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January 2012



## ***Shaking up the Western blot***



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## education

The results of the 2011 ASBMB  
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Additional information is also available  
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## New initiatives for 2012: public outreach and professional development

BY SUZANNE PFEFFER

**T**he start of a new year is always a good time to reflect on the successes of the previous year and to set goals for the months ahead. The American Society for Biochemistry and Molecular Biology Council met in early December to discuss two new initiatives that I am pleased to describe for you here.

The ASBMB Council and Public Affairs Advisory Committee feel strongly that public outreach and increasing scientific literacy are two very important society goals. To forge ahead in these areas, the ASBMB has assembled a Public Outreach Task Force chaired by Lee Gehrke of the Massachusetts Institute of Technology. The goal of this task force is to enhance the ability of ASBMB members to contribute to the public understanding and appreciation of science. Because this is a highly ambitious undertaking, it will be important for the us to leverage the resources of other existing programs and organizations. During this first year, the Public Outreach Task Force will survey the outreach landscape and determine how ASBMB can have the greatest impact toward promoting science communication and scientific literacy worldwide. The task force will investigate the activities of a number of existing organizations, including the Coalition on the Public Understanding of Science, the Science Festival Alliance, sciencecafes.org, the International Public Science Events Conference and the Alfred P. Sloan Foundation.

To support the work of the task force, we are looking for an energetic, enthusiastic, innovative and organized individual to serve as a new public outreach coordinator. This individual should exhibit a vision for establishing a broad contact network and great initiative to help establish our new program. We seek applicants with a passion for promoting science and strong interpersonal and communication skills to galvanize the ASBMB membership to promote science communication and scientific literacy. The coordinator will facilitate volunteer activities that promote public understanding of science. The top candidate will write well, be fluent in the use of modern media and have the ability to make science both relevant and accessible to nonscientists. A Ph.D. in biological



**Lee Gehrke, Massachusetts Institute of Technology, chairman of the Public Outreach Task Force**

or chemical sciences is helpful but not required.

Concrete goals include the generation of a toolkit to help members initiate science cafés and festivals, the creation of a Web portal to help ASBMB members learn from each other how to plan local community events, and the establishment of mechanisms to motivate members to initiate events and foster partnerships with local organizations to promote scientific literacy.

In the first year, the science outreach coordinator will prepare a white paper for the Council describing existing outreach and science communication programs and how ASBMB can have the biggest impact in outreach and science communication by coordinating with existing programs. As soon as possible, we hope to facilitate new grassroots science communication activities, including encouraging ASBMB members to talk to civic groups, to present lectures or start science cafés, to visit local schools to promote science careers, and to participate in established science fairs and in programs at their own institutions devoted to increasing the public's awareness of science. In the future, the Public Outreach Task Force also will sponsor workshops on science communication at the annual ASBMB meeting.

If public outreach is your interest, watch for our new blog and website to be launched in the near future. We welcome the input and participation of all ASBMB members to make this program a success.

### **A new Mentorship Committee**

The ASBMB Education and Professional Development Committee, led by Peter Kennelly, oversees a number of wonderful programs that support high-school and

undergraduate students, graduate students, and postdoctoral fellows who share an interest in biochemistry and molecular biology. Yet all of our members can benefit from professional-development activities. To bolster the ongoing activities of the EPD, the Council proposes to establish a new Mentorship Committee with the mission of providing members of all ages with tools to enhance their own personal mentorship and professional development.

The goals of the proposed Mentorship Committee will be to develop and sustain a monthly column for ASBMB Today on topics of relevance to the professional development of ASBMB mentees of all ages. These would relate to professional skills, lab management, personnel issues, how to apply for a postdoc or job and so forth. The columns will be written by committee members and by other invited authors. The Mentorship Committee will develop ideas for mentorship and professional-development programs for each annual meeting and possibly also ideas for



**Fred Maxfield, Weill Cornell Medical College, chairman of the Mentorship Committee**

stand-alone courses that could be offered biannually for members. This year's annual meeting will include a time-management and work-life balance workshop; the Mentorship Committee will plan similar events for future years. In addition, the Mentorship Committee will work hard to identify other programs that would benefit our members in terms of mentorship and professional development. Should ASBMB offer methods courses in advanced proteomics or single-molecule analysis? Would a workshop in high-content, high-throughput screening be of value? Fred Maxfield of Weill Cornell Medical College has agreed to chair the committee, and I look forward to watching it take flight.

Should these new programs prove successful, we will consider adding them as standing committees of the society via a change in the ASBMB bylaws.

I wish all of you a new year full of many new discoveries — both of the scientific and personal variety. Happy new year to you! XXXX



ASBMB President Suzanne Pfeffer (Pfeffer@stanford.edu) is a biochemistry professor at the Stanford University School of Medicine.

A promotional graphic for the Journal of Biological Chemistry (JBC). The background is a light blue gradient with a pattern of molecular structures. On the left, the JBC logo is written in a large, white, cursive font. To the right, the text "WE MADE THE MOVE ONLINE ONLY IN 2012" is displayed in white and yellow. Below this, it says "JOURNAL OF BIOLOGICAL CHEMISTRY" in yellow, followed by "New Topic-Specific Affinity Websites" and "One of the Quickest Publication Turnaround Times" in white. At the bottom right, it says "SUBMIT TO THE JBC" in yellow and "www.jbc.org" in white.

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New Topic-Specific Affinity Websites  
One of the Quickest Publication Turnaround Times

**SUBMIT TO THE JBC**  
[www.jbc.org](http://www.jbc.org)



# DEADLINE EXTENDED!



## *It's not too late to submit your entry for the Experimental Biology 2012 poetry contest sponsored by ASBMB.*

*W*e know some of you are probably on the fence about this whole poetry-contest thing, so we thought we'd give you a little more information about what we're looking for.

We want you to send us lines that will make us laugh, that will make us feel warm inside, that will make us shiver, that will make us say to the person next to us, "Hey, you've got to hear this." Put simply, we want to be moved one way or another.



**GUIDELINES:** Entries should be unpublished free-verse poems up to 25 lines long in the EB2012 "bench-to-bedside" theme. Simultaneous submissions are allowed, but notify us immediately to withdraw your entry if it is accepted for publication elsewhere. Send your poem as an attachment, without identifying information on the file, to [asmbmtoday@asbmb.org](mailto:asmbmtoday@asbmb.org).

**ELIGIBILITY:** Members of the societies participating in EB2012 and registered attendees may enter. Each entrant is allowed only one entry, so send us your best work.

**WINNERS:** The top 10 finalists will be invited to read their work at EB2012, if they plan to attend. Attendance is not required for submission to the contest. The top three prizes will be \$100, \$75 and \$50. Finalists' poems will be published in ASBMB Today.

**JUDGES:** The panel includes both scientists and poets.

**DEADLINE:** January 31, 2012



## 2012 through our crystal ball

BY BENJAMIN CORB



**A**s the calendar flips from 2011 to 2012, we in the Public Affairs Office reflect on the year that was and try to predict the year that will be. Unfortunately, Carnac the Magnificent refused to take our calls, and predicting politics in this era of partisanship is about as easy as particle physics. First, a brief look at what Washington did, and didn't, do in 2011:

**Congress:** The 112th Congress has, to date, seen 54 bills signed into law by President Obama. By comparison, the 111th Congress had 383 bills signed into law by Obama. Of course, in the 111th, Democrats controlled the U.S. House and Senate; whereas, in the 112th, Republicans control the House. The last time there was a Democratic president and the House switched to Republican rule was after the Republican Revolution of 1994, with Newt Gingrich as speaker of the House of the 104th Congress and rival President Clinton in the White House. As contentious as that time was, Congress still saw 333 bills signed into law. The track record of the 112th Congress is atrocious, and both parties are to blame. The House continues to pass legislation so extreme there is no chance of it passing the Senate, let alone being signed into law by the president, and the Senate does... well, the Senate doesn't do very much.

**Budget:** Congress, in one of its last actions of 2011, managed to pass a budget for fiscal 2012. The good news is that agencies that fund biomedical research like the National Science Foundation and the National Institutes of Health saw increases. The bad news is the NIH increase was modest and well below the president's request. Additionally, Congress authorized creation of a translational science center at NIH, a central pillar in NIH Director Francis Collins' 2011 activities.

**The not-so-super committee:** Things got so bad in Washington when our (ahem) "leaders" brought the nation to the brink of default for the first time in our 228-year history that Obama established a "super committee" of 12 members of Congress (equally divided by party and chamber) to put politics aside and do the heavy lifting the full Congress was unable to do. They were tasked with developing a plan to cut \$1.5 trillion in spending over the next 10 years. After 111 days, the committee disbanded, having failed to come to a bipartisan agreement.

After a dysfunctional 2011, 2012 may not be too different, as all 435 representatives and 33 senators are up for re-election. And then there's that pesky 2012 presidential election. Fear not, biomedical community! The Public Affairs Office and Public Affairs Advisory Committee will work diligently all year to tackle the most important issues facing you all. Here's a peek at some of the issues on our list:

**Funding:** Although the NIH budget over the past few years has been stable or modestly increased, when adjusted for inflation, the NIH actually has been losing purchasing power for the past five years. We will work with Congress to ensure strong support for funding at the NIH and other research-funding agencies and work with the NIH leadership, sharing our thoughts on how to increase the amount of investigator-initiated research being done even in a tightening fiscal environment.

**Regulatory burden:** We understand that increased regulation on research (be it in the usage of animals or the tracking of time) puts an unnecessary and frequently expensive burden on you, the researcher. We will work to identify ways Congress can ease the regulatory burden on the scientific community.

