-depth critical analyses of published studies, similar to the research highlights and journal clubs that are found in many publications and lab meetings. Blogging and live-tweeting of scientific conferences serve as meeting reports. Sacred tips about grant writing and information about how study section reviews work, once confined to career-development workshops, is now posted, archived and updated online. Social media has become another method for sharing valuable information with the scientific community.

### More than medium

Although digital platforms provide content similar to traditional forms of scientific communication, social media also radically changes these communications. Scientific journals and society publications will continue to be useful resources, but in some matters, they can quickly become echo chambers – select individuals given the podium, another voice or two providing counterpoints, the whole debate taking place in just a few issues before being left behind for the next topic. These commentaries now can be transformed into incredibly dynamic discussions! Social media is not static; it is a living, growing, morphing thing. A post can be shared across multiple platforms, reaching a variety of audiences and sparking new conversations while often remaining connected to the original. Rather than waiting weeks for a response to be reviewed, edited and published, it can go up within minutes. This might sound like a recipe for disaster to some, but comments are typically subject to rapid response too, with participants correcting errors, extolling virtues and pointing out bias.

Social media brings in another powerful element: diversity. People from an array of backgrounds at different stages of different career tracks in different

career tracks in different sectors are using social media to talk about the practice, culture and findings of scientific research. Online, people are not just sitting quietly at the back of the lecture hall listening to others debate some piece of research or the fate of the scientific establishment. They're participating.

Everyone, from the undergrad to the institute director, has a voice. There are no time constraints for organizing one's thoughts. It is not necessary to compete for the attention of the moderator or editor. An argument is more readily judged by its essence than the number of publications or titles of its presenter. It is far more difficult to interrupt a response midstream and drown out that voice.

Eavesdropping on social media can provide a wealth of information for scientists at all stages, and some users simply choose to listen. But active participation can bring even more value. Social media is a testing ground to flesh out ideas, improve writing and even build confidence. Individuals who might often go unheard, who are perhaps too timid to speak in public, can find their own voices through social media.

Many scientists choose to use their professional identities online, but pseudonymous scientists also contribute to the great diversity of social media. The reasons for choosing to write under pseudonyms are varied but rarely nefarious. Credentials lend credibility, but in the digital age trust is built on behavior. Every individual engaged in social media creates an identity, and that identity is established by the content he or she creates and promotes. To borrow again from Zivkovic, "I don't care about Samuel Clemens; I care about Mark Twain." Whether you choose to use your professional identity or not, you can find your voice.

### More than material

Scientists are discovering direct benefits from being online. Some scientists use blogs for data sharing or public outreach, which are critical elements for many funding applications now. In fields such as ecology and astronomy, social media networks are leveraged to collect and analyze data. You will find scientists troubleshooting experiments in different cities, even different countries, at all hours of the day and night. We are sharing samples of cover letters and grant components and providing feedback on job and funding applications, often for people we have never met. Scientists are expanding networks, finding people with shared and diverse interests and expertise from all over the globe.

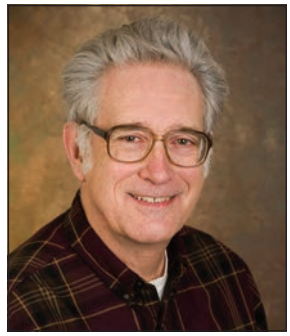
It works because social media has moved far beyond content; it has become another place to create community. We connect and nurture relationships with people from curious nonscientists to established experts. We catch up from time to time, chatting about the silly, the serious, the mundane and the extraordinary. If we posted only the profound, then we would lose the camaraderie we share. This is what transforms social media. Relationships may begin as an exchange of tweets but become friendships and collaborations, bonds with mentors and peers that reach beyond the confines of a social media website.

We accept that chance connections at conferences or seminars have sparked lifelong professional relationships. The same is possible in virtual space. Not every scientist needs to have a blog or Twitter or Tumblr. But just like the phone call or the walk down the hall to chat with a colleague, social media are tools that can broaden our reach and enable us to build rich, diverse networks of peers and mentors.

# From horse stingers to courtship and cuckoldry

## *Harold White's Delmarva-lous reflections on the fascinating world of Odonata*

**BY JAMES T. HAZZARD**

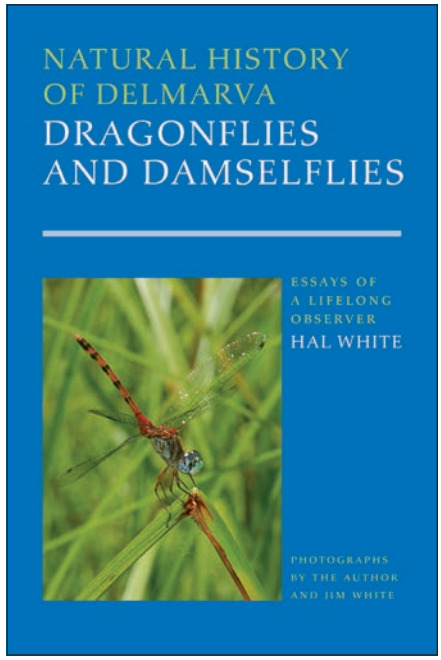


Immediately before beginning a seven-week summer session nonmajors biochemistry course, I was quite surprised to receive an autographed copy Harold White's book "Natural His-

tory of Delmarva Dragonflies and Damselflies: Essays of a Lifelong Observer" (1). Before receiving this book, I had just read White's article "Visualizing the Perception Filter and Breaching It with Active-Learning Strategies" (2), in which he suggests that a primary goal of student-centered learning is "to generate situations and activities that open holes in the perception filter and allow information to invade the student's working memory space." Standing on the precipice of a once-a-year teaching obligation, my memory space already was fairly overwhelmed, and, not being an Odonata aficionado, there was certainly a need for something to poke a hole in my self-imposed perception filter. Fortunately, that was primarily accomplished by my great admiration of Hal's passion for and leadership in transforming undergraduate education in biochemistry and secondarily by the fact that, having been born and raised on the Delmarva Peninsula, I am very familiar with many of the collection and observation sites White reveals in his book.

In the preface, the author candidly states that he has not written this book to be a formal field guide describing the 85 dragonfly and 44 damselfly Delmarva inhabitants. Rather, he uses the detailed photographs and colorful descriptions of each species as the basis for an eclectic series of reflections on subjects ranging from the development of his own interest in these amazing creatures to natural selection and evolutionary biology, the ethics of obtaining voucher specimens for collections as opposed to photographic documentation (a dragonfly enthusiast's version of catch-and-release), the humorous opportunity to use his knowledge to discreetly identify the species depicted in a woman's dragonfly body art, and the lamentable fact that many younger bioscience students are disconnected from the natural world and seldom go outdoors for extended periods of time. This latter chapter prompted me to reflect on the fact that while those of us who are of pre-Nintendo/ Xbox/Wii generations often were stimulated to pursue careers in the biosciences because of our interest in the outdoor world (this was certainly the case for me, as I spent copious amounts of time paddling a canoe along the upper reaches of the Nanticoke River and duck hunting in a variety of lower Delaware marshes), we spend so much time investigating the intricacies of the molecular world that we tend to neglect studying the intricacies of the creatures with which we co-exist in our biosphere.

This charming, humorous and well-written book is such a joy to read because it reminds us of the first principles we learned in traditional biology courses many years ago and instills in us the desire to learn more about the living things about which we have little knowledge, whether we live in the arid Sonoran Desert or the more water-rich Delmarva Peninsula. To that end (and being the consummate educator), White sprinkles suggestions for interesting research projects for young scientists throughout his book. These suggestions, coupled with the fact that natural habitats are being lost at an alarming rate, makes one realize that it is incumbent upon those of us who are in a position to do so to engage in greater outreach activities, mainly in the form of field trips, with K–12 students to give them a better sense of the astounding natural world in which they live as well as "how science is done and the people who do science."




Interestingly, after looking through "Dragonflies and Damselflies" one evening, my 14-year-old granddaughter (who is "terrified" of insects) casually informed me that she had seen a couple dragonflies down near our horse corrals. Now we are determined to know whether they are Spot-winged Gliders, Cardinal Meadowhawks or Mayan Setwings; being amateurs in the "Ode" field, we will have to wait until the dragonflies perch on a greasewood branch, because we lack the skill to identify them in flight. But as a direct result of White sharing his passion for these amazing insects in his wonderful book, another young person has become more knowledgeable about the world in which she lives.

James T. Hazzard (jhazzard@email.arizona.edu) is a senior lecturer at the University of Arizona department of chemistry and biochemistry.

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# TAKE THE ASBMB GRADUATION SURVEY

**The American Society for Biochemistry and Molecular Biology is actively seeking to better connect with, serve and represent the many future biochemists and molecular biologists in our colleges and universities and the educational professionals who instruct and advise them.**

When we ask our elected representatives for greater financial support for education and research, we anticipate that officials will try to gain some perspective on these issues by asking questions such as:

- How many students graduate with bachelor's, master's or doctoral degrees in biochemistry and molecular biology nationally? What about in my state?
- How many institutions of higher education offer a bachelor's degree in biochemistry and molecular biology? How many faculty members do they have? How large are these programs?

Science, technology, engineering and math disciplines have a reputation for attracting primarily males and the socio-economically advantaged. We need to know:

- How is your field attracting and graduating young women and persons of diverse backgrounds?
- Are there any institutions that are particularly successful at recruiting and educating students of diverse backgrounds?

*To answer these seemingly straightforward questions,* **WE NEED YOUR HELP.**

Recently, we sent instructions for accessing our annual graduation survey to the chairs of more than 800 departments/programs that offer degrees at undergraduate and/or graduate levels in biochemistry, molecular biology, the biochemistry track in chemistry, or biotechnology. This survey is particularly focused on following trends in demographics, identifying programs especially successful in minority graduations, and comparing data on minority progress within our discipline with data from other scientific organizations.

Those of us working on the ASBMB Minority Affairs Committee, Education and Professional Development Committee and Undergraduate Affiliates Network are fellow faculty members and department chairs. We know that you, our colleagues, are extremely busy. Therefore, we have kept the survey short and put it in an easy-to-access online format.

**You need only to request from your university registrar the information for the survey and fill it out.**

We need a high response rate to generate reliable and informative data. If you are a chair who did not receive an email request, please contact us at education@asbmb.org so that we can update our contacts and forward the information to you.

Faculty members can help by asking their department leaders or coordinators if they have received and replied to the survey. If not, perhaps you could volunteer to oversee its completion.

Those of you involved in educating the next generation of biochemists and molecular biologists are doing wonderful things under increasingly difficult circumstances. Help us to better recognize your successes and help you overcome the challenges you face by providing the information we need to be good stewards.

James K. Zimmerman for the Education and Professional Development Committee

Peter Kennelly, Education and Professional Development Committee

Squire Booker, Minority Affairs Committee

Takita Sumter, Minority Affairs Committee

Benjamin D. Caldwell, Undergraduate Affiliation Network

# AT THE FOREFRONT WITH AVANTI

BY RAJENDRANI MUKHOPADHYAY

**How Walter and Rowena Shaw grew Avanti Polar Lipids into the company it is today**

Avanti Polar Lipids probably would not exist if it hadn't been for a brother and sister born of incest. The siblings suffered from a genetic disease. A researcher got involved in understanding some of the molecular details of the disease. That researcher was Walter Shaw.

As a series of events unfolded in the 1960s and 1970s, his project spun off into what would become one of the most recognized suppliers of lipid products. Today, Avanti Polar Lipids, which 72-year-old Shaw owns and runs with his wife, Rowena, has 110 employees in Alabaster, Ala.

**Aerial view of Avanti's campus.** IMAGE COURTESY OF WALT SHAW

In 1967, when he was a laboratory director at the Medical College of Virginia, tubes of blood from the brother-sister pair landed in Walter Shaw's hands. The siblings had type I hyperlipidemia, which meant they couldn't metabolize fats properly. The brother and sister "would periodically come to the emergency room to be treated for pancreatitis caused by eating a fatty meal," says Shaw. Shaw's boss, clinician-researcher William Harlan, had the siblings' permission to take blood samples for research purposes during their hospital visits.

Harlan already had established that the siblings were missing the adipose tissue lipase commonly called lipoprotein lipase. They had problems with processing neutral triacylglycerols. But the patients had phospholipase activity. What enzyme produced this phospholipase activity? Shaw was tasked with finding that out.

Shaw and others in Harlan's group developed an assay to track the phospholipase activity. The mysterious enzyme was very slow and required lots of substrate egg phosphatidylcholine. A single incubation consumed 10 grams of the substrate. Shaw and Peter Jezyk, now a veterinarian in Arizona, were in charge of purifying kilos of phosphatidylcholine from eggs. The researchers soon switched to a radioactive substrate that could be used in smaller amounts, but by then Shaw and Jezyk knew how purify buckets of egg phosphatidylcholine and happened to have some left over.

When not cracking eggs with Jezyk, Shaw had another project to worry about. He and Harlan were trying to figure out why the red blood cells of severely burned patients looked like spiky balls instead of the usual biconcave disks. It was Shaw's responsibility to collect the weepage from the victims' third-degree burns, which covered more than one-third of their bodies. To this day, Shaw says he has horrible flashbacks to the weepage collections.

In trying to understand why the red blood cells of burn victims turned spiky, Shaw needed to learn a purification technique. To learn the method, he had to go to The Ohio State University, where he had earned his master's degree, to visit a researcher who could teach it to him. While he was in Cleveland, Shaw decided to drop by a company called Grand Island Biological Company. The company is better known today as GIBCO and is now part of Invitrogen. On the Friday he walked into the company's office, its leaders were grappling with a problem. Their lipid supplier in India had had a facility fire and was unable to deliver materials. When Shaw mentioned he had several kilos of egg phosphatidylcholine handy, "They bought it on the spot," he says.

His first sale wasn't anything to make him rich, says Shaw, but it did land him an annual contract of $12,000 to supply GIBCO with lipids. When he got back to Virginia, he and Jezyk established a company called Laboratory Pure Biochemicals. An assistant professor at the Medical College of Virginia, Joseph Liberti, who later joined Virginia Commonwealth University and passed away in 2009, knew the executives at GIBCO. "He said, 'If you let me in on this deal, we can sell them millions of dol-

lars' worth of lipids instead of $12,000 a year,'" says Shaw. The trio rented laboratory space from the University of Richmond for the business endeavor.

But first, Liberti, an Italian by blood, objected to the company name. He told his partners that "Laboratory Pure Biochemicals" was terrible and instead suggested "Avanti," the Italian word that means to go forward.

## 'I WROTE A CATALOG'

In January 1969, Avanti Biochemicals began business. Shaw, Jezyk and Liberti quickly learned the ropes of making high-quality lipids and began shipping them to GIBCO. But it was arduous. Each day, after doing research at MCV, they drove to their rented space and worked well past midnight making lipids. Despite their hard work, "From January to July, sales of lipids to Grand Island Biological did not increase by leaps and bounds," says Shaw. "Joe and Pete got tired of this in a hurry."

That summer, Jezyk and Liberti told Shaw they wanted out of Avanti Biochemicals. Shaw bought each out for $500. At the same time, Harlan informed Shaw that he was going to move to the University of Alabama at Birmingham. He asked if Shaw would like to move with him as a graduate student and do his Ph.D. work on the brother-sister phospholipase activity. Shaw agreed. In September 1969, Walter and Rowena Shaw moved to Alabama with their young children.

For four years at UAB, Walter Shaw did his thesis work, oversaw two university lipid laboratories and ran Avanti, which by then was supplying GIBCO with lipids worth $16,000 a year. "I was a busy guy," he says.

But it wasn't smooth sailing. Shaw's initial thesis project based on the brother-sister project at MCV was to isolate the enzyme responsible for the phospholipase activity. But after a year, "my results hit a stone wall, and my research ground to a halt," he says.

Alarmed, he began to consider changing projects. But one day, he came across a research article published by W. Virgil Brown's group at the University of California, San Diego. The paper described a liver enzyme that had triacylglycerol hydrolytic activity. Shaw called Brown "and told him that I had the other half of the story, phospholipase activity," he recalls. Brown invited Shaw to work with him in California, which Shaw did. They eventually demonstrated that the enzyme, a liver lipase, has both triacylglycerol and phospholipase activity. Shaw says this time was a major turning point in his life and taught him that "research is unpredictable, and hard times are growing experiences."

In 1973, after Shaw graduated with his Ph.D. from UAB, he suggested to GIBCO that he set up a lipid division for it in Ohio. But GIBCO executives had other plans. "They informed me that lipids had absolutely no future. They didn't want me to set up a lipid lab for them," says Shaw. "In fact, they were going to cancel the contract."

For some reason, GIBCO's rejection didn't faze Shaw. "It went right over my head," he says. He decided instead to rent a 900-square-foot cement-block garage in Pelham, a town outside of Birmingham, change the company name to Avanti Polar Lipids, because that's all the company was making, and put out a catalog. "I never wrote a résumé after I graduated," says Shaw. "I wrote a catalog."

At that time, Shaw thought he was going to sell lipids as standards for thin-layer chromatography. But changes in lipid research were happening. In 1965, Alec Bangham at the Institute of Animal Physiology in the U.K. had discovered liposomes. By the late 1960s, researchers were very interested in recreating these tiny balls of lipids and learning about their properties. After Shaw's catalog came out, orders started to come in from all over the U.S. so researchers could make liposomes. "Everyone thought this was the best stuff they had ever seen," says Shaw. "Orders kept progressing."

**L-R: Stephen Burgess, Rowena Shaw, Walt Shaw, Trevor Shaw.** IMAGE COURTESY OF WALT SHAW

John Weinstein at the National Cancer Institute used Avanti lipids to make liposomes that could deliver drugs to solid tumors. The New York Times ran an article about Weinstein's work in the spring of 1979, and sales of Avanti lipids rose.

At first, it was just the husband-wife team running Avanti. Rowena Shaw worked out of the home basement, making phone calls, taking orders and shipping out materials. Walter Shaw was in the rented garage, purifying lipids and developing new processes to make synthetic ones. Every morning, Rowena Shaw and a helper thoroughly cleaned the garage. "I would cover all the equipment and clean the rafters," she says.

In 1979, the Shaws hired a 16-year-old high-school student named Stephen Burgess. Burgess' father was a grocery store manager with whom Walter Shaw grew friendly because he helped Shaw buy 100 pounds of animal brain, liver and heart for lipid purifications every week (see sidebar). Burgess' father mentioned he had a son who was interested in science. On the day he turned 16, Burgess started to work at Avanti in the afternoons after school.

At first, Burgess washed the laboratory glassware. But as Shaw taught him lipid chemistry, Burgess moved on to synthesizing and purifying lipids. When Shaw asked the teenager what his scientific interests were, Burgess recalls saying "microbiology." Shaw passed him a batch of Escherichia coli and told him to extract the lipids. As Burgess got to work, he asked Shaw if all microorganisms smelled as bad. Shaw cheerfully told him there were others that smelled worse. Burgess decided to devote his scientific career to lipids and is now the director of research and development at Avanti.

## EXOSURF

By the early 1980s, Avanti was steadily supplying research-grade lipids. At that time, representatives from the pharmaceutical company Burroughs-Wellcome approached the Shaws. They wanted to know if Avanti could supply pharmaceutical-grade dipalmitylphosphatidylcholine for a drug they were developing. The drug was to be Exosurf Neonatal.

Exosurf is an artificial lung surfactant used to help premature babies breathe. Before Exosurf, premature babies were placed inside hyperbaric chambers to force oxygen into their lungs. But the high-pressure gas also damaged kidneys and optic nerves, so the babies commonly would go blind and suffer renal failure.

Making dipalmitylphosphatidylcholine for Burroughs-Wellcome meant the Avanti team had to learn how to make a synthetic lipid in kilo quantities under the guidelines of good manufacturing practices so that the product would gain the U.S. Food and Drug Administration's approval. Rowena Shaw says she had misgivings about the venture at first. "I was concerned, because I didn't think our place might be big enough for [Burroughs-Wellcome's] needs," she says, "but they just loved our product."

When Exosurf went on the market in 1990, it was the first-ever synthetic lipid product and squarely landed Avanti in the pharmaceutical business. Until that point, Avanti had operated out of the Pelham garage, which had passed FDA inspection for the manufacturing of pharmaceutical-grade products. "It was clean for a cement-block garage. Like I said, I cleaned the rafters!" quips Rowena Shaw. But the company needed more

## AVANTI POLAR BEARS

The iconic cartoon polar bear in Avanti ads grew out a joke, says Stephen Burgess, Avanti's director of research and development. "Walter would go to the grocery store to buy all this animal tissue," he says. "When you go through the checkout line with 100 pounds of brain, you are going to raise some eyebrows." The cashiers would ask Walter Shaw what he was going to do with the pile. When he tried explaining he was going to extract the lipids to produce materials for biomedical research, his audience's eyes glazed over. So Shaw began to tell cashiers and other nonscientists that he was making polar bear grease. Polar bears were an endangered species, according to his yarn, because they'd sit on ice with wet fur, get stuck, starve and die. When slicked up with his special grease, polar bears didn't get stuck on ice. The joke went down so well, Burgess says, that the company decided to adopt the polar bear as its mascot. Within the organization, the polar bear is informally known as Oscar, after Walter Shaw's father.

**The Shaws with Avanti employees.**

IMAGE COURTESY OF WALT SHAW

space to comfortably supply Burroughs-Wellcome, so in 1990 it moved five miles to Alabaster to a 16,000-square-foot building.

Exosurf ultimately changed neonatal care. Neonatal nurses could now use a dropper to administer the drug into the lungs of a preemie and get the baby to breathe. Shaw says it's not uncommon for people to come up to him after his lectures to tell him that Exosurf saved their children's lives.

Exosurf epitomizes Walter Shaw's attitude toward science, says his wife. He "always wanted to do something for the science community. He didn't start out just to make a big pile of money. That was never our focus. He wanted to make a difference," she says.

## BUSINESS TRAINING

Walter Shaw was born and raised in Minerva, a small town in Ohio. His father, Oscar, worked at the local bank, which was so small that it had a cap of $5 million. Shaw credits his father for instilling in him a solid work ethic. "Dad was unbelievable. He worked at the bank, and he kept books for companies at night," remembers Shaw. Shaw's mother aspired to be a physician but never got the opportunity. Instead, she instilled in her son that he ought to do something in the biomedical field.