**Workforce issues:** With regard to issues such as Ph.D. training, K-12 science education, and immigration and student visa reform, we will search for ways to ensure there is a robust workforce pipeline to keep America a global leader in biomedical research.

Didn't see an issue you want addressed? Looking for ways to get involved in shaping policy? Eager to learn more about the issues? Visit [www.bit.ly/sUOe1L](http://www.bit.ly/sUOe1L), read our blog ([www.asbmbpolicy.wordpress.com](http://www.asbmbpolicy.wordpress.com)), which is updated several times a week, or email us at [publicaffairs@asbmb.org](mailto:publicaffairs@asbmb.org). ☺☺☺



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



## 2011 ASBMB graduation survey

Last year's survey elicited a somewhat lower response rate than the 2010 one (136 responses out of 818 surveys sent). Nonetheless, the number of undergraduate degrees awarded to persons from ethnically diverse backgrounds increased in every category. Both the raw numbers and overall pattern constitute hopeful signs that our programs are reaching and attracting more underrepresented minorities. Conversely, the reported number of graduate degrees conferred was down substantially. Also, for the first time in many years, more men than women were reported to have graduated with bachelor's degrees in biochemistry and molecular biology.

We ask that you take special notice of those programs that have reported the largest number of undergraduate degree recipients from traditionally underrepresented groups (listed below).

Data regarding the number of minority students graduating from each school may be obtained at <http://bit.ly/tlY4fz>.

### James Zimmerman

*Emeritus professor of biochemistry, genetics and biochemistry department, Clemson University*

### Peter Kennelly

*Professor and head, department of biochemistry, Virginia Polytechnic Institute and State University*

### Benjamin D. Caldwell

*Undergraduate Affiliate Network Committee, professor and chairman, department of chemistry, Missouri Western State University*

### Takita Felder Sumter

*Minority Affairs Committee, professor of chemistry, department of chemistry, physics and geology, Winthrop University*

### Squire J. Booker

*Minority Affairs Committee chairman, associate professor of chemistry, associate professor of biochemistry and molecular biology, chemistry department, The Pennsylvania State University*

	B.S./B.A.			M.S./M.A.			Ph.D.		
	M	F	Total	M	F	Total	M	F	Total
<b>American Indian or Alaskan Native</b>	21	20	41	0	0	0	0	1	1
<b>Asian</b>	171	188	359	7	15	22	21	14	35
<b>Black, not of Hispanic origin</b>	38	60	98	0	5	5	2	5	7
<b>Hispanic</b>	46	43	89	2	1	3	3	5	8
<b>Pacific Islander</b>	5	8	13	1	0	1	1	1	2
<b>White, not of Hispanic origin</b>	735	577	1312	20	30	50	63	42	105
<b>International students</b>	57	81	138	15	23	38	42	34	76
<b>Unspecified</b>	105	80	185	7	4	11	4	5	9
<b>Totals</b>	1178	1057	2235	52	78	130	136	107	243

**The programs here have reported the largest number of undergraduate degree recipients from traditionally underrepresented groups.**

1. American Indian or Alaskan Native: The biochemistry/molecular biology program at Centre College in Danville, Ky., and the chemistry and biochemistry department at California State University, San Marcos.

2. Blacks: The chemistry department at Oakwood University in Huntsville, Ala., and the chemistry and biochemistry department at Jackson (Miss.) State University.

3. Hispanic: The chemistry and biochemistry department of Arizona State University, the chemistry department of the University of Washington and the biochemistry and

molecular biology department of the University of New Mexico.

4. Pacific Islanders: The department of chemistry and biochemistry at the University of North Carolina at Greensboro, the microbiology and molecular biology program at Brigham Young University and the chemistry department at the University of North Carolina at Chapel Hill.

## Meet Vicky Minderhout

***She was named the Washington state winner of the U.S. Professors of the Year Award***

BY JOHN NELSON

**V**icky Minderhout, a professor of chemistry, has been teaching at Seattle University for the past 31 years. Although her research training is in clinical chemistry, it was during her postdoctoral work that her interests turned to teaching. Late last year, Minderhout was named the 2011 Washington state winner of the U.S. Professors of the Year award, sponsored by the Carnegie Foundation for the Advancement of Teaching and the Council for the Advancement and Support of Education. Minderhout was one of 27 state-level winners; four others were named national-level winners. We asked Minderhout to elaborate on her teaching strategy and to what she hopes the award will draw attention.

**Q. What piqued your interest in teaching?**

**A.** I taught part time one year during my postdoc and had so much fun working with students that I seriously began wondering about the career path I had chosen, which was clinical chemistry, not teaching.

**Q. Was this an opportunity you actively looked for or were you volunteered to teach? And whom did you teach?**

**A.** I was recruited from my postdoctoral program in clinical chemistry at the University of Washington to teach clinical chemistry to undergraduates. Seattle University was unusual for offering a bachelor's degree in clinical chemistry.

**Q. How is your strategy for teaching — for getting through to your students — different from that of your peers?**

**A.** My classroom strategy utilizes (what is known as) active learning and involves students working in small groups answering instructor-designed questions — as opposed to lecture. My chemistry colleagues at Seattle University use active learning in the classroom to varying extents; however, nationally, the use of active-learning strategies is not as prevalent. This approach engages students by actively involving them in the learning process. They feel challenged, but most eventually take pride in their development personally and intellectually.



Vicky Minderhout assists student Halina Walker and her team.

PHOTO COURTESY OF CHRIS TAYLOR

**Q. Does active learning essentially follow the Socratic method, involving dialogue and challenge?**

**A.** Yes, that's correct. And in large classes, the dialogue and challenge can be between the students themselves; it does not always require the instructor to lead the challenge. In fact, it is probably best if students take on this role, although the instructor may assign a specific student to be the skeptic.

**Q. When did you begin teaching in this different way?**

**A.** After my first sabbatical in 1993, I redesigned one upper-division course to focus on the primary literature and became very interested in teaching problem solving and critical thinking in more direct ways than I had done previously. I attended an active-learning workshop in 1997 that focused on process education. This workshop helped me translate my ideas about what I wanted my teaching to accomplish for my students into real

classroom practices that I could implement. Since the workshop modeled classroom practices while delivering content about learning, I actually was able both to learn new material and watch it being implemented in ways I could adapt to my classroom.

**Q. Have favorite teachers of yours informed how you teach? Do you emulate their methods?**

**A.** Initially, I was taught by interactive lecture, and I had the good fortune to have several teachers who did this extremely well. It can be very motivating for students. However, my undergraduate quantum mechanics course was taught entirely without lecture. Students worked in pairs to answer the end-of-chapter problems. We could seek help from other students and the professor, but eventually we had to explain our answers to the professor. I worked very hard in that course and passed my qualifying exam in graduate school. So motivating students is important, but, in the end, they have to do the heavy lifting that learning requires. My courses have students explaining answers first to each other and then to the class. So my teachers helped me to shape my teaching and to be confident that I could get students to achieve understanding without lecturing while at the same time they could develop other skills.

**Q. Do you have any concrete examples of how your teaching method has improved your students' abilities to understand or better appreciate the topics you present?**

**A.** First of all, this method is basically what is stated in the book "How People Learn" published by the National Research Council, which has 600 references. Also, the success of the method is consistent with data collected over many years in the cognitive sciences. As you might imagine, doing side-by-side controlled studies on learning is exceedingly difficult, since there are many variables and controlling those variables is difficult.

Additionally, our students who have graduated have returned to report how well prepared they are compared to others. One student felt his biochemistry course at an Ivy League health-professions school was extremely easy following what he had done with us. Also, we have shared our exam questions with others, and they are

impressed with how well our students perform on the complex questions we ask. Many of these questions transfer into other scientific contexts.

In our biochemistry courses, we have students write final growth reports that reflect on their maturation in learning as a result of the course. Now, because we know their names, the reporting is not blind, and students could be brown-nosing, but when you read comments like "I figured out how to learn in this course and wish I had known how to learn in my freshman year" or "I never really organized my problem solving very effectively until this course" or "I am using strategies I developed from this course in all my other courses," it is persuasive. The students could have said "This course really helped me learn," "The course helped me improve my problem solving" or "This course helped me improve my study strategies," but, when students give you the additional context for their growth, it makes their statements much more believable.

**Q. What do you want to occur as a result of receiving this award? For your students and your university?**

**A.** My students already have a great education — if they embrace this classroom strategy! I am hopeful that more faculty will embrace more active-learning strategies in their classrooms. Faculty members are doing this in classes of 700 and classes of 10, so there are ways that we can engage students and coach the learning process in any class size. As more foreign-born individuals earn (science, technology, engineering and math) degrees than do U.S. citizens, we should be concerned that we are no longer attracting young minds into these fields — and wonder why that is so. Is this because the drinking-from-the-fire-hose approach and the emphasis on coverage at all costs turns many students off to our fields? Science is data driven and interdisciplinary. We need to create environments in which students at all levels work with raw data so they will understand that everything in the textbook actually originates from raw data and offer students opportunities to make connections across disciplines. This will be exciting for us and them and will model how science really works. ∞∞∞

## Bassler receives L'Oreal-Unesco award

Princeton University's Bonnie Bassler, a Howard Hughes Medical Institute investigator and National Science Board nominee, recently was lauded as the L'Oreal-UNESCO laureate for North America. Five



female scientists, each from a different global region, are chosen yearly, based on their contributions to science. Bassler's work on quorum sensing, or group communication among bacteria so that they function as an entity, has opened up research into how chronic infections and bacteria-based biofilms may be thwarted. ∞∞∞



# National Research Council report calls for new disease taxonomy

*Molecular biology findings must be included, it says*

BY RAJENDRANI MUKHOPADHYAY

Late last year, the National Research Council released a report calling for a new data network to integrate the latest research on the molecular causes of diseases with clinical data from individual patients. The report said that the network could lead to a more accurate classification of disease and, in turn, a new taxonomy, which would improve clinical diagnoses and treatments. The committee that put together the report argued that the time was right to embark on this change, given the richness of current biological data, advances in information technology and the changes needed in the U.S. health-care system. The

NRC undertook this study at the request of Francis S. Collins, the director of the National Institutes of Health.