Shaw says he got the best business training in his hometown. Between the ages of 12 and 16, he held a paper route. That required delivering newspapers every day, no matter what the weather brought, to customers who wanted their newspapers to be in specific spots. "If it was not where they wanted it, you got a lot of complaints," says Shaw. Every Saturday, Shaw had to collect money from his customers to pay the people who gave him the newspapers to sell. "A paper route is a microcosm of a business. You have customers whom you have to satisfy, you have to make a profit, you have to handle the finances," says Shaw. "You can't take a Saturday off to go play ball."

The only difference between his paper route and Avanti, says Shaw, is that as a newspaper delivery boy, he had no control over the quality of the product. But at Avanti, Shaw can ensure the quality of every shipment.

Shaw met his future wife at Asbury College in Kentucky. He was a chemistry major. She majored in music, specializing in piano and voice. Asbury College had a strict rule segregating men and women. But one day, Rowena, a self-described rule-keeper, disobeyed. "I went to hear the boy's glee club choir in Lexington. I went with a young man who had a car. I don't know why I did this," she says. "Walt also happened to be going."

The group later went out for hamburgers. Rowena didn't have any money, so she first declined to join the meal. But then Walter offered to pay for her meal, "which was probably 75 cents!" she says with a laugh. The two have been married for 52 years. "He's the one with the sense of humor," says Rowena Shaw of their partnership. "I am the very serious one."

Rowena Shaw was a year ahead of her husband in college, so as he completed his degree, she worked at the University of Kentucky Medical School's purchasing department as the assistant to the secretary of purchasing. "I took care of emergency purchase orders," she says. "It taught me a lot for starting up [Avanti], because I created all the paperwork and everything."

The Shaws then moved so Walter could pursue his master's degree at The Ohio State University. By the time they got to Virginia so that Walter could take up his laboratory director position, their children were born, so Rowena stayed home to take care of them. In Alabama, she took on running Avanti's daily operations full time in 1978 and has been doing it ever since. Rowena is the vice president of the company.

## KEEPING AVANTI AHEAD

Avanti now has 75,000 square feet of manufacturing and office buildings spread over 25 acres. The Shaws' son, Trevor, has joined the family business. Their two daughters have chosen other careers.

Walter Shaw says Avanti has been successful because the company makes sure it can stand behind the quality of its products and always listens to its customers. "We used to just make a few simple phospholipids. Now we make a whole host of lipids, from sterols to neutral and biologically active lipids," says Shaw. "All of these have evolved because the customer has come to us and asked, 'Can you make this?'"

George Carman of Rutgers University says that, indeed, custom orders for specialized lipids are one of the best services the company offers. Carman was the 2012 recipient of the Avanti Award in Lipids that is given through the American Society for Biochemistry and Molecular Biology and funded by Avanti.

Both Burgess and Rowena Shaw say Walter Shaw's commitment to quality is what has helped Avanti earn its good reputation. Rowena Shaw recalls a time when she received inquiries from Europe about making lipids for cosmetics. Although the thought of the revenue was tantalizing, the Shaws decided against going into the cosmetics business, because it would mean making less pure lipids.

Because of Avanti's commitment to quality and willingness to help customers, lipid researchers view the company as "more of a collaborator than a supplier," says Daniel Raben of Johns Hopkins University, who heads the ASBMB's Lipid Research Division. In line with its philosophy of always thinking of customers, says Walter Shaw, Avanti is a generous supporter of the ASBMB because many of his customers are members of the society. Starting in 2013, the ASBMB's Lipid Research Division will give out a young investigator award in Walter Shaw's name.

The Shaws and Burgess say they are constantly exploring the next frontiers in lipid research. For example, on the side of the research-grade lipid products, the company is working on biologically active lipids, which are emerging as important molecules in cell function. On the pharmaceutical side, the company is exploring the use of lipids as bioactive ingredients in analgesics and anti-inflammatory agents. Since 2003, Avanti has been a licensed supplier of mass spectrometry lipid standards for the multi-institutional initiative called LIPID Metabolites and Pathways Strategy, or LIPID MAPS for short. LIPID MAPS aims to identify and quantitate the majority of lipids in mammalian cells, as well as to quantitate the changes in them in response to environmental and chemical signals.

In telling the story of how Avanti grew into the company it is today, Walter Shaw reflects on the moments that seem insignificant but change life's course: "Just think, if this brother and sister born of incest hadn't shown up in the emergency room with stomach cramps, we would have never had their blood to do the study. If I hadn't been working on the blood of burn victims, went to Cleveland and called up Grand Island Biological, who knows what I would have been doing?"

But Shaw pays the biggest tribute to the moment when he treated a woman to a hamburger. He says, "If I hadn't married Rowena, I can't imagine where life would have taken me."

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## PHOTOGRAPHY

When not focused on work, Walter Shaw does photography. He caught the photography bug in college when he showed up for a yearbook meeting. He was handed a speed-graphics camera, pointed in the direction of the darkroom and informed that he was the yearbook photographer. In the first three decades of Avanti, Shaw found it hard to spare time for darkroom processing of photos. But with digital photography, he has taken up his old hobby with gusto in the past decade, simply because "you can start and stop anytime you want." These days, he packs 35 pounds of camera equipment when he travels. ("My wife thinks I am crazy," he says.) Shaw is now putting together a photo collection of icons of the world and preparing for his first trip to Africa next year.

IMAGE PROVIDED BY WALT SHAW

# ASBMB
## ANNUAL MEETING
### BOSTON, *April 20–24, 2013*

Dear students, postdoctoral fellows and colleagues,

We cordially invite you all to attend the American Society for Biochemistry and Molecular Biology annual meeting April 20–24 in Boston.

This meeting is the product of an extraordinary amount of program planning by the organizational committee. It will feature 10 scientific themes, each composed of several symposia of distinctive flavors and foci.

The meeting will showcase the latest research breakthroughs not only in the established fields of biology (e.g., gene transcription) but also in the emerging disciplines of chemical biology and systems biology. There will be award and plenary lectures honoring distinguished scientists whom you likely admire but may not have had the pleasure to meet in person.

Numerous poster sessions will present findings from laboratories the world over. Short platform talks will be selected from the submitted abstracts, and there will be a poster competition with cash awards in each of the scientific themes. Competitive travel awards will be available for eligible students and postdoctoral fellows.

For those of you who have not attended an ASBMB annual meeting before, it provides a truly superb venue for networking – for prospective postdoctoral fellows and mentors to become acquainted, for example – and for forging collaborations.

In this issue of ASBMB Today and the next, you'll find synopses of some of the themed symposia that you surely will find informative and entertaining.

Mark your calendar now and plan on presenting your exciting work at the meeting!

Carol Fierke and Patrick Sung
Co-chairs, ASBMB 2013 annual meeting

# From motor to metalloproteins: the wonderful world of biocatalysis

BY ENRIQUE M. DE LA CRUZ AND CATHERINE DRENNAN

The catalytic mechanism theme has something for everyone. With the diversity of the field in mind, we have developed four sessions depicting frontiers of enzymatic catalysis.

Molecular motor proteins convert chemical bond energy into force generation and mechanical work. One session will highlight common mechanistic features and functional diversity among ATPase motor proteins via discussion of three systems: RNA helicases, nonmuscle myosins and kinesins. Speakers will discuss the chemical mechanisms of these enzymes, focusing on how their catalytic cycles are linked to thermodynamic and structural changes associated with force production and directed motility.

Meanwhile, enzymes long have been noted for their effective catalysis toward specific substrates. However, many enzymes are promiscuous in that they can metabolize multiple chemical substrates and/or catalyze different reactions on an individual substrate. Speakers in the thematic session on catalytic and substrate promiscuity will discuss the molecular origins of enzyme promiscuity as well as its critical role in the evolution of new catalytic activities and functions.

With a renewed national focus on alternative energy and the environment, our third session presents contributions that biochemists are making to the emerging field of bioenergy. Speakers will highlight recent advances in our understanding of the enzymatic machinery of photosynthesis, the assembly of the biological cofactors required for hydrogenase activity, and the enzymatic sequestration of the greenhouse gas carbon dioxide.

Once thought to represent a small subset of reaction mechanisms, identification of radical-based enzymatic chemistry is on the rise. In the "Cool Catalysis & Radically New Reaction Mechanisms" session, we will hear about enzymes with cool catalytic centers that perform dramatic chemical transformations. These enzymes will range from well-studied radical enzymes such as ribonucleotide reductase to newly discovered biosynthetic enzymes.

Enrique M. De La Cruz (enrique.delacruz@yale.edu) is a professor at Yale University. Catherine Drennan (cdrennan@mit.edu) is a Howard Hughes Medical Institute investigator and a professor at the Massachusetts Institute of Technology.

**Catalytic Mechanisms Thematic Sessions**

Molecular Motor Proteins – Force & Work as Products

Catalytic & Substrate Promiscuity

Bioenergy & Enzymatic Catalysis

Cool Catalysis & Radically New Reaction Mechanisms

# RNA biology: There's nothing boring about it

BY RACHEL GREEN AND DAN HERSCHLAG

Our annual meeting theme, rather mundanely entitled "RNA Function and Protein Synthesis," will include a wide range of exciting talks highlighting the diverse and remarkable roles of RNA in biology.

It has become increasingly clear in recent years that much of the genome is actively transcribed, and yet we still know little about what the many noncoding transcripts in the cell do and how they behave.

This theme covers the roles of RNAs in splicing, in translation, in regulating gene expression, and in bacterial and viral defense strategies. Some of the talks will be very biophysical in nature, discussing critical aspects of RNA structure and dynamics, while others will be more philosophical in nature, discussing protein evolution entwined with RNA regulation throughout the kingdoms of life.

Together, these talks will convince you that there is much to be discovered and that RNA biology, while now a vibrant field, has an even more vibrant future. Come join us in Boston for an exciting series of RNA sessions.


Rachel Green (ragreen@jhmi.edu) is a Howard Hughes Medical Institute Investigator and a professor at Johns Hopkins University School of Medicine. Dan Herschlag (herschla@cmgm.stanford.edu) is a professor at Stanford University.

**RNA Function & Protein Synthesis Thematic Sessions**

How RNA Molecules Behave & Misbehave

Making & Using RNA in the Nucleus

RNA in the Cytoplasm: Translation & Degradation

Frontiers in RNA Biology

# Lipids and membranes uncensored: The devil is in the greasy details

BY TOBIAS BAUMGART AND MARION B. SEWER

Although the past several decades have seen the role of lipids expand from mere structural cellular components to signaling mediators and regulators of protein function, the integral roles that these macromolecules are known to play in coordinating physiological and pathophysiological functions are ever increasing.

Identifying novel roles for lipids and membranes in biological processes has been facilitated by the development of innovative analytical and biophysical techniques, including live-cell, single-organelle imaging, mass spectrometry and fluorescence microscopy.

The integration of novel experimental approaches with classical biochemistry and in vivo rodent models has had a profound impact on our understanding of lipid biology and revealed many unexpected roles for these molecules. Indeed, it is now becoming apparent that the local lipid environment plays a critical role in dictating protein function and thus cell physiology.

Intriguingly, a recent research emphasis on the intricate synergy between the shape of cellular membranes and their function is beginning to yield mechanistic insight into localized signaling, trafficking and protein sorting.

The impact of signal-transduction cascades on lipid homeostasis in distinct organelles is also an important mechanism for controlling cell function. For example, nuclear phospholipid and sphingolipid metabolism is emerging as a key regulator of gene expression.

Moreover, a growing body of discoveries is defining new roles for detergent molecules such as bile acids as prominent contributors to metabolic dysfunction.

Mechanistic insight into the roles that sphingolipids, glycolipids and phosphoinositol phosphates play in the etiology of cancer, cardiomyopathy, inflammation and type II diabetes is becoming apparent.


Tobias Baumgart (baumgart@sas.upenn.edu) is an associate professor at the University of Pennsylvania. Marion B. Sewer (msewer@ucsd.edu) is an associate professor at the Skaggs School of Pharmacy and Pharmaceutical Sciences at the University of California, San Diego.

**Lipids & Membranes Thematic Sessions**

Lipid Signaling in Health & Disease

Lipid Membrane Curvature in Membrane Function

Lipid Trafficking & Sorting

Lipids in Nutrient Metabolism & Metabolic Dysfunction

# Chemical and systems biology

BY ANNA K. MAPP AND SHELLEY COPLEY

Molecules of all sizes function within complex networks in cells. Understanding cell physiology requires an understanding of the network components individually, their interactions with each other and the function of the entire network. The annual meeting sessions on chemical and systems biology will feature exciting new research on the function and evolution of interactions at scales ranging from small molecules to cellular networks.

The sessions on systems biology focus on the function, evolution and manipulation of metabolic networks. Two speakers will describe the use of quantitative systems-biology approaches to reveal a fascinating picture of the dynamics of cellular metabolism in bacteria and mammalian cells. Two speakers will focus on the evolution of metabolic pathways from different perspectives: the use of genomic resources to analyze the historical evolution of pathways and the use of experimental approaches to analyze the emergence of a novel pathway patched together from promiscuous activities of enzymes that normally serve other functions. The final speakers will show how a greater understanding of metabolic networks provides the framework for efforts to manipulate networks in applications as diverse as the production of chemicals and the treatment of cancer.

The chemical biology sessions will focus on communication within networks. Two talks will address the mechanisms of communication between bacteria and their hosts, including the discovery of small molecules that regulate the communication and behavior of both the bacteria and the eukaryote. Hubs of the signaling networks that underlie cellular communication and phenotype rely on multicomponent complexes that assemble and disassemble in a dynamic fashion. Because of their often transient existence and the inherent conformational dynamics of the constituent macromolecules, these complexes have been challenging to define and control. In four talks, we will learn about cutting-edge spectroscopic methods for capturing the structure and dynamics of these complexes as well as the latest strategies for regulating their assembly and function using artificial modulators. In one case, for example, designer ligands are used to control B-cell signaling through modulating receptor cluster assemblies.


Anna K. Mapp (amapp@umich.edu) is a professor in the department of chemistry and the director of the chemical biology program at the University of Michigan. Shelley Copley is a professor in the department of molecular, cellular and developmental biology at the University of Colorado at Boulder.

**Chemical & Systems Biology Thematic Sessions**

Function & Evolution of Metabolic Networks

Controlling Cellular Communication

Manipulating Metabolic Networks

Assembly & Control of Dynamic Protein Complexes

# Controlling gene expression in the dynamic genome

BY STEPHEN BURATOWSKI AND GEETA NARLIKAR

Controlled changes in gene expression drive the transitions from stem cells to differentiated tissues, and many diseases are caused by misregulation of gene expression. This theme will cover four cutting-edge areas in transcription and chromatin research that will be of interest to a wide range of people. Talks will span multiple levels of analysis, from detailed molecular and genetic experiments to genomewide studies and continuing on up to looking at organism development.

The first session, on chromatin remodeling during transcription, will cover factors that assemble, move and dissociate nucleosomes to control access to the DNA template. The subject for our second day is mechanisms of transcription. It will address the events needed to create RNA from the DNA template. In addition to covering the fundamental processes of gene activation and transcription initiation, this session will address the hot topic of gene expression control during early elongation. The third session will cover co-transcriptional coupling mechanisms, a rapidly growing field that looks at how RNA processing and chromatin-modifying enzymes are physically and functionally linked to the transcription machinery. The final session will address the mechanisms in targeting and maintaining different types of heterochromatin. Large parts of the genome are heritably silenced during differentiation and development, and this process must be reversed to create induced pluripotent stem cells. Exciting new work suggests that these mechanisms involve not only histone

modifications but also noncoding RNAs.

We hope to attract a wide range of scientists and provoke stimulating questions and discussions. Invited speakers include established leaders as well as emerging stars. We look forward to rounding out the sessions with speakers picked from the most exciting submitted abstracts as well as highly interactive poster sessions.


Stephen Buratowski (steveb@hms.harvard.edu) is a professor at Harvard Medical School. Geeta Narlikar (geeta.narlikar@ucsf.edu) is an associate professor at the University of California, San Francisco.

**Mechanisms of Gene Transcription & Regulation Thematic Sessions**

Transcription Mechanisms

Chromatin Remodeling During Transcription

Co-transcriptional Coupling Mechanisms

Repressive Chromatin

# Protein modifications: the proteome in high gear

**BY DANIEL FINLEY AND MAURINE E. LINDER**

Although the central dogma of molecular biology is DNA ⟶ RNA ⟶ protein, we can't declare victory once the protein is made. A major focus of biological regulation is the chemical modification of amino-acid side chains of proteins with molecules as large as a protein or as small as a methyl group. These myriad modifications enable rapid, flexible and finely tuned responses to changing conditions in the cell. The ability to follow these chemical modifications globally and quantitatively by mass spectrometry is having a marked impact on our understanding of biological regulation and human health. The "Protein Modification, Trafficking & Degradation" theme examines the mechanisms and consequences of protein modification in four sessions, which are complemented by a workshop at which experts will share the state of the art on the proteomics of post-translational modifications. Misfolded proteins are toxic and have been implicated in tens of diseases. We will examine how the ubiquitin-proteasome pathway identifies such proteins, tags them covalently, and rids them from the cell. The elimination of membrane proteins also involves ubiquitination, although they are directed to the lysosome for elimination rather than the proteasome. The relevant trafficking pathways, endocytosis and the multivesicular body, form a novel and rapidly developing area of cell biology.

Bacteria usurp the eukaryotic cellular machinery to invade and sicken their hosts. We will learn how bacteria attempt hostile takeovers, how the host fights back and how the mycobacterial proteasome might represent a new target for treating tuberculosis.

An inviting site for chemistry, cysteine residues in proteins are modified in ways that control protein localization, sense changes in the environment and regulate enzyme activity. The versatility of cysteine modifications in proteins will be highlighted in a session that explores topics from a redox regulatory switch with implications for diabetes and obesity to oxygen sensing in plants.


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**Protein Modification, Trafficking & Degradation Thematic Sessions**

Ubiqutin & Ubiqutin-like Modifications

The Multivesicular Body & Endocytosis

Mechanisms of Bacterial Pathogenesis

Regulatory Thiol Modifications

Proteomics of Post-translational Modifications (workshop)

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# Science gets the interview, but you get the job

## *A perspective from a hiring manager in industry*

BY MELISSA A. STAROVASNIK

As a biochemist and leader of a large function at Genentech, I often am asked by graduate students and postdocs, "What are good strategies for getting jobs in industry?" Yet I am no expert. I have solicited only one industry job for myself, a postdoc position that put my foot in the door at Genentech, where I have continued my career for the past 19 years. Nevertheless, over that time, I have been involved in the hiring for hundreds of positions at every level from research assistant to senior director. So I will offer my advice from the perspective of the hiring manager looking for top talent and share common pitfalls. As challenging as those new on the job market find it to break in and be seen, we too find it exceedingly difficult to identify and recruit great candidates, so let's help each other!

### Be seen with four C's

Four main mechanisms are available to help you be seen by the hiring manager:

(1) curriculum vitae,
(2) cover letter,
(3) colleagues or network, and
(4) communication of your distinguishing characteristics.

The way in which you communicate how and why you are qualified for the position is of utmost importance. The goal is to effectively and succinctly convey your accomplishments to differentiate yourself from others in a compelling fashion. As your CV plays a crucial role in communicating your expertise and accomplishments, you should tailor it along with the cover letter to the specific job opening and company. While you may be open to a variety of opportunities, the manager reading through hundreds of CVs is looking for specific criteria relevant to his or her opening, so try to make that pop.

Have several colleagues review all application documents before submission to ensure they are formatted properly, read well and include no misleading information or typos. (And offer to do the same for them!) You may be surprised how often a simple mistake in your CV will be interpreted as a lack of attention to detail and put you out of the running before your application gets serious attention.

Always submit materials to the online application system, but also use your network to help identify the likely hiring manager or department head and send your CV and cover letter directly to him or her. If you are unsure who the department head is, consider sending it to the person you think may hold that position and ask him or her to pass the materials along to the appropriate hiring manager.

### Baseline scientific requirements are essential

For every opening, there is the expectation of specific technical/scientific skills and experience, so make sure evidence of the necessary expertise is clear in your application. If your most important work is still in preparation or under revision for publication, include a credible description of the key findings and your role in achieving them so that your work is not immediately disregarded as a pipe dream. Ideally, your adviser will provide a quick follow-up reference to the hiring manager validating the nature of your work and contributions and the status of the impending paper(s) to ensure your application will have a chance of more serious consideration.

Alternatively, for competitive research positions, your job pursuit will be much more productive if you hold off applications until your best work is in press. As you only get your first industry job once, you should start your career trajectory on as strong a footing as possible.

### Science gets the interview, but you get the job

Given that there are usually too many applicants who have the baseline requirements, the one who ultimately gets the job likely has additional soft skills: passion,

flexibility, leadership potential and communication.

As managers, we look for self-motivated individuals who are passionate about what they do. Just as important, though, is a willingness to be flexible and adapt to changing environments. In most industry settings, teamwork and collaboration are critical, so evidence of good communication, leadership and people skills will be helpful in distinguishing yourself among candidates with similar training and expertise. Go after jobs that will inspire you, and many of these traits will come more naturally.

I also would caution ambitious people to avoid the pitfall of assuming they should aim only for higher titles or for the ability to rise quickly in an organization. Instead, focus more on thoroughly embracing each step. Those who relish their work each day tend to be the ones who find or, more likely, create opportunities that ultimately propel their advancement. So relax and enjoy yourself. (And, if you are not having fun, it's better to recognize this early and change course.)

## Common misperceptions

Many candidates have mistakenly confessed during interviews for research positions that they are "more interested in the business side or management." If that is true of you, then you should not be pursuing research positions. We indeed conduct rigorous experimental science in industry! Nevertheless, there are other roles that would benefit from science-trained applicants. Thus, if never touching a pipette again is your preference, make sure you are interviewing for the right jobs! In smaller companies, you will find that nearly everyone pitches in on various aspects of research and business, making the lines more blurred. However, in major pharmaceutical companies, if you are not interested in doing science, you typically need to look beyond the research organization for job opportunities.

## Beyond the bench: many science-related jobs in industry

Most are stunned by the numerous important and exciting roles outside of the research organization within a pharmaceutical company where science training is highly valued. These include jobs within product development, project management, clinical operations, commercial strategy, market planning, manufacturing, process development, regulatory affairs, patent law and business development.

In such roles, successful candidates will have sufficient understanding of the science behind their projects and business opportunities to navigate various landscapes effectively. In many cases, additional training may be required to enhance skills not emphasized during graduate school, so assess carefully the job requirements and consider additional coursework to gain the necessary skills and demonstrate your commitment to your new career.

What if you don't know what you want to do? Go to conferences and job fairs, pursue internships or temporary work, or find other ways to interact with folks who work in various roles in industry – and ask questions!