“Currently, a disconnect exists between the wealth of scientific advances in research and the incorporation of this information into the clinic,” Susan Desmond-Hellmann, co-chair of the committee that authored the report and chancellor of the University of California, San Francisco, said in a statement. “Often it can take years for biomedical research information to trickle to doctors and patients, and in the meantime wasteful health care expenditures are carried out for treatments that are only

effective in specific subgroups. In addition, researchers don’t have access to comprehensive and timely information from the clinic.”

To develop the new disease taxonomy, the committee recommended creating an “information commons” to bring fundamental molecular research (such as findings in epigenetics, metabolomics, genomics and proteomics) together with medical histories, environmental exposures and treatment outcomes of individual patients. The information commons then would be mined to understand and integrate the connections between the different types of data to produce a knowledge network. The new disease taxonomy would rise from a better understanding of the connections between molecular biology and clinical data derived from large patient numbers within the knowledge network.

Molecular biologists and biochemists stand to benefit



The proposed framework for building a biomedical knowledge network for basic discovery and medicine IMAGE: NATIONAL RESEARCH COUNCIL OF THE NATIONAL ACADEMIES

from this proposed setup. Keith Yamamoto, a molecular biologist at the University of California, San Francisco, who served on the committee, explains that the information commons and knowledge network will broaden the scope of fundamental research. With a database at their fingertips that links disparate types of data — for example, genomic analyses and behavioral studies — investigators will find it easier to identify interesting hypotheses to pursue and to find potential collaborators with the specific expertise to build the multidisciplinary team necessary to tackle the hypotheses. “The knowledge network will allow you to find things you were not looking for, much the way that Google does,” explained Yamamoto.

Validation of information within the proposed setup was a focus in the report. Yamamoto envisions a Wikipedia-like model in which researchers confirm or dispute research findings. Claims of new links between different research areas can be validated by other investigators. If the claims don’t stand up to scrutiny, they will disappear. Upon meeting a rigorous validation standard, information within the knowledge network will create a new taxonomy of disease that will affect clinical practice by changing the way clinicians make diagnoses, choose therapeutic routes and advise patients on the need for intervention.

One of the committee’s recommendations was to set

up pilot studies. These pilot studies should assess the feasibility of integrating molecular parameters with medical histories in the ordinary course of care. These studies also will explore how to gradually eliminate institutional, cultural and regulatory barriers to the sharing of patients’ molecular profiles and health histories while still protecting their privacy.

Both Desmond-Hellmann and co-chair Charles Sawyers, a Howard Hughes Medical Institute investigator at Memorial Sloan-Kettering Cancer Center, emphasized that the data network and the taxonomy won’t appear overnight. In a statement, Sawyers said, “Developing this new network and the associated classification system will require a long-term perspective and parallels the challenges of building Europe’s great cathedrals — one generation will start building them, but they will ultimately be completed by another, with plans changing over time.”

The report can be obtained at <http://bit.ly/vEnths>. XXXX



Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the senior science writer for ASBMB Today and the technical editor for the JBC.

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*Exceptional shots will be considered for the cover, and you may be interviewed about the meeting you attended.*

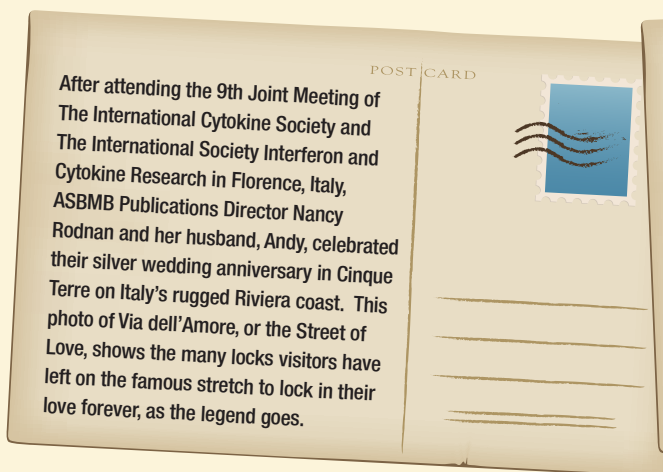


PHOTO COURTESY OF ANDY RODNAN

# Retrospective: Har Gobind Khorana (1922–2011)

BY ROBERT D. WELLS

**H**ar Gobind Khorana, the Sloan professor emeritus of chemistry and biology at the Massachusetts Institute of Technology, died on Nov. 9 in Concord, Mass., at age 89. He was my postdoctoral mentor from 1964 to 1966 and a dear, lifelong friend. During the mid-1960s, his research team, consisting of about 16 postdoctoral fellows (a large group even for that time), solved the genetic code. This achievement was remarkable, because this moniker had not even been coined when I joined his team at the Institute for Enzyme Research at the University of Wisconsin. However, when I assumed my professorship in the department of biochemistry in Madison 24 months later, all 64 codon assignments as well as the stop and start codons had been determined by two different experimental strategies and were published. In 1968, Gobind shared the Nobel Prize in physiology or medicine with Robert W. Holley of Cornell University and Marshall W. Nirenberg of the National Institutes of Health for these discoveries and, over the years, was the recipient of numerous other prizes and accolades.

Gobind pioneered the interface of biology and chemistry long before this topic became popular. His contributions spanned peptides and proteins, carbohydrates, nucleic acids and membranes.

## Vancouver and Madison

In 1952, he began his academic career in Vancouver at the British Columbia Research Council, where he pioneered methodologies to synthesize nucleotides and achieved international recognition for synthesizing coenzyme A. He also developed, almost single-handedly, the steps to synthesize small ribo- and deoxyribo-oligonucleotides. He moved eight years later to the Institute for Enzyme Research in Madison, Wis., where he undertook his Nobel Prize work. Undoubtedly, his knowledge of enzymology and the biochemistry of peptides as well as oligonucleotides provided a trove of experience for the genetic code problem. He could both strategize and organize, skillfully marrying the research programs of a large number of postdoctoral fellows. I and other fellows worked hard during this time, but Gobind's brilliance deserves the credit.

In 1970, he quickly moved on to report another breakthrough: the construction of the first synthetic gene (for yeast alanine transfer RNA) using commercially available chemicals. Then, six years later, he showed that the synthetic gene for a different tRNA with all the necessary signals for expression *in vivo* functioned in a bacterial cell. The current biotechnology industry and genetic engineering methodologies are dependent on chemically synthesized segments of DNA or RNA, and Gobind's discoveries were critical to these developments.

## MIT

He joined the MIT faculty in 1970 and retired in 2007. During this period, his lab focused mostly on biological membranes and bioenergetics and elucidated the mechanism of proton transport in light transduction by bacteriorhodopsin in the purple membrane. His most recent work was in the mammalian visual sensory system and involved G-protein-coupled receptors. His approach continued to be multidisciplinary, involving biochemistry, genetics, chemistry and cell biology.

He mentored more than 150 postdoctoral fellows and several graduate students. A notable number of these scientists are now leaders in academia, biotechnology industries and government service. Gobind was a prodigious contributor to the scientific literature, with more than 450 original, refereed publications. After the synthesis of the alanine tRNA gene, an entire issue (Dec. 28, 1972) of the *Journal of Molecular Biology* was devoted to publishing a series of 13 of his papers; I can't recall ever observing this feat by another scientist.

## The beginning

Born in the village of Raipur, which was then nestled in India's Punjab region and now within the bounds of Pakistan, Gobind was the youngest of five children. While his father was a Hindu tax clerk for the British colonial government and the family lived in poverty, Gobind once wrote that his was "practically the only literate family in the village of 100 people." He repeatedly told stories of his early education from his teacher under a tree. Moreover,



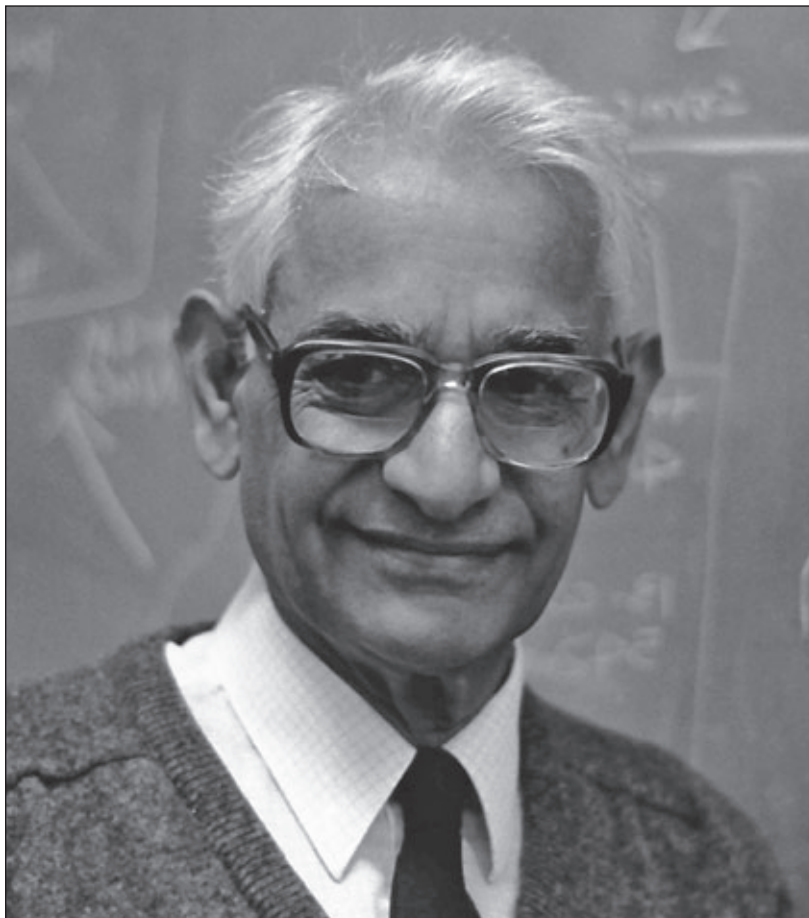


PHOTO COURTESY OF MASSACHUSETTS INSTITUTE FOR TECHNOLOGY NEWS OFFICE

I remember his glee in telling me of his pride when his father gave him a pencil for one of his birthdays but then broke it in half and told him only to use half at a time.

His university training began at Punjab University, where he studied chemistry on a scholarship and earned his bachelor's degree in 1943 and his master's degree in 1945. He was admitted although he had been too shy to attend the required admissions interview. He earned a Ph.D. in organic chemistry from Liverpool University in 1948 and then spent a year as a postdoctoral researcher at the Swiss Federal Institute of Technology, now known as ETH Zurich. There, he secretly camped out in a lab until Cambridge University came through with some funds. For this further training in England, he worked with Lord Alexander Todd on the chemistry of small molecules. Cambridge had become a stronghold of protein and nucleic acid biochemistry; Watson and Crick would discover the double-helical structure of DNA in 1953.

## Dedication

Always humble and hardworking, Gobind embodied dedication and drive. He treated his students and staff thoughtfully and fairly, and he demonstrated his loyalty to them time and again. Although quiet by nature, he was not timid when it came to upholding ideals and pursuing goals. In fact, I repeatedly saw him attack grand challenges that I was confident he had little idea how to solve, but I nonetheless trusted that he would succeed. He had tremendous scientific courage. This is a very rare trait in these days of limited funding, which strongly selects against such ambitious projects. He had high expectations for himself and his fellows.

His lectures were a model of organization and clarity. He always stressed the concept of informing his audience and not trying to impress them. And one of his favorite quotes, attributed to Otto Loewi, was, "We must be modest except in our aims." I believe this sums up well a part of his philosophy.

His wonderful wife, Esther, who died in 2001, was his close love and helpmate; in fact, for some years, she was even his chauffeur, as he chose not to drive

to keep his mind on his science. He is survived by his daughter Julia and son, Dave, and was predeceased in 1979 by his daughter Emily.

Gobind was famous for his long walks and talks, usually about science or nature, with friends and associates around the world. During one of my visits to his Rockport, Mass., retreat along with my wife, Dotty, we decided to walk into the hamlet for an afternoon tea; unfortunately, it was raining, but we proceeded anyway. On the entire two-hour walk, he happily recited a poem by heart with great gusto.

Our science was strengthened immeasurably by his efforts. XXXX

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Robert D. Wells (bodow1938@comcast.net) is the Welch and Regents professor emeritus at the Institute of Biosciences and Technology-Houston. The editorial contributions of Uttam RajBhandary (MIT) are gratefully acknowledged.

# Revamping the Western blot

*Researchers are pursuing efficiencies, automation and higher throughput*

BY RAJENDRANI MUKHOPADHYAY

**E**ver dreamed of the things you could accomplish if you weren't stuck babysitting a Western blot? Help may be on the way. Some researchers and at least one company are looking to liberate molecular biologists and biochemists from the manually cumbersome and time-consuming process by rethinking the protein immunoblotting technique.

Since its inception in 1979, Western blotting has been a mainstay in molecular biology and biochemistry laboratories and is used as a confirmatory diagnostic for HIV-AIDS. The power of the method lies in its ability to detect a specific protein in a complex mixture. However, the multistep technique takes hours and demands technical skill. It can't process large numbers of samples at once and requires micrograms of proteins, an amount that can be hard to come by for rare or precious samples. Its performance is inconsistent and gives rise to variable blotting efficiencies, especially with high-molecular-weight proteins.

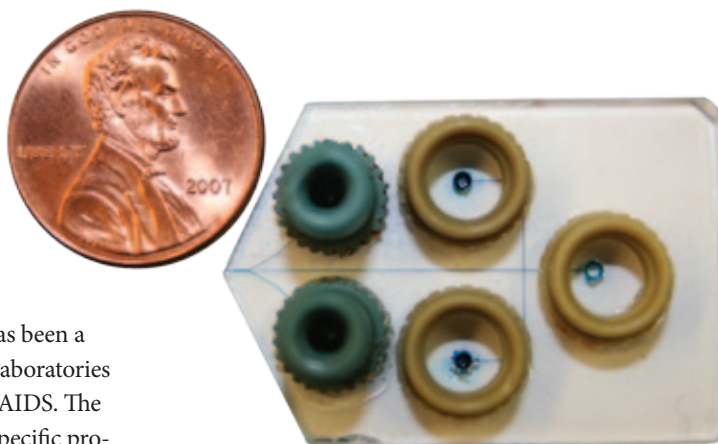
Instruments are available to speed up some stages of the process, such as automating the incubation steps with antibodies and blocking buffers or improving visualization and quantitation of the final blot. But the fundamentals of "this technique have been around for more than 30 years and have hardly changed. Maybe it's time people go back and see if there is anything that can be

done" to improve it, says Robert T. Kennedy at the University of Michigan, Ann Arbor.

Kennedy acknowledges redesigning Western blotting can be controversial, because it's valid to question whether there is a need to change something that works. "But it's also true that people spend a lot of time doing Western blots," says Kennedy.

Rajini Rao is a biochemist at Johns Hopkins University who welcomes a redesign. "Traditional Western blotting is tried and trusted, but there are so many limitations to the standard approach. I think the time is right" to introduce some innovations to the process, she states. Rao says, for example, that her laboratory would love to see an increase in the throughput of Western blotting, because often, "we end up designing our experiments around the number of lanes available on a gel, which is not at all ideal!"

Protein research can be shaken up if Western blotting is automated and made faster with the capacity to analyze many samples at once. Today, "there isn't high-throughput methodology for looking at the protein content and changes in



Robert T. Kennedy's group developed a microfluidic format that separates and blots proteins onto a membrane. The separated proteins emerge from the arrowhead section of the device. Penny shown for scale. PHOTO COURTESY OF SHI JIN OF THE KENNEDY LABORATORY



ProteinSimple's Simon uses capillary electrophoresis to fully automate the protein immunoblotting process.

PHOTO COURTESY OF PROTEINSIMPLE

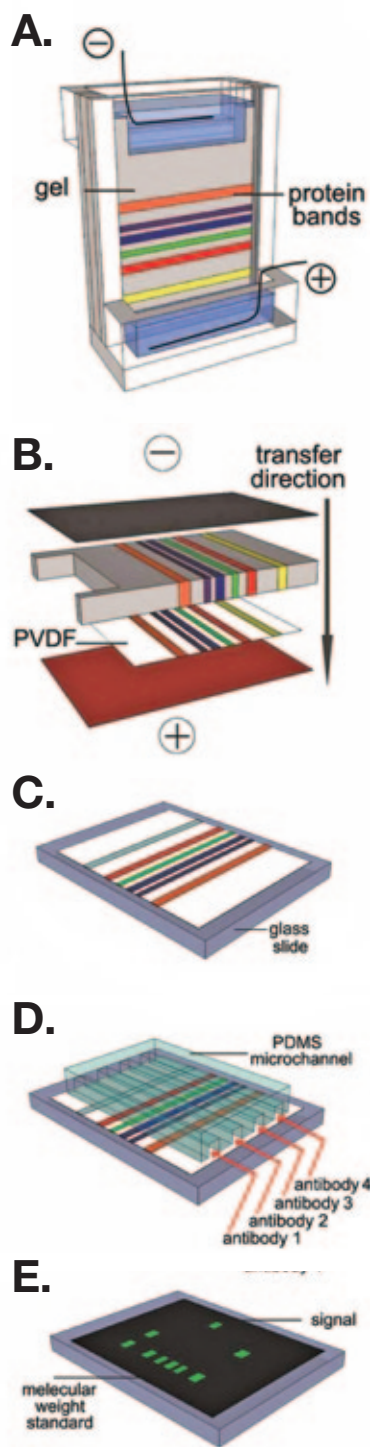
expression and post-translation modifications in large numbers of samples” in an average biology research laboratory, says Amy E. Herr at the University of California, Berkeley. “There are very few proteins that are currently used in disease diagnostics of any type, and it’s just because looking for protein biomarkers can be really daunting.”

Both Kennedy and Herr envision an automated system where the researcher can just pop in samples and let the instrument do the grunt work. In fact, a new instrument for Western blotting has appeared on the market that matches that description. Furthermore, by increasing the capabilities of Western blotting, those interviewed for the article point out, biologists will be able to formulate more ambitious hypotheses.