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## ASBMB TODAY ESSAY SERIES: DERAILED BUT UNDETERRED

***Deadline: Dec. 31, 2012***

ASBMB Today is seeking personal essays for a special series called "Derailed but Undeterred." The series will speak to the resilience required for success in science. We hope these first-person essays will impart emotion and insight into how scientists endured — or are still enduring — trials and tribulations, both uncommon and widespread.

Share with our readers how you navigated unexpected life events and scientific setbacks that threatened your professional and personal goals. Your story can be humorous, serious or something in between, but it must be, above all, true and personal. We welcome submissions from scientists and students at all stages.

*Guidelines: Essays must be unpublished, between 300 and 1,000 words and emailed to asbmbtoday@asbmb.org by Dec. 31, 2012. Please send your manuscript with a brief cover letter, including the title of your submission, complete contact information and an author bio of no more than 100 words.*

# HOPES seed-grants program to enhance K–12 education in STEM: an update

BY REGINA STEVENS-TRUSS

The American Society for Biochemistry and Molecular Biology's Hands-on Opportunities to Promote Engagement in Science program, or HOPES, held its second annual workshop in April in San Diego during the society's annual meeting. The workshop, titled "Fostering Partnerships Between Colleges, Universities and K–12 Schools," was a three-hour session that brought together research scientists and teachers to talk about ways hands-on activities can be incorporated into science lessons to enhance student experiences.

This program, first launched during the society's 2011 annual meeting in Washington, D.C., is supported in part by the National Science Foundation and provides $2,000 grants to seed new partnerships to support the development of science, technology, engineering and math projects among workshop attendees. Ten proposals were funded in 2011. (Read about them at http://bit.ly/onrLgH.)

A requirement of the HOPES grants is that awardees submit end-of-year reports that outline outcomes of the projects. All of the grantees reported successes and challenges. The most common challenge reported was insufficient time to execute the plans thoroughly – a challenge we all experience. Several projects involved multiclassroom or multischool activities, and some of those projects' organizers had difficulty getting K–12 teachers' buy-in and implementation of the projects in classrooms. Regardless, all the awardees reported successes and have plans to continue their partnerships and projects. In fact, several outlined plans for expansion of the projects.

As part of the reports, the awardees were sent a questionnaire that probed at the following:

(1) success of the project,

(2) number of students affected and their demographics,

(3) students' knowledge before and after the project, and

(4) dissemination and long-term plans.

The results reported by the first round of grant awardees and the newly granted projects are exciting and encouraging. This program was initiated to promote partnerships between educators in the STEM fields who are seeking ways to enhance their teaching by incorporating hands-on classroom activities. A long-term goal of the HOPES program committee is that partnerships blossom all over the country and that K–12 students learn the joy of science through hands-on classroom activities.

Regina Stevens–Truss (Regina.Stevens-Truss@kzoo.edu) is an associate professor of chemistry at Kalamazoo College and a member of the ASBMB Minority Affairs Committee and Educational and Professional Development Committee.

**2012 SEED-GRANT WINNERS**

Seven proposals from the 2012 competition were funded:

**From genes to proteins: bringing hands-on molecular biology activities into middle-school classrooms to promote STEM education,** a collaboration between Robert Dutnall at the University of San Diego and Valentyna Banner, Aja Booker and Emily Vizzo from San Diego Global Vision Academy

**Nurturing interest in biomedical science education among elementary students,** a collaboration between Carmel McNicholas–Bevensee and J. Michael Wyss at the University of Alabama at Birmingham and Wayne Richardson at Deer Valley Elementary School

**Promoting in-depth science exploration through guided individual projects,** a collaboration between Maarten Chrispeels and Tamara Bhandari of the University of California, San Diego, and Camille Fowler from Garfield High School

**One health: disease diagnostics, surveillance and emerging infectious diseases,** a collaboration between Brinda Rana of the University of California, San Diego; Karen Ferran, Esmeralda Iniguez–Stevens and Sarah Marikos of the California Office of Public Health; Nikos Gurfield of the Department of Environmental Health Vector Disease and Diagnostic Laboratory; and Kate O'Connor of San Diego High School

**Botano tech incorporated comparative plan genomics module,** a collaboration between Cheryl Wlodarksi, Michael Goodbody and James Morris of Roosevelt Middle School; Laurie Smith of the University of California, San Diego; and Shirley Demer of Grant School

**Research collaboration between Rodriguez High School and University of the Pacific,** a collaboration between Kevin Scully and Sophia Straun of Rodriguez High School and Kirkwood Land of the University of the Pacific

**Stimulating fifth-grade science students' interests through engaging hands-on, inquiry-based lessons,** a collaboration between Rachell Booth, Marilyn Banta and Corina Maeder of Texas State University–San Marcos and Addie Woodard, Susan Brown and Cindy Matias of Hernandez Elementary School

## EVALUATING THE 2011 GRANT WINNERS' PROJECTS

### No. 1: success of the project

Michele Bahr of Woods Hole Marine Biological Laboratories (Woods Hole, Mass.) and Whitney Hagins of Lexington High School (Lexington, Mass.) headed up the project "Wolbachia and students: Discover the scientist within." Hagins reported, in part:

"(The) initial plan to have students teaching students worked out very well. I decided to jump right in with my 10th-grade (advanced placement) biology students and do the Wolbachia investigation as their first lab experience of the year … It was interesting to watch how tentative and scared they were as they began. My assurances that this was an adventure and there was no penalty for screwing up helped some, but for most, since this was their first AP class and first lab, they were nervous.

"(T)he best part of this project was watching these same students teach other students. They were phenomenal! It was so exciting to listen to the formerly tentative and shy students explain how to use each piece of equipment and how to do the complicated protocol. It was interesting to hear them mimic my instructions and, as time went along, adding their own variations and explanations — making the instructions more student-friendly and helpful.

"During the first month of school, the students in my class gave up their free periods to go into other classes and teach the background and techniques. Overall, this was very successful, as we had a total of 148 students run through the Wolbachia investigation."

### No. 2: number of students affected and their demographics

Mary Jo Koroli of the University of Florida Center for Precollegiate Education and Training (Gainesville, Fla.), in partnership with biology teacher Janet Bisogno of Celebration High School (Celebration, Fla.), headed up "Teach tech: increasing the use of biotechnology in high-school science classrooms." They conducted four professional-development workshops, each with a different science theme, for the high school's life sciences teachers during their regularly scheduled Professional Learning Communities time. Fourteen teachers participated.

Koroli and Bisogno report that by the year's end,

- five teachers had implemented the pipetting lab, affecting about 530 students;
- four teachers had implemented the gel electrophoresis lab, affecting about 375 students;
- three teachers had implemented the blood-typing lab, affecting about 350 students; and
- two teachers had implemented the ELISA, affecting about 200 students.

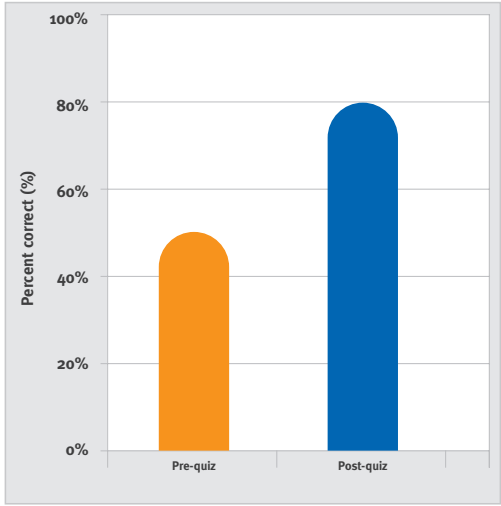
Of the 1,717 students involved, 49.1 percent were female, 49 percent were Hispanic, 10.6 percent were black and 10.8 percent were Native American or Pacific Islander.

### No. 3: students' knowledge before and after the project

J. David Holtzclaw of Transduction Technologies, in partnership with Kristin Swanson of Norris Middle School (both of Omaha, Neb.), Shelly Avery of Santee Community Schools (Santee Indian Reservation, Niobrara, Neb.) and Carol Moravec of Lincoln Southeast High School (Lincoln, Neb.) reported that the following students participated in their project, "Inquiry-based learning of K–12 physiology and nutrition concepts using pedometers":

- 40 middle-school students (67.5 percent of whom were from underrepresented minority groups),
- 45 high-school students (26.7 percent from underrepresented minority groups) and

Figure 1

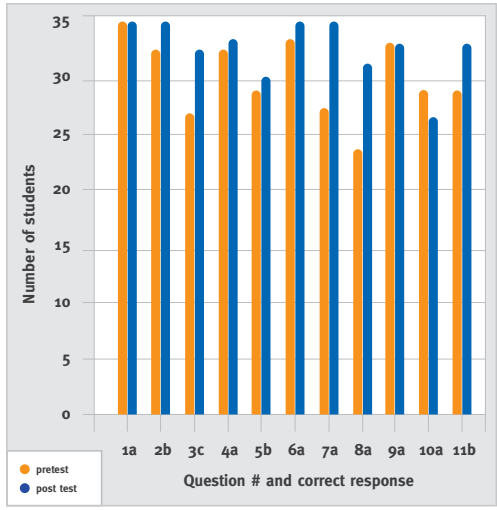


- 23 students in the Santee Community School (95.6 percent of whom were from underrepresented minority groups).

They further report a 30 percent increase in the number of correct answers given by the students in a pre- and post-project quiz (Fig. 1).

Patricia Halpin of the University of New Hampshire at Manchester, in partnership with fourth-grade teacher Heather Cantagallo of Sunapee Central Elementary School (Sunapee, N.H.), also reported data for their project titled "Getting fourth-graders excited about the cardiovascular system." For this project, the entire fourth-grade class (20 female and 17 male students, all Caucasian) participated in a three-day project. The students were given a questionnaire before and after the project to assess the impact of the activities.

Figure 2




The most significant changes (Fig. 2) were obtained for the following questions:

- Question 3: What is blood pressure?
- Question 7: After you exercise for five minutes, your breathing [respiration] rate should go _____ .
- Question 8: After you exercise for five minutes, your blood pressure should go _____.

## No. 4: dissemination and long-term plans

The project by Dorothy Belle Poli of Roanoke College (Salem, Va.) in partnership with Amy Chattin and Ashly Dowdy of Franklin County High School (Rocky Mount, Va.), titled "Bryological respiration and photosynthetic comparisons: a case to connect Virginia high-school students to active research," affected more than 100 high-school students of various grades. The students worked on a real research problem alongside scientists at Roanoke College. The organizers reported:

"Originally this project was only targeting 30 mixed-level students, because of costs. However, once the materials were prepared, several additional teachers were excited to try out the laboratories and iBook materials, and the school gave additional funds to the experiments. Even an ecology teacher used the bryophyte systems to show how respiration and photosynthesis was impacted using current drink choices (i.e., soda pop) on the plants. Therefore, over 100 students of varying levels (grades 9–12) and abilities (noncollege-bound to AP courses) were exposed to this project."

Although the organizers' initial goal of publishing the results of the project in a scholarly journal – and having students as co-authors – was not realized, the information was disseminated at a conference with very positive results. The organizers explained:

"The academic bryophyte community received the iBook with enthusiasm during the MOSS 2012 and 3rd International Symposium on Bryophyte Systematics joint meeting at the New York Botanical Garden in June 2012. This community of researchers and teachers has requested to use and contribute to this iBook to enrich the opportunities to educators of all levels. One researcher has already contacted Dr. Poli to add his reproduction videos to this interactive media product."

### 2013 SEED-GRANT OPPORTUNITIES

The third annual HOPES: Fostering Partnerships Workshop will take place in April in Boston as part of the society's 2013 annual meeting. Registration and program information for the workshop will be available in February. Awardees from the 2011 and 2012 competitions will be invited to present their findings. Though all ASBMB members are invited to submit proposals, preference is given to workshop attendees. Information regarding the HOPES seed grants can be obtained at http://www.asbmb.org/hopesgrant/.

*While university administrators seek out and reward faculty members who serve their communities, they're not focused on the greater good. But they should be.*

# Service is in our best self-interest

BY THOMAS O. BALDWIN

Advertised descriptions for faculty positions in American universities almost always refer to "research, teaching and service" as expectations of successful applicants, and the merit and promotion procedures in universities almost universally address faculty members' activities in these three areas.

Success in research and teaching usually can be gauged relative to some clear standards, but success in service is generally much more difficult to ascertain. Faculty on review teams look for evidence of professional service, such as editorial work and grant reviews; service to professional societies; or college or university service, such as academic administration, committee assignments, student advising and mentoring.

But service to the larger society, to the public we serve, seldom gains much traction in the merit and promotion evaluation systems. This seems to me to be strangely out of sync with the needs of both science and society.

## Good intentions with diminishing returns

The Morrill Act of 1862 established the land-grant university system that has served the United States so well for the past 150 years. Even in the darkest days of the American Civil War, President Lincoln and the Congress realized that the future of the nation depended upon a strong, accessible system of higher education.

Today, however, higher education is threatened by devastating funding cuts that are making it inaccessible to all but the wealthy, and the public seems to be unaware of the potential grave impacts on future generations.

At the same time that the core infrastructure of public higher education is waning, public trust of science and scientists is eroding. Recent polls suggest that events such as the Fukushima nuclear plant disaster and the overestimation of the H1N1 influenza pandemic have compromised public trust in science, and public misunderstanding of such matters as vaccine risks, stem-cell research and the use of animals in research also contributes to this decline.

To reverse this worrisome trend, it is essential that university faculty members take it upon themselves to inform the public of the value of America's great university system, to engage the public in discussions of the nature of science and the scientific process, and to recruit the passion of the people to move higher education closer to the top of the national agenda. But even when faculty members do get involved, without buy-in of the top administration of universities, their efforts are muted.

For more faculty to become engaged in K–12 math and science outreach, to devote more time to working with middle- and high-school students on science-fair projects, to develop science cafés, to deliver lectures for the public, and so forth, the reward system needs to be restructured.

## The responsibility is shared

The challenge is twofold. First, university administrators have to come to respect, support and reward faculty efforts to advance the public opinion of science. Second, faculty members have to take advantage of the added dimension of the meaning of service and outreach as they attempt to do that for which they receive a paycheck.

This is a matter of changing the culture of academic science. It is vital that American universities accept that outreach to and engagement with the lay public is a most serious form of service that should be rewarded through the merit and promotion systems. The culture of universities is based on many decades of tradition, and changing it will not happen quickly unless the top leadership of American universities accepts the challenge to debate and, ultimately, to redefine the parameters by which the service efforts of their faculty members are evaluated and rewarded.

Thomas O. Baldwin (thomas.baldwin@ucr.edu) is the executive associate dean for external relations at the University of California, Riverside, College of Natural and Agricultural Science and a member of the ASBMB Public Outreach Committee.

# Implementing 'Vision and Change'

## *Developing and using assessment tools to promote student-centered teaching*

BY J. ELLIS BELL

The "Vision and Change in Undergraduate Biology Education: A Call to Action" report, the final version of which was released last year, outlined a blueprint for undergraduate education in the biological sciences that focuses on student-centered learning of foundational concepts and skills necessary for their future success in science or whatever careers they choose. Despite the participation of the major funding agencies in the preparation and dissemination of the report, it is surprisingly clear that few outside the immediate participants have heard of "Vision and Change."

Recognizing that widespread implementation of the concepts of "Vision and Change" would require much broader buy-in, the American Society for Biochemistry and Molecular Biology applied for and won a Research Coordination Networks–Undergraduate Biology Education grant from the National Science Foundation to engage the biochemistry and molecular biology community not only in discussion but also in the development of assessment tools focused on the student-centered skills and the foundational concepts of our discipline (and the associated fields of chemistry, physics, math and computer science).

Going into the third year of a five-year project, the ASBMB has sponsored regional meetings across the country that have engaged faculty members from all types of institutions in the discussion of what are the foundational concepts and skills that our students should acquire from their degree programs. These meetings also have disseminated information about developing tools that can be used for both formative and summative assessment of student outcomes. The regional meetings were complemented by well-attended symposia at the annual meeting and a session at the ASBMB's small education meeting in Richmond, Va., in 2012.

As we go into the third year of the grant, the project's steering committee is working on three white papers summarizing the discussions on

1) the foundational concepts of the discipline;

2) the necessary skills for biochemistry and molecular biology graduates; and

3) the underlying concepts of chemistry, physics, math and computer science necessary for our students in the increasingly quantitative and interdisciplinary world of modern biochemistry and molecular biology.

These three white papers should be available on the ASBMB's project website before the annual meeting in April in Boston. The outlines for developing appropriate assessment tools also will be available on the website.

The annual meeting also will highlight the transition to the development and use of validated assessment tools with the following presentations:

- Jennifer Momsen, North Dakota State University: "Will this be on the test? Characterizing cognitive skills of undergraduate science assessments"
- Cheryl Sensibaugh, University of New Mexico: "Problem solving in biochemistry: assessment, learning strategies and preconceptions"
- Kim Linenberger, Iowa State University: "Bio chemistry students' misconceptions regarding enzyme-substrate interactions"
- Karen Sirum, Bowling Green State University: "Assessing student development of scientific thinking skills using the experimental design and analysis of data ability tests."

The national meeting presentations will be followed by two RCN–UBE-focused workshops and a steering committee meeting at the small education meeting to be held in Seattle in August 2013.

To lower the energy barrier for the development and use of these tools, a section of the website will be dedicated to illustrating best practices for faculty members using such approaches in their classrooms as well as making the tools themselves available as they are developed and validated.

Finally, just as the "Vision and Change" initiative was a community project, the ASBMB RCN–UBE project

quickly has expanded from the original group of principal investigators to engage a wide segment of the biochemistry and molecular biology community, bringing together pedagogy and assessment experts with classroom faculty interested in engaging their students in the best possible learning environment.

Have we implemented "Vision and Change"? In some instances, yes, but communitywide there is a long way to go, and, as we move along the path, it is clear that "Vision and Change" will evolve, and must evolve, to engage more than just the biological science community and the four-year college student community if it is truly to transform life-science education. In particular, it is critical that the two-year college community is engaged in the discussion of how the first two years look and what concepts and skills are involved.

Given the emphasis of "Vision and Change" on engagement in research early in the curriculum, it is important that the biochemistry and molecular biology community seriously think about those first two years for all students. Perhaps as we develop assessment tools we should focus on a tiered assessment, asking, "What do we expect students to understand and be able to do as they enter their third year?" (which is when often they get their first exposure to a traditional biochemistry course) rather than just, "What do we expect a graduating student be able to do?"

The discussion of what the first two years of the curriculum should look like puts the allied fields of chemistry, physics, math and computer science into the spotlight. Combined with the emphasis on skills and early exposure to research, this suggests a need for a concerted implementation of the approaches envisioned in "Vision and Change" among the various disciplines and departments involved in educating students in the molecular life sciences.

This year and during the next two years of the project, there will be many more regional meetings, so look out for a meeting near you. If you are interested in getting more involved, don't hesitate to contact me.

J. Ellis Bell (jbell2@richmond.edu) is professor of chemistry at the University of Richmond.

RESOURCES

1. Vision and Change in Undergraduate Biology Education main website: http://visionandchange.org/
2. 2011 final report from Vision and Change: http://visionandchange.org/finalreport (requires registration but is free)
3. Implementing Vision and Change website (by the ASBMB): http://www.asbmb.org/NSF/NSFHome.aspx
4. Slideshows from the ASBMB's small education meeting at the University of Richmond in July 2011: http://www.asbmb.org/CareersAndEducation.aspx?id=14095

jbc THE JOURNAL OF BIOLOGICAL CHEMISTRY

# Cytochrome P450 research pioneer

BY ADITI DAS

In a new collection of three Classics articles, the Journal of Biological Chemistry features the contributions of F. Peter Guengerich to the fields of drug development and toxicology through his pioneering studies of the cytochrome P450 enzymes. Guengerich, now a JBC associate editor and professor at Vanderbilt University, was introduced to the heme-containing enzyme in the early 1970s as a postdoc at the University of Michigan. He then went on to build a research team at Vanderbilt that set out to address several mysteries shrouding its actions by purifying it from rat samples. In the early 1980s, about 40 percent of candidate drugs failed because of adverse side effects. Guengerich soon realized that his team's initial endeavors into rodent enzyme characterization would not be enough to explain the toxicity of drug candidates in the human body, so he was able to partner with a Nashville transplant agency to obtain human liver samples, for which specimen collection calls often came late in the night. During those days, before the advent of recombinant DNA technology, his team had to work with liver microsomal preparations followed by traditional native enzyme purification and gas chromatography-mass spectrometry assays to characterize the human P450 enzymes. But Guengerich's team eventually isolated four of the five most important human P450s, which catalyze about 90 percent of the oxidations leading to drug metabolism. Their work was reported in the three successive JBC publications, which for the first time elucidated the body's most powerful detoxicating enzymes and served as a platform to understand failure of drug candidates and the basis of adverse interactions. The field of cytochrome P450 research has developed considerably over the past 40 years. Fifty-seven human forms are now known, with hundreds of genetic variations. Bioactivation by cytochrome P450s and understanding how to make intelligent decisions about the potential toxicity of candidate drugs at an early phase is one of the biggest challenges for the pharmaceutical industry today. None of these development efforts would have taken off without the efforts of the group led by Guengerich, who is still actively pursuing the fundamental biochemistry of these drug-metabolizing enzymes.

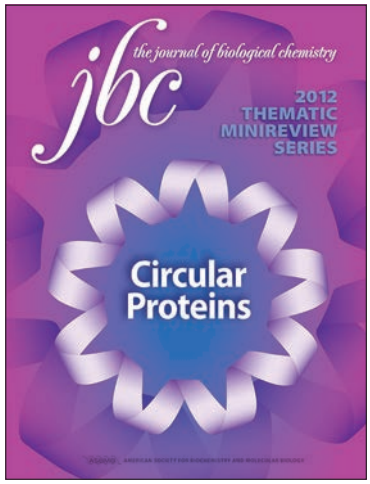
GUENGERICH

Aditi Das (addas06@gmail.com) is a Washington, D.C.-based science writer and research consultant at AGTII.

# Circular proteins thematic series

BY DIEDRE RIBBENS

A new thematic review series on circular proteins appears in the August issue of the Journal of Biological Chemistry. The series focuses on ribosomally synthesized circular proteins, which begin as linear peptides before they are post-translationally modified by the addition of an extra peptide bond to join the N- and C-termini. Topics covered in the review include the families of organisms – from microorganisms to mammals – that produce circular proteins, their discovery, their activities, and their chemical and biological synthesis in the lab. Understanding how circular proteins are produced and the advantages they have over their linear counterparts has broad applications in the fields of pharmaceuticals, agriculture, diagnostics and food safety.