### Capillary electrophoresis meets protein immunoblotting

Capillary electrophoresis is one way investigators are overhauling the Western blot. The method separates molecules by their size-to-charge ratio inside a narrow electrolyte-filled tube and was the workhorse with which the Human Genome Project was completed (1). The advantage of CE is that the sieving matrix for separations can be automatically pumped in and out, because it contains entangled polymers rather than the typical crosslinked polymers of gels, explains Kennedy. He adds, “It’s what made the big difference in the Human Genome Project. It didn’t sound like much, but if you’re talking about running many samples over and over again, that simple automation step made life so much easier.”

CE also requires less sample than gel electrophoresis and has a better resolution of protein size. Kennedy’s laboratory has now swapped the gel electrophoresis step for CE. Proteins travel down a capillary and separate according to size. As the individual proteins emerge at its mouth,



Xingyu Jiang and colleagues created a microfluidic device out of a plastic called PDMS to assay a Western blot with 10 different antibodies at once.

IMAGE COURTESY OF SHA HE AND WENYING PAN, JIANG LABORATORY

they drop onto a blotting membrane moving steadily across the capillary opening. In this way, the researchers drop the time-consuming gel-to-membrane transfer step of conventional immunoblotting and develop the blot as usual. The researchers have shown they can separate classic protein standards like carbonic anhydrase and lysozyme within an hour using only a few nanoliters of sample (2).

In September, the company ProteinSimple released the SimpleWestern technology in an instrument called Simon. The technology is based on CE and, according to the company, is a “gel-free, blot-free and hands-free solution to the entire Western blotting process.” Mixtures of proteins in nanoliter aliquots are taken into 12 capillaries filled with a sieving matrix and separated by size. The separated proteins are immobilized at the capillary walls in their positions by exposing the capillary to a ultraviolet-light source that activates proprietary chemistry. The separation matrix gets removed, and the reagents for a standard immunoassay flow into the capillary. The primary antibody enters first, followed by a horseradish peroxidase-conjugated secondary antibody, which generates a chemiluminescent readout. Including the time for sample preparation, the totally automated process takes three to five hours, say company representatives.

The instrument allows for quantitative protein measurements. “The biggest challenge with a traditional Western blot performed today is that you separate your proteins in a polymerized acrylamide matrix and transfer it to a solid membrane surface,” says Peter Fung, ProteinSimple’s Simon product manager. “You have no idea how much of your protein that you loaded into that gel is actually transferring to a solid membrane surface. With our technology, we know the proteins that are separated will be captured on the walls of the capillary.”

Trent Basarsky, ProteinSimple’s vice



president of corporate development, and Fung both say that their approach gives more reproducible data. No matter “who is in front of the machine, it’s going to give the same answer,” says Basarsky. Although Basarsky declined to reveal the price of the instrument, he and Fung say that the cost of each run in Simon is comparable to that of traditional Western blotting.

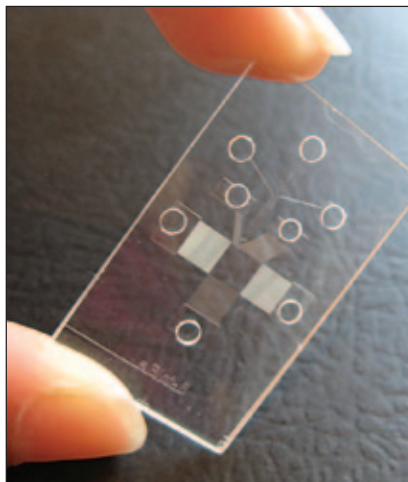
## Downsizing to microfluidics

The other approach to changing Western blotting is microfluidics, a technology by which small volumes of fluids and molecules move through microscale channels. Kennedy’s group is looking into using microfluidics to further reduce the amount of sample needed for their method and reduce the size of their setup by swapping the centimeter long capillaries for micrometer long microfluidic channels.

Xingyu Jiang and colleagues at the National Center for NanoScience and Technology in Beijing recently incorporated microfluidics for the immunoblotting step. They designed a microfluidic system with channels that allowed 10 different primary antibodies to probe the membrane. Once the incubation step with the primary antibodies was completed, Jiang’s team incubated the whole membrane in a secondary antibody solution. They were able to analyze the expression and molecular weights of 10 proteins, not just a single protein, from a single sample (3). Jiang explains that, because multiple proteins are detected simultaneously, “researchers can save [themselves] the labor of preparing multiple samples.”

Rao says Jiang’s work is an example of how rethinking Western blotting could change the game. She points out biologists now have to strip and reassay blots if they want to test a sample with multiple antibodies, a process fraught with pitfalls. “If you don’t get a signal, you don’t know if the protein is just not there or you lost it” during the stripping process, she says.

Herr’s group hopes to change the entire Western blot procedure with microfluidics. They recently described an automated system made from polyacrylamide gel that automatically does the electrophoretic separation, transfer and blotting all within its confines (4). Herr says the system requires only 0.01 to 0.5 micrograms of protein. She emphasizes that the system is still a prototype, although her team is collaborating with an industrial partner to commercialize



The microfluidic device developed by Amy E. Herr’s group does separation, blotting and antibody binding all in one shot. PHOTO COURTESY OF AMY HERR

it. Herr wouldn’t reveal the company’s identity except to say it was large.

One of the goals of Herr’s team is to determine precisely the absolute abundance of proteins from rare cells. The group is kicking off a project to characterize proteins in mouse hematopoietic stem cells. “Right now, those [cells] are so sparingly available,” says Herr. “There really isn’t any capability for protein or biochemical characterization of proteins, because levels are so small.”

This is the type of application in which Gary D. Smith, a molecular physiologist at the University of Michigan, Ann Arbor, is very much interested. His laboratory studies glycogen synthase kinase 3’s role in gamete and embryonic development in mammals.

Smith explains, “It takes us 300 to 400 oocytes to run one lane on a Western blot. If we do it in triplicate, we’re talking about 1,200 oocytes. Each mouse gives 30 to 40 oocytes.” That’s a lot of dead mice for a Western blot. For this reason, Smith says he is very excited to see the development of miniaturized platforms that could drastically reduce the amount of protein, cells and mice needed for an experiment. Furthermore, both Herr and Smith explain that if microfluidic protein immunoblotting systems let researchers quantify the levels of proteins with different post-translational modifications from just a few cells, and perhaps even single cells, that capability could open new avenues of investigation.

So far, aside from ProteinSimple’s Simon, these methods aren’t commercially available. But the researchers say once they have taken their laboratory prototypes through the development process to become commercial products, they will give biologists the gift of time. ∞∞∞



Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the senior science writer for ASBMB Today and the technical editor for the JBC.

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## W. Neal Burnette: the man behind the Western blot

*Burnette made his seminal contribution to molecular biology and biochemistry as a postdoc and went on to have an unusual career.*

BY RAJENDRANI MUKHOPADHYAY

**T**hirty-one years ago, W. Neal Burnette published a paper that described a technique called Western blotting (1). The paper initially was rejected by the journal *Analytical Biochemistry*, but it went viral among molecular biologists as a preprint. Eventually the journal agreed to publish the paper, which now has been cited more than 6,000 times. Because Burnette didn't bestow his name on the blot, it's likely that the current generation of investigators don't know he was involved in developing the technique that is now ubiquitous in molecular biology and biochemistry research laboratories and used as a clinical diagnostic for HIV-AIDS.

Burnette's story is an unusual one: After a quick dip into acting school after high school, he went through the academic training mill. In the early 1980s, he went to work for a then-small biotechnology company. At the same time, Burnette served his country for 35 years, in both reserve and active duty, as a U.S. Army officer, a field medic and an infectious diseases expert.



W. Neal Burnette is now an avid golfer.

PHOTOS COURTESY OF BURNETTE

### Early years

Born in 1944 in New York state, Burnette traveled with his family all over the U.S. and Japan while his father served in the U.S. Air Force. Burnette wanted to be a military pilot like his father, who was a bomber pilot during World War II and a fighter pilot during the Korean war, but his bad eyesight put an end to that dream. He was very much interested in science, but, in his junior year of high school, his mother encouraged him to take speech and drama classes after he got injured during football spring training. Burnette says he became "a starry-eyed kid who wanted to be an actor."

As a senior in a Texas high school, Burnette acted in the lead role of King Creon in a production of Jean Anouilh's "Antigone," which won him and his school theater awards from the state. The award led to a theater scholarship from Texas Christian University. "I went to college to study theater and ballet," he says. "But my then-girlfriend, and now wife, convinced me to change course." Aware of Burnette's interest in science, she told Burnette she would marry him only if he went into science.

Burnette heeded her. "I lost my

theater scholarship. I worked 48 hours a week as a surgical scrub” to make ends meet, recalls Burnette. “It was tough getting through school.”

With mentorship from his organic chemistry professor, Manfred Reinecke, Burnette graduated with two bachelor’s degrees, one in biology and the other in chemistry. He then got a master’s degree in bio-organic chemistry at the University of Central Missouri, a location chosen partly because his father was teaching there. He then went to Vanderbilt University to work toward a Ph.D. thesis on RNA tumor viruses (now called retroviruses) under the guidance of William Mitchell. This was followed by a postdoctoral stint with J. Thomas August, who was at that time at the Albert Einstein College of Medicine, where Burnette honed his skills in SDS-PAGE and radioimmunoassays.