In the first article of the series, "Circular proteins from plants and fungi," Ulf Göransson and colleagues discuss three families of circular proteins – cyclotides and circular sunflower trypsin inhibitors from plants and amantia toxins from fungi. The authors discuss the biological origin, structure and activity of each class, highlighting the different ways nature has devised to produce these molecules. They also speak to the benefits of circularization that offset the energetic cost of this post-translational modification.

Mercedes Maqueda and colleagues focus on bacterial circular proteins in the second minireview, "Discovering the bacterial circular proteins: bacteriocins, cyanobactins and pillins." The genetic organization of circular protein biosynthetic pathways is well understood in bacteria

and contributes to the understanding of these proteins in higher organisms. The authors explain how bacteriocins, in particular, are being tapped as potential preservatives in the food-safety industry or as therapeutics for systemic bacterial infections, because they are toxic to other bacteria but not eukaryotic cells. The exquisite stability of cyclic peptides is a valuable attribute in these applications.

Next, Robert Lehrer, Alex Cole and Michael Selsted review the only known circular proteins produced by animals in "Theta-defensins: cyclic peptides with endless potential." The unique biogenesis of theta-defensins sets them apart from other circular proteins, because each one is the product of two separate precursor peptides that become spliced together into a single molecule by a mechanism that is still unknown. The authors give examples of how theta-defensins, both biologically and synthetically derived, contribute to host immune defense against viral and bacterial agents.

Circular proteins also can be produced in the lab, as James Tam and Clarence Wong discuss in "Chemical synthesis of circular proteins." The authors explain how the entropic barrier to coupling the N- and C-termini of large peptide segments has been overcome by using a chemoselective capture step that generates a covalently linked ester intermediate and a subsequent acyl shift to convert this ester intermediate to an amide. Many current ligation methods use cysteine-rich peptides due to the supernucleophilicity of thiol side chains during the initial capture step.

Finally, Teshome Aboye and Julio Camarero describe the recombinant DNA expression techniques used to generate circular proteins in "Biological synthesis of circular polypeptides." Covalently linking the N- and C-termini of proteins can be useful, because the circularized protein becomes resistant to degradation by exoproteases, increasing protein stability. The authors discuss the production of circular polypeptides in vitro or in vivo, by expressed protein ligation, protein trans-splicing, protease-catalyzed transpeptidation and genetic-code reprogramming. The authors outline how circularization of proteins aids in the exploration of the relationship between protein topology and folding kinetics as well as the generation of genetically encoded cyclic protein libraries that can be used to screen the properties of these molecules.

The five review articles in this series highlight the fascinating roles of circular proteins in all manner of organisms and bring to light the various ways these molecules may affect various industries. While the articles show the progress that has been made toward finding these proteins and elucidating their activities, there is still much to be learned in this field. In their editorial commentary on the thematic series, David Craik and Norma Allewell, a JBC associate editor, note some of the remaining challenges, including the need to develop a robust way of rapidly discovering new examples of circular proteins because genomes or transcriptomes do not give hints as to an eventual circular structure and standard proteomic approaches to peptide sequencing do not detect proteins that have no beginning or end. They also highlight the common feature of cyclic peptides and the "endless potential of these ultra-stable mini-protein nuggets."

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THE JOURNAL OF LIPID RESEARCH

# Sleep apnea-related atherosclerosis and leukotriene B4

BY MARY L. CHANG

Obstructive sleep apnea is a common condition in which breathing while sleeping is blocked by soft tissue of the throat, decreasing oxygen flow. Left untreated, it can lead to heart disease and stroke. Atherosclerosis has been linked to moderate to severe sleep apnea, as those with the condition show signs of early atherosclerosis, but the connection between the two has remained unclear.

Cytokines are one group of signaling molecules that act as chemical messengers, allowing for communication between cells. Sometimes, when there is too much of a cytokine in one place, damage can occur. Recent studies have shown the cytokine group of leukotrienes are related to both obstructive sleep apnea and atherosclerosis, but the mechanisms linking leukotrienes to either condition had not been adequately investigated.

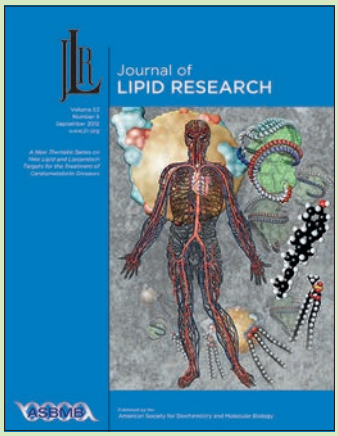
In a paper in the September issue of the Journal of Lipid Research titled "Leukotriene B4 pathway activation and atherosclerosis in obstructive sleep apnea," Françoise Stanke-Labesque and colleagues of France's National Institute of Health and Medical Research, known as INSERM, examined the production of a specific LT, leukotriene B4, in polymorphonuclear neutrophil cells from sleep apnea patients and healthy people.

Leukotriene B4 causes white blood cells to adhere to and cross into endothelial walls, a key step in the development of atherosclerosis; this leukotriene also increases the production of other inflammatory cytokines by transcriptionally activating their related genes.

In the study, the cells obtained from patients with sleep apnea had increased production of leukotriene B4 associated with increased messenger RNA expression of 5-lipoxygenase-activating protein, known as FLAP, which is directly involved in production of leukotriene A4, the unhydrolyzed form of leukotriene B4.

In vitro results indicate that the activation of the leukotriene B4 pathway and increased production of leukotriene B4 induces two other proinflammatory cytokines, interleukin-6 and monocyte chemotactic protein-1, both of which are major players in the development of atherosclerosis. Because atherosclerosis is such a complicated disease involving many different lifestyle and hereditary factors, the authors concede that this leukotriene pathway activation may not be the sole mechanism for the vascular remodeling that occurs. Still, the findings from Stanke-Labesque et al. point to this particular leukotriene pathway and FLAP as possible therapeutic targets.

### Thematic reviews on new ways of treating cardiovascular disease by targeting lipids and lipoproteins




The September issue of the Journal of Lipid Research features a special section marking the beginning of a new thematic review series that explores new therapeutic targets. Entitled "New Lipid and Lipoprotein Targets for the Treatment of Cardiovascular Diseases," the series is being coordinated by Associate Editor Stanley L. Hazen of the Cleveland Clinic. Hazen has written an introduction to usher in this first installment of five reviews in this series, which surveys topics as varied as bile acid receptors to treat dyslipidemias (abnormal levels of lipids in the blood) as reviewed by Geoffrey Porez et al. of Université Lille Nord de France and the ongoing debate of lecithin:cholesterol acyltransferase in a piece by Sandra Kunnen and Miranda van Eck of Leiden University in the Netherlands. Additional reviews in this series with a clinical focus will follow in future issues.

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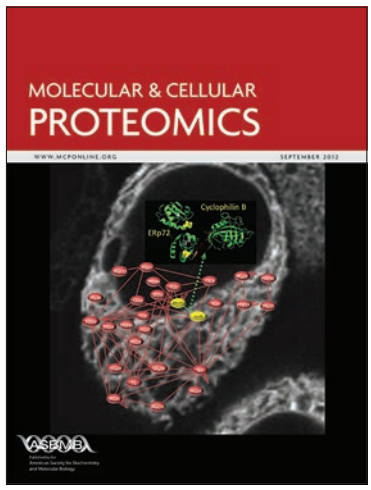
MCP **MOLECULAR & CELLULAR PROTEOMICS**

## How human milk nurtures the gut microbiome

BY RAJENDRANI MUKHOPADHYAY




Breastfeeding is a major influence on the makeup of a baby's gut microbiome, because human milk has been shaped by evolution to nourish and protect infants. "Notably milk guides the development of the infant gut microbiota, in particular enriching for certain Bifidobacterium species," explains David Mills at the University of California, Davis. Bifidobacteria are symbiotic bacteria in the human colon. In a recent paper in Molecular & Cellular Proteomics, Mills and colleagues analyzed how bifidobacteria digested N-glycans from complex milk glycoproteins (1). Babies can't digest these N-glycans, so the study, says Mills, is the first "to explain how these glycoproteins might serve as growth substrates for bifidobacterial enrichment." To break down N-glycans, Mills and colleagues established that the bifidobacteria had special endoglycosidases. The most interesting enzyme was EndoBI-1, the endoglycosidase from a particular bacterium called Bifidiobacterium infantis that is predominant in the infant gut microbiome. EndoBI-1 "was amazingly unique in its ability to cleave any type of N-linked glycan away from the corresponding protein," says Mills, adding that the finding strengthened the argument that B. infantis "evolved in concert with mammals and lactation." Furthermore, the researchers discovered that EndoBI-1 is heat stable. "This feature, combined with the ability to cleave any type of N-linked glycoprotein, potentially makes this enzyme a very useful tool in proteomics and pharmaceutical research," notes Mills. He adds that because bifidobacteria are eaten as probiotics, EndoBI-1 could have "a slew of applications in food processing as well."

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1. Garrido, D., et al. Mol. Cell. Proteomics (2012) DOI 10.1074/mcp.M112.018119.

# Insights into the regulation of phosphatidate phosphatase activity and lipid homeostasis have come to light through studies with yeast

BY GIL-SOO HAN AND GEORGE M. CARMAN

The obesity epidemic and derivative metabolic diseases, such as diabetes, have stimulated much interest in controlling fat (triacylglycerol) metabolism. Of many enzymes involved in fat production, phosphatidate phosphatase, or PAP, has emerged as an important regulatory enzyme. PAP, which catalyzes the dephosphorylation of phosphatidate to produce diacylglycerol, functions at the penultimate step of triacylglycerol synthesis and controls the pathways by which membrane phospholipids are synthesized. Because the lipid precursors phosphatidate and diacylglycerol also play roles as signaling molecules, the importance of PAP activity is implicated in the control of diverse cellular processes, including transcription, activation of cell growth, membrane proliferation, secretion and vesicular trafficking.

The yeast Saccharomyces cerevisiae serves as an excellent eukaryotic model in elucidating the enzymological, kinetic and regulatory properties of PAP. A gene (PAH1) encoding PAP was first identified in S. cerevisiae, leading to the identification of homologous PAP-encoding genes in humans, mice, flies, worms and plants. The phenotypic characterization of yeast cells lacking or overexpressing the PAP gene has revealed the importance of the enzyme in lipid metabolism and cell physiology. The PAP-deficient cells, which contain reduced levels of diacylglycerol and increased levels of phosphatidate, exhibit a great reduction in triacylglycerol synthesis and a marked increase in phospholipid synthesis. The elevated level of phosphatidate also is associated with the induced expression of phospholipid synthesis genes and an abnormal expansion of the nuclear/endoplasmic reticulum membrane. The reduced level of diacylglycerol correlates with defects in the formation of the lipid droplet (fat storage organelle) and in vacuole homeostasis. Reduced ability to synthesize triacylglycerol renders the PAP mutant acutely sensitive to fatty acid-induced lipotoxicity. On the flip side, higher PAP activity is also deleterious to lipid homeostasis and cell physiology. For example, the overexpression of an unregulated phosphorylation-deficient form of PAP is lethal, and the toxic effect is attributed to the depletion of phosphatidate required for phospholipid synthesis and to the accumulation of diacylglycerol to a toxic level. Thus, a tight regulation of PAP activity is essential to balance the synthesis and turnover of lipids.