## Going west

At the end of 1977, Burnette took on another postdoctoral fellowship with Robert Nowinski at the Fred Hutchinson Cancer Research Center in Seattle. Nowinski, who went on to become the founder of the biotechnology company ContraFect, describes Burnette as an “eager and enthusiastic” postdoctoral fellow who worked fairly independently.

Nowinski’s group was prominent in the retrovirology field and was engrossed in the analysis of antigenic epitopes of retroviral structural proteins. But they were using tedious chromatographic separations and radioimmunoassays to probe each individual protein of the viral capsid with a series of antibodies. Burnette offered to find a way to speed up the process so that all the proteins in a viral capsid could be tested with an antibody in a single shot. “When you ask a carpenter to do something, the tool he’s always going to use is a hammer,” says Burnette. “My tools were SDS-polyacrylamide gels and immunoassays.”

The main development of the technique took Burnette two weeks in 1979 followed by a few more weeks of tweaking. One of the major problems Burnette had to grapple with was how to get antibodies to bind to proteins that were separated in the polymer matrix of a gel. But in a moment of inspiration, he realized that, just like the DNA and RNA blots that were all the rage at the time, he could make a replica of the gel-resolved proteins and use the replica for the immunoassay.

DNA blotting was called Southern blotting after its inventor, Edwin Southern at Oxford University (2). RNA blotting, developed in 1977, was called “Northern blotting” by James Alwine, David Kemp and George Stark at Stanford University as a play on Southern blotting (3). During a quick chat, Nowinski and Burnette decided to continue the directional joke. They dubbed Burnette’s method “Western blotting” simply because the laboratory was located on the West Coast.

As Burnette was developing his technique, a paper appeared in Proceedings of the National Academy of Sciences that described a similar approach (4). But Burnette was convinced that his method made it easier to transfer the proteins from gel to membrane, get antibody detection and analyze the blot. So he began to put together a manuscript. At this point, Nowinski says he told Burnette, “I didn’t think it would be appropriate for me to come on the paper as an author, because it was really all his work.”

When Burnette, the sole author of the manuscript, sent his work to Analytical Biochemistry, it was promptly rejected. The rejection wasn’t because of the method’s similarity to the technique in the PNAS paper but because it seemed pedestrian, and one reviewer had taken particular offense to the whimsical name.

On receiving the rejection, “I thought, ‘What the heck,’ and didn’t pay much attention,” says Burnette. But he had given preprints of the paper to his friends. They photocopied the paper and gave it to their friends, who repeated the process. “Pretty soon, I was running a daily seminar on blotting by telephone. I was talking to everyone on the planet who was trying to reach me because they couldn’t read the Xeroxed copy they had,” says Burnette. “I had moved to the Salk Institute from Fred Hutchinson by then. [Western blotting] was taking up all my time by talking on the phone.”

Frustrated, Burnette called back the editors of Analytical Biochemistry. “I told them, ‘This is crazy. Everybody knows about this technique now that I’ve not published for two years. You think you might like to publish it now?’” The journal at this point agreed and published the paper in 1981. “Then I got deluged with reprint requests!” says Burnette.

Burnette really had not thought much more about the paper between its acceptance and publication. “I just wanted another publication on my CV. What I didn’t realize [was] that it would be cited so many times that it would be cited orders of magnitude more than all my other papers put together!” Nowinski says had he or Burnette had any inkling of the paper’s impact, they would have handled the paper more deliberately.

## Academia to industry

By now, Burnette was at the Salk Institute as a research associate. Biotechnology companies were starting to pop up, and someone suggested to Burnette that he check out a tiny company in Thousand Oaks, Calif. Burnette interviewed with the company and landed a job that doubled his salary, offered something called stock, and made him one of the company’s earliest employees. The company was initially called Applied Molecular Genetics but soon became famous as Amgen when it released its blockbuster drugs Epogen and Neupogen for treating anemia in the 1980s.



Burnette was given independence to pursue his own research interests in recombinant vaccines. He led programs that resulted in the first experimental recombinant vaccines for hepatitis B, pertussis, cholera and a number of animal infectious diseases. “The best work I ever did was on developing what I call genetic toxoids,” he says. These toxoids are versions of the toxins produced by pathogenic bacteria. “I could make very selective site-specific substitutions within certain subunits of these multimeric toxins and inactivate toxic activities but allow them to retain their immunogenic properties so they could be used” for vaccine development, Burnette explains. “I enjoyed doing that work at Amgen, but Amgen really didn’t care about it. They had EPOgen and some other big money-makers, and vaccines weren’t thought to be big money-makers.”

Burnette left Amgen in 1992. Thanks to the stock options he had received when he signed on at Amgen, Burnette now was at a point where he “didn’t need to work too hard.” He went on to become a director and executive of a number of smaller biomedical companies but “none of that was very successful.”

## Military career

Despite not getting to be a military pilot, Burnette still served his country over the course of 35 years. Burnette joined the army reserves in the 1970s and went on active duty periodically. But his biggest contribution to national security came after 9/11. In 2001, at the age of 57, Burnette was mobilized for active duty as an infectious diseases specialist. He developed the first quantitative algorithm that assessed the threats of indigenous infectious diseases to military operations in regions around the world. He was an adviser to the chemical and biological defense program at the Pentagon. Among other things, Burnette was responsible for the acquisition of smallpox and anthrax vaccines for protecting the U.S. and allied forces against bioterror threats.

But the military also gave Burnette a chance to make something like a full circle to his childhood dreams of movies and Hollywood. Between 2004 and 2005, he served at a U.S. Army Reserve public affairs unit in Los Angeles. The



W. Neal Burnette retired in 2005 as a colonel in the U.S. Army after serving 35 years in various positions.

unit helped screenwriters and TV and film producers create movies with greater military authenticity. “We often read scripts and commented on them to help” filmmakers understand how the military worked, says Burnette. “We got a lot of goofy scripts!”

## Enjoying life to a tee

Burnette retired from the army in 2005 as a colonel. He now lives with his wife in Chapel Hill, N.C., on a property that has a Jack Nicklaus-designed golf course in its back yard. Burnette flies airplanes as a licensed commercial pilot, feeds his golf addiction (he plays, by his own admission, “terribly”) and occasionally consults for biotechnology companies.

For a man who’s worn many hats, he sounds wistful when talking about research, something he hasn’t done since he left Amgen. “I had the best time when I worked at the bench, filling a pipette,” he says. “I think that’s when I was most effective.”

Of the status of the Western blot today, he says, “I am happy to have done it and made a contribution to science that everybody uses. I could have never imagined that I would have my 15 minutes of fame last this long.” ☺☺☺



Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the senior science writer for ASBMB Today and the technical editor for the JBC.

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# Surviving a bioscience Ph.D.

## *Part 2: Mitigating the hurdles and pitfalls faced by doctoral students*

BY MICHAEL J. BRADLEY

**Y**ou spent four-plus years becoming inspired by the biosciences. You were told that you were among the best and the brightest and were encouraged to pursue a Ph.D. You were fortunate enough to choose from among your favorite doctoral programs. Yet now you're struggling: juggling coursework, pondering rotation research, preparing for the qualifying exam and the thesis proposal, making steady thesis research progress, and figuring out how to finish and defend on time. At the heart of your struggles are nagging internal questions: Do I really belong here? Do I have what it takes to get through this? Do I *want* to do this?

Most graduate students in the biosciences (and elsewhere) must struggle with these issues while pursuing a Ph.D. I'm not talking about fixing failed experiments, struggling with techniques or having a publication get scooped, which are all difficult aspects of bioscience research. Instead, I'm talking about figuring out what a Ph.D. means to *you*, finding out the hard way what it takes to get one and developing a career plan to leverage your degree (1).

### Qualifying as a doctoral candidate

After getting into a bioscience Ph.D. program, the next hurdle between you and defending your thesis is “qualifying” as a doctoral candidate. This includes passing your coursework, doing research rotations, choosing a thesis lab or mentor, passing a preliminary exam and proposing your thesis research

project. Keeping in mind that the time to degree has become increasingly lengthy in the biosciences (six or seven years is not unusual), a student's choices leading up to Ph.D. qualification can dramatically accelerate or delay the period between matriculation and commencement.

The quality of graduate courses varies widely in part because of your dependence on faculty members whose primary job descriptions and reward systems do not require high-quality teaching. One of the best approaches for students is to form small (three- to four-person) study groups that meet regularly (two to three times a week) to go over the material in detail and teach each other. However, students should keep in mind that coursework is not the main point of graduate school; the most important material any student will learn comes from direct application to her or his research project. *Do not* take extra courses based solely on interest. *Do* learn and apply new techniques that help answer interesting research questions.

Getting the most out of research rotations and ultimately choosing the right thesis or lab mentor, thesis research project and thesis committee are all topics that could fill separate articles. The main points include the following: 1) Keep research rotations short (six to eight weeks) but sufficiently long to make an informed decision. The sooner you get rolling on your thesis project, the sooner you'll graduate. 2) Be aware of both your hands-on and hands-off mentoring needs. Hands-on mentoring involves detailed instruction and oversight, whereas hands-off mentoring consists of top-level project administration only. Some mentors are capable of balancing both as the situation demands. 3) Find a lab that is doing interesting research, but, more importantly, make sure it is a good fit for you scientifically and personally. It's incredibly important not to feel isolated or in conflict during your thesis research. 4) Choose research rotations carefully to give yourself an opportunity you might not have initially expected, but never rotate into a lab that you wouldn't consider joining. 5) You'll probably start on an existing project, but sticking with it for three to five years of thesis research will require that you take ownership and develop your own driving questions and research methods.

The qualifying exam and thesis proposal

occur at a time when many graduate students falter. It's a difficult process that requires lots of hard work and creative thinking to identify important questions and the best approach(es) to answer them. Use the time-management strategies discussed below. Ask for help as necessary (or allowed), but first spend time trying to answer questions and understand key concepts by yourself.

## Conducting, finishing and defending your thesis research

To help take ownership of your thesis project, develop your own interests within your discipline and within your thesis lab. Stay in frequent, open communication with your adviser to keep your project on track. If possible, never go more than a week without discussing your science with him or her, including your weekly research goals and accomplishments.

Use your thesis committee for more than just a stamp of approval. These fellow scientists form an important part of your nascent scientific network. If you ask for advice, you can benefit from their experience, not only for your thesis project, but also in other areas of your education and professional development.

Getting from the thesis proposal to the defense requires a large amount of time and sustained effort. Staying motivated is not usually the central issue unless something is wrong in your relationship with your project, your thesis adviser, or your friends and family outside the lab. It's important to realize that you're likely to go through a low-motivation period at some point during a five- to seven-year span. Be clear and honest with yourself about the causes of motivation problems, and don't wait to seek counseling or other help.

Besides creative thinking, hard work, dedication and perseverance, the completion and defense of your thesis require other skills. Chief among these are organization, time management and pride in your work. Scientific research is a kind of knowledge work, meaning that it requires you to generate and analyze data; attend, organize and present at meetings; and write reports and proposals. The main problem in knowledge work is managing how *effectively* you work on your own. There are many tools and resources for best practices in knowledge work. I recommend using books, including "Getting Things Done" by David Allen (2), and online sources, including "Study Hacks," a collection of essays by Georgetown University computer science professor Calvin Newport (3, 4). The key is to set reasonable project

goals, milestones and timelines with input from your thesis adviser. Project execution requires deliberate practice (3, 4) and working effectively each day (2).

## A healthy, productive lifestyle

Stress stemming from hard work over a long period can affect other aspects of your life, including personal relationships. Getting regular exercise and healthy amounts of sleep and eating well provide disproportionate research benefits in comparison with spending more time in the lab. A "work hard, play hard" mentality helps us lead rich, rewarding lives outside the lab while nourishing our creativity for solving research problems. Nevertheless, making steady progress in bioscience research probably requires more than 40 hours per week dedicated to designing and performing experiments, analyzing data, reading

the literature and writing manuscripts or proposals. My typical work week is 50 to 60 hours, including time spent working at home. Each individual must find a balance that provides for steady research progress while leading a fulfilling life. Finally, mismanaged stress and traumatic events both in and outside the lab can harm Ph.D.

students' mental health. It is vitally important that grad students utilize counseling when needed and take any other necessary steps to protect their mental health along the road to defending their theses. ∞∞∞

**“ Use your thesis committee for more than just a stamp of approval. ”**



Michael J. Bradley (michael.bradley@yale.edu) is a postdoctoral fellow in the department of molecular biophysics and biochemistry at Yale University.

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# America needs more deep innovation

BY KEN DILL

Over the past half-century, a troubling trend has emerged. America's research has drifted away from deep innovation toward incremental innovation. Deep innovation is about exploring uncharted territory — where the payoffs are not obvious and the time scales may not be short. Some deep innovation can be transformative and the stuff of economic revolutions. Who would have guessed when Russell Ohl studied how current flowed through a cracked crystal in 1939 that it would lead to the P-N junction, the basis for semiconductors, enabling a revolution in modern computers and telecommunications, which have markets now worth hundreds of billions of dollars? Who would have guessed, when Barnett Rosenberg applied electric fields to growing bacteria in 1965, that the platinum metal from the electrode would leach into the solution and hinder cell division, resulting in cisplatin, the penicillin of cancer drugs, now a billion-dollar industry?

Since World War II, deep innovation in America has largely come through federal funding of academic research. Government funding is essential for supporting national needs like defense and for helping our technology industries. Some research simply is not done by industry. It is considered too basic, too blue sky, too expensive or too diffusible, meaning that certain research efforts can leak out beyond a company's walls and pay off for other companies. Take the computer mouse. It was researched and developed by Xerox Corp. But the mouse paid bigger dividends for computer companies than for copier companies like Xerox. These days, industrial research is more targeted; it is mostly "D," not "R," aimed at making better widgets for tomorrow's store shelves. The government plays an irreplaceable role in supporting research that is deep, broad and diffusible — the kind of work that has the potential to transform our science and create new industries.

## By definition, deep innovation is often unpredictable

Imagine having written years ago a grant proposal to invent the iPad. Reviewers would have rejected it. There were already larger versions (computers). There were already smaller versions (iPhones). And there was no apparent market: Existing tablet computers were flops. So on the day the iPad appeared, it was panned by the media, and Apple stock dropped 4 percent. The result? The iPad sold 15 million units the first year.

Deep innovation is less about guessing the future than it is about supporting the people who can lead us to it.

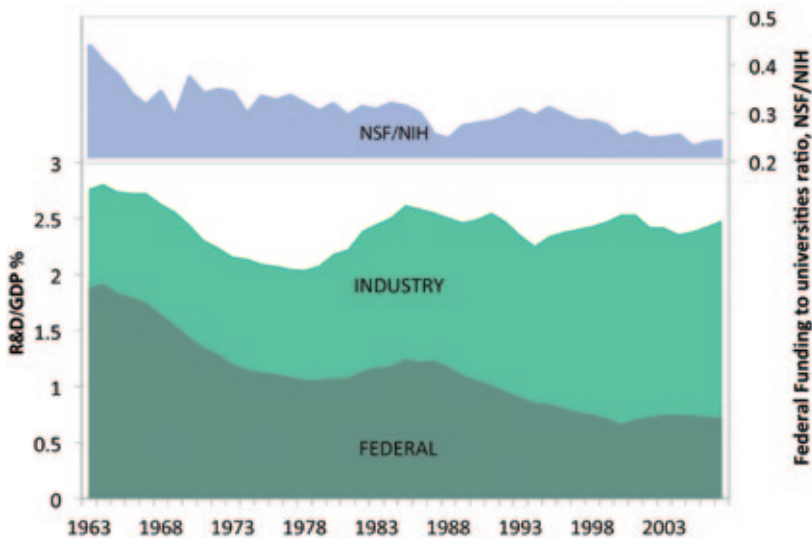
Seeking, finding and supporting deep innovation is very different than promoting incremental innovation. A reviewer of an incremental-innovation proposal decides whether the problem is important and the solution feasible, whether the preliminary results give sufficient proof of success, the possible ways it might fail, and how quickly the investigator can achieve his or her goals.

But judging deep innovation requires nearly the opposite set of determinations. Rather than asking whether the problem is important, one must ask whether it is interesting. Rather than hoping for an expected outcome, one must hope for surprises. Instead of minimizing the time to payoff, the goal is to maximize how long the consequences will reverberate. Instead of more scrutiny and longer proposals, deep innovation requires less scrutiny and shorter proposals. Controversy is not something to be avoided. Instead of looking for the next iPad, those interested in deep innovation look for the next Steve Jobs. Does the investigator have the passion to focus on a problem, the sensitivity to recognize a small signal in a large amount of noise, the ability to connect the dots, the tenacity to withstand the objections of critics and the perseverance to follow a road wherever it may lead? It's not that we need better reviewers. Nobel Prize winner Linus Pauling objected that quasicrystals could not exist when Dan Schechtman, winner of this year's Nobel Prize, discovered them in 1982. With deep innovation, even our best reviewers are usually wrong.

Some agencies have made progress supporting deep innovation. The National Institutes of Health, for example, has recently developed Pioneer Awards, the Eureka Program, Transformative RO1s and New Biomedical Frontiers at the Interface of the Life and Physical Sciences.

## But we need much more

The two bottom curves on the figure (from <http://www.nsf.gov/statistics/>) show that our federal R&D (divided by gross domestic product, to normalize for the size of the economy) has diminished since the 1960s while industrial R&D has grown. In the 1960s, the U.S. invested \$2 in basic research for every \$1 companies invested. Now, it's the opposite: The U.S. invests \$1 for every \$2 invested by companies. If this trend continues,



10 different flavors of biology departments (biochemistry, systems biology, bioengineering, genetics, physiology and so on), while still having only one for each of the other basic sciences. Biology, of course, is crucially important. But the NSF provides the broad underpinnings of all sciences. We don't know where to look for the next unexpected, transformational technology. We should not foreclose our options. Tomorrow's science, engineering and technology may spring up from discoveries that are unimaginably unrelated to the disciplines in which they are born.

### What I propose

Here's what I would say to a national innovation czar, if we had one. First, to solve

who's going to generate tomorrow's industrial revolutions?

Taxpayers tend to focus on immediate threats. The peak of R&D spending in the '50s and '60s arose from military threats. To end World War II and respond to Russia's launch of the Sputnik satellite, the U.S. created new funding agencies. Taxpayers see more clearly the benefits of research that is mission-oriented (i.e., targeted: the U.S. Department of Energy's mission is energy, the U.S. Department of Defense's mission is defense, NASA's mission is aerospace, the NIH's mission is health), rather than discipline-oriented, such as that of the National Science Foundation.

Our research universities are looking for quicker payoffs too. Universities are becoming more entrepreneurial as their federal support shrinks. For example, as our pharmaceutical industry grows more risk averse, academics are stepping up. By one estimate, nearly 80 academic research units have sprung up in the last four years focused on pharmaceutical discovery, which is traditionally the business of industry. Of course, we all benefit from the start-up companies that universities spin off. But there's also a potential downside. If our universities divert too many resources to short-term payoffs, we risk losing the basic-science wellspring of tomorrow's science and technology.