Recent studies with yeast PAP have shown that phosphorylation/dephosphorylation is a major mechanism by which the enzyme activity is controlled. PAP is a peripheral membrane enzyme, which translocates from the cytosol to the nuclear/endoplasmic reticulum membrane via interaction with the Nem1p-Spo7p phosphatase complex. The enzyme in the cytosol is highly phosphorylated, and the phosphorylated form is recruited to and dephosphorylated by the membrane-associated phosphatase complex. Upon its dephosphorylation, PAP directly associates with the membrane using its N-terminal amphipathic helix. Phosphorylation of PAP is mediated by multiple protein kinases that include cyclin-dependent kinases (e.g., Pho85p and Cdc28p), protein kinase A, protein kinase C and casein kinase II. Identification of phosphorylation target sites and the interdependencies of the various phosphorylations are being interrogated with the aim of understanding how PAP activity is fine-tuned to control lipid homeostasis.


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# Reader feedback

**Below is a selection of what readers are saying about the August issue of ASBMB Today. All letters and comments are edited for grammar, clarity, length and style. Have something to say? Email asbmbtoday@asbmb.org or comment online.**

## Balancing act

The scientific community as a whole – men and women – needs to have this issue brought to the forefront of discussion. Don't even get me started on the lack of jobs, generally poor salary and benefit structure, and pressure to get funded and publish four to five peer-reviewed manuscripts a year in addition to having to have a real come-to-Jesus moment when … deciding whether or not you can afford to have a child, much less take time to raise one. Over the past five years as a postdoc, almost everyone I know, including myself, is just clawing our way to get the hell out of science – whether it be academia, industry or government – with the general consensus being that the pressure and lack of opportunities in this economic climate are simply not worth it anymore. "Disenchantment" is the best word to describe it. – R.O.

The lack of paid postpartum leave is appalling, especially when sick/vacation time is as limited as it is during student/postdoc years. I had one child while a postdoc and a second as a staff scientist. I've had to realize that, no matter what I do, I'm going to feel guilty about shortchanging some aspect of life. Move past it – that isn't productive and won't help you toward your goal – or so I tell myself daily! For me, the biggest factor in success is having an understanding and incredibly helpful partner, especially as he is the one who usually gets shortchanged first. I'd also point out that issues affecting men/dads and women/moms overlap but are divergent – an obvious example is access to pumping facilities. I also suspect that moms harbor more guilt at being away from their children, but perhaps that is just my perception. – CHRISTINA B. IN OKLAHOMA

THANK YOU SO MUCH FOR WRITING THIS! I am not a biologist, but this was passed to me by a colleague. Very nearly all of the challenges I have faced since becoming a parent as a postdoc have been addressed here. I would like to echo other comments in that I am nearly certain I will leave academia, but I am also nearly certain I will return later in my career as a more experienced, confident and laid-back professional. Two facets of parenthood not included here are the aspects of unexpected pregnancy and early termination of pregnancy. These also present unique challenges. In sum, I would suggest to others that developing a close-knit, diverse network of scientist–parent and parent supporters is paramount to success in both of these roles. – ANONYMOUS

## An "honorable" career in academia vs. an "alternative" career in the private sector

I just obtained my (bachelor's) in biotechnology this year (from the Universitat Autònoma de Barcelona). I am currently working in the business development department in a small biotech company. I simply would like to thank you for your article: That's exactly what I have found during these four years studying in a public institution. Your article made me feel I was not alone, in fact, I would say that around 80 percent, (if not more) of the content given by the university was closely related to what we could classify as basic research. One had to go beyond university to learn about the biopharmaceutical sector itself, preclinical and clinical development, marketing, management or biobusiness. Also, I had never thought that some of the obstacles I have found when trying to understand biotechnology as a whole at university were also present in the USA. – GERARD CAELLES

## Good outcomes

Well said. Only by placing highly qualified scientists in educational settings can we hope to shift the dominant view toward one that accepts rational explanations and values logic and problem solving. The journey of a scientist is long and varied – and worth every sacrifice and detour. Mentors who supported me, encouraging me to explore different paths, are the reason I'm where I am today. I'm incredibly fortunate to be combining my loves of research, teaching and science outreach/communication as a new assistant professor at Reed College. Even if mentors start out clueless, the examples (in this article) illustrate that they don't have to stay that way. Thanks for sharing! – KARA CERVENY

## Thanks, but we need more

The article by Benjamin Corb has a number of statements that are misleading or erroneous. The most egregious is the phrase "today's trainees are sold promises that their hard work in the lab will pay off with tenure-track positions in academia." This is an unwarranted allegation. The statement incorrectly portrays the faculty in our profession. The Ph.D. never promised a specific type of employment. The Ph.D. aims to develop critical thinking and analytical skills, experimental design, communication of science, creation of new knowledge and problem solving. These are the tools/fundamentals that are essential for a variety of employment opportunities. There are many ongoing initiatives today at universities and professional organizations, such as the ASBMB and (the Federation of American Societies for Experimental Biology), that address the variety of career pathways for Ph.D. scientists. It is unfortunate that the strides being made now and the opportunities that we see for the future are not fully recognized and applauded. – JUDITH BOND

I am overjoyed to see this topic being discussed at this level. While I agree with Judith Bond that the Ph.D. does not promise a specific type of employment, there is a clear expectation in most departments that most students will pursue academic careers. Given the results of this study (by the National Institutes of Health Advisory Committee to the Director's Biomedical Workforce Working Group), perhaps the first step is to stop referring to nonacademic positions as "alternative" careers for Ph.D. scientists. Fundamental changes to training programs will not happen until there is a cultural shift in the attitude toward nonacademic career paths. – JULIE MONTGOMERY

This article raises a number of important and complex issues that deserve further discussion. One of these is highlighted by the comment by Judith Bond. The key issue is the relationship between what trainees are "sold" compared with what they perceive. Many individuals enter graduate school with the anticipation that they will pursue academic careers, because that is the only career path that they have been exposed to in any depth. Furthermore, some components of academia have, intentionally or otherwise, placed academic careers on a higher plane than other careers, as noted by Martin Rosenberg in his essay in this issue. Dr. Bond is correct that many institutions and organizations have taken steps to provide trainees with clear perspectives on the wide range of career options that are potentially available to individuals with Ph.D. training in biomedical fields. It is important that such efforts continue and reach earlier into the training period. To Julie Montgomery: See the accompanying essay by Jon Lorsch on this issue. I agree completely that acknowledging that there is a range of successful career outcomes, academic and nonacademic, for biomedical Ph.D.s is an important step. We tried to raise this issue in the Training Strategic Plan that I was involved in at the National Institute of General Medical Sciences, and we need to reinforce this point, both with faculty and with trainees. – JEREMY BERG

As a Ph.D. graduate in molecular biology, I very much understand the challenges that face graduate students. While I fully believe the training is valuable and your training is much more than the technical skills, businesses want more than your academic training. They want real-world experiences. Currently, I am a scientific recruiter, and I daily work with businesses to connect them to the right talent. I am constantly told that Ph.D.s can't do this job because they have no experience, they want too much money, they aren't good team players, they are "weird," they don't know how to work on a fast timetable. While these (statements) are untrue, graduate students need more outside-of-lab time to develop their unique talents (both technical and nonbench skills), understand the market and figure out how they can sell their individual skills/value to the private sector. – IDELLA YAMBEN

### ALICE IN GRANTLAND*

You are old, Doctor Williams,
The postdoc said,
And your hair has become very white,
And yet you incessantly trouble your head.
Do you think, at your age, it is right?

In my youth, Doctor Williams
Replied to his chum,
I used to get grants without pain,
But now that I'm perfectly sure I'll get none,
Why, I write them again and again.

**A poem composed between grant applications by George Stark while channeling his inner Lewis Carroll.*

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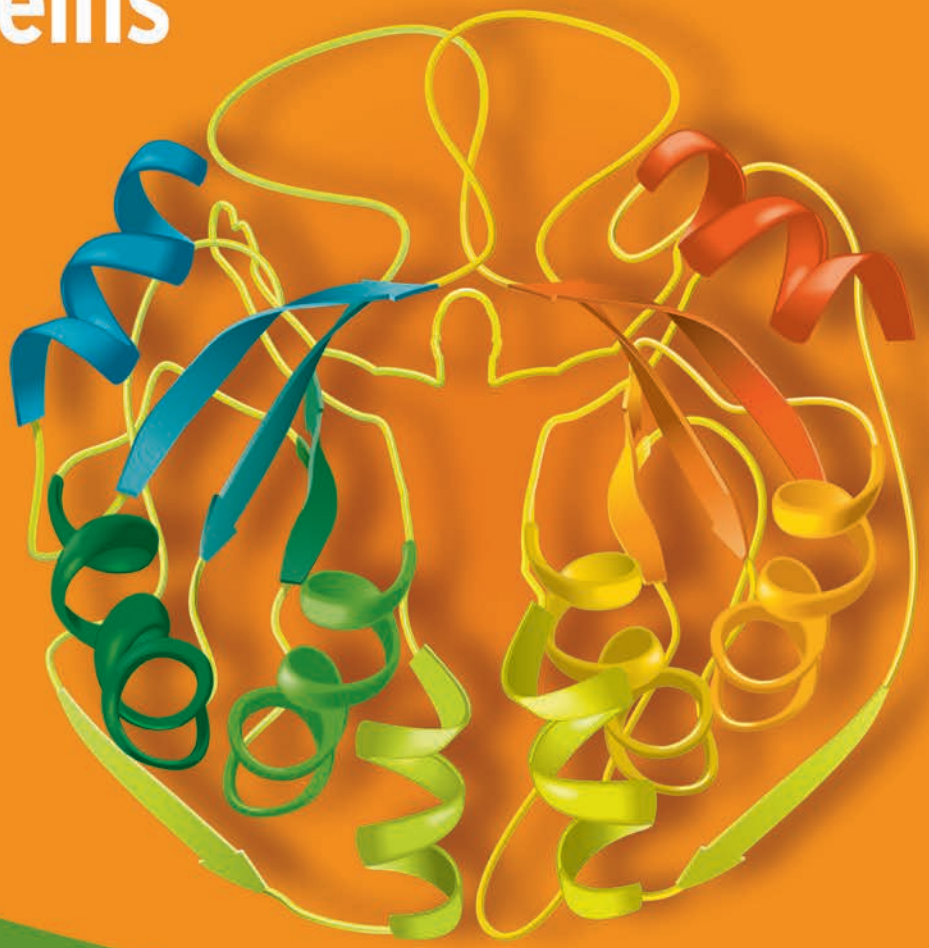

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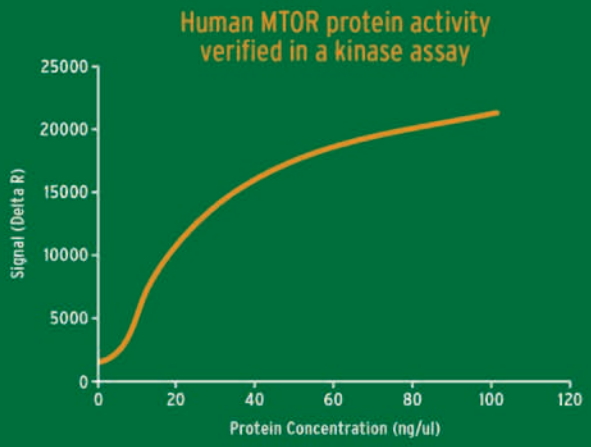


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