The top panel of the figure shows the shifting balance between the two main funders of academic research. Until recently, NIH budgets roughly have kept pace with the economy. But NSF budgets have not. The NSF's discipline-driven funding is a shrinking part of university funding.

And, look at the shifting balance in university departments. A typical university used to have one department each for biology, chemistry and physics. Now a university may have five to

a country-size problem — like our current jobs crisis — by creating the next \$100 billion-per-year technical industry, we need to increase the federal R&D budget to 1.7 percent of GDP. That was the level that worked in the 1960s when President Kennedy made good on his commitment to land a person on the moon. Increased funding would mean raising federal R&D to two-and-a-half times its current level. Today's NSF budget should be around \$17 billion, and the NIH's should be around \$78 billion. That seems like a lot of money, but, as former U.S. Rep. John Porter, R-Ill., once told me, the issue is not dollars; the issue is priorities. Even at those amounts, we would still be unable to fund many meritorious proposals. And today's entire NSF budget (around \$7 billion) is smaller than the single-company R&D budgets of Pfizer, Merck, Microsoft or Ford.

Second, I would suggest that our innovation czar develop new initiatives to protect deep innovation. After the 1960s and '70s, our portfolio of deep innovation has become inadequate to power an economy as large and technology-based as ours. For the disruptive technologies that have driven economic revolutions — and that could create the jobs of the future — we need more academic research, and we need a protected portfolio of deep innovation.

Thanks to Alberto Perez and Jim Larimer for their assistance. ∞∞∞



Ken Dill (dill@laufercenter.org) is the director of the Laufer Center for Physical and Quantitative Biology and is professor of physics and chemistry, Stony Brook University.





## A protein with protective qualities for HIV patients

BY MARY L. CHANG

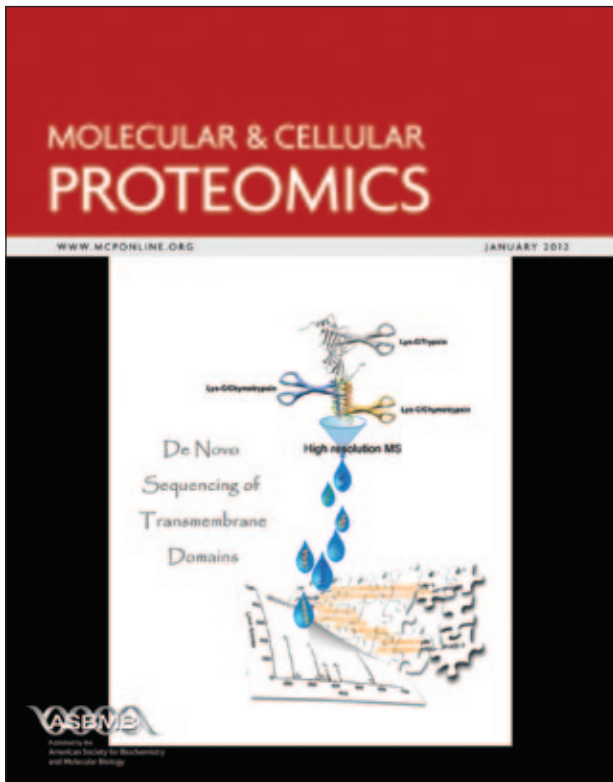
People infected with HIV often develop metabolic complications and atherosclerosis. Treatment of these individuals, therefore, must take into account ways to prevent or slow the development of these concomitant, potentially life-threatening conditions, and treatment decisions can be confusing, because different classes of the medications used to battle HIV differ in their side effects. Serum paraoxonase-3 is a protein that has been associated with lowering the risk of developing coronary artery disease and atherosclerosis. PON3 also prevents the formation of atherogenic, oxidized low-density lipoproteins, which are part of atherosclerotic plaques.

In May, Gerard Aragonés of Hospital Universitari de Sant Joan de Reus in Spain and colleagues published an article in the Journal of Lipid Research describing their new assay to measure serum PON3 concentrations using high-throughput, enzyme-linked immunosorbent assay. In a follow-up article published in this month's issue of JLR, Aragonés et al.

report in "Serum paraoxonase-3 concentration in HIV-infected patients: Evidence for a protective role against oxidation" their results upon examination of serum PON3 concentrations in HIV-infected individuals as compared with those in healthy controls.

Compared with healthy study participants, HIV patients had significantly higher serum PON3 concentrations. Also observed in these patients was a significant inverse relationship between serum PON3 concentration and levels of oxidized LDL. The researchers say that this is the first in vivo evidence of PON3's possible protection against infection, suggesting further study is warranted on exactly how PON3 affects the course of HIV. HIV patients taking a class of drugs called non-nucleoside reverse transcriptase inhibitors had decreased serum PON3 concentrations, a result that correlates negative changes to metabolism with long-term NNRTI use and may drive clinicians to reconsider their patients' treatment plans. XXXX

Mary L. Chang ([mchang@asbmb.org](mailto:mchang@asbmb.org)) is managing editor of the JLR and coordinating journal manager of MCP.

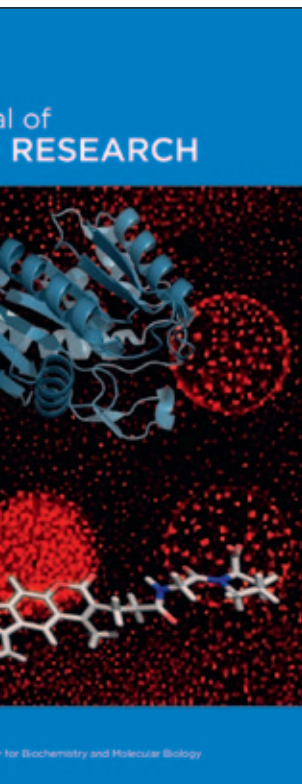


## MCP MOLECULAR AND CELLULAR PROTEOMICS

### Understanding precocious puberty

BY RAJENDRANI MUKHOPADHYAY

When stricken with precocious puberty, children begin sexual development too soon. In boys, the condition can strike before age 9, and it can begin in girls before age 8. The condition causes the children to be short in stature and suffer from psychological and social problems. "Researchers think childhood obesity may be playing a role in the phenomenon, since body fat increases production of estrogen, which helps trigger puberty," explains Wei Jia at the University of North Carolina at Greensboro. To diagnose the condition, doctors have to go through a time-consuming process of physical exams, MRI scans and other tests. To better understand precocious puberty and to diagnose it more efficiently and effectively, Jia, along with Yongyu



Zhang at the Shanghai University of Traditional Chinese Medicine and Guoxiang Xie at UNC-Greensboro, led a team to identify metabolic markers in urine samples from more than 100 patients and 50 healthy children. In a recent paper in *Molecular and Cellular Proteomics*, the investigators described their finding that three major metabolic pathways — catecholamine metabolism, serotonin metabolism and the tricarboxylic acid cycle — didn't function normally in precocious puberty patients, probably because the sympathetic nervous system and the endocrine system were disrupted. They also found hints that patients who suffered from a subtype of the condition that directly involves the endocrine system had alterations in their gut microbiome. In separate research, constituents of the gut microbiome have been correlated with a propensity to obesity. XXXX

Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the senior science writer for ASBMB Today and the technical editor for the JBC.

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BIOLOGICAL CHEMISTRY

## How *H. pylori* deals with stomach acid

BY RAJENDRANI MUKHOPADHYAY

*Helicobacter pylori* can cause stomach ulcers and cancer. The pathogenic bacterium survives in the acidic conditions of the human stomach by hydrolyzing urea into ammonia to neutralize the stomach acid. Urease is the critical enzyme that undertakes the hydrolysis, but it only becomes active with the help of the accessory proteins, which include UreF, UreH and UreG. "Although UreF, UreG and UreH are well-known players involved in urease maturation, their biochemical roles have remained enigmatic over the years," explains Kam-Bo Wong at the Chinese University of Hong Kong. In a recent Paper of the Week in the *Journal of Biological Chemistry*, Wong and colleagues established the crystal structure of the complex formed by UreF and UreH. They found that UreH induced conformational changes in UreF,

which in turn recruited the third accessory protein, UreG, to form the essential complex for urease activation. During their study, the investigators had to solve a puzzle: "Our biochemical experiments initially showed that the highly conserved C-terminal tail of UreF was essential for interaction with UreH. But when we solved the structure of UreF, we found that this highly conserved region of UreF was missing," says Wong. "It wasn't until we solved the UreF-UreH complex structure that we discovered that the conserved C-terminal residues of UreF become structured only when in complex with UreH." Wong says the work has clinical potential. With the complex's crystal structure in hand, researchers can now search for small molecules that disrupt the assembly of the complex and halt urease maturation. XXXX

Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the senior science writer for ASBMB Today and the technical editor for the JBC.



The *Journal of Biological Chemistry* has such a rich history that the editors and staff members thought it was only fitting that the final print edition's cover convey the vibrant colors of past editions. They wrote, in part: "We... recognize that inspiration often emerges in unexpected ways — thanks to a patchwork of people and ideas. Next week, the JBC will begin a new phase of its existence... enabling us to roll out new forms of scientific communication that were not possible with conventional print. But, rest assured, showcasing images that tell scientific stories remains a priority, and we're looking forward to presenting our authors' finest artwork in innovative ways on the Web."

## Tailoring journal content online

**JBC Editor-in-Chief Fedor says new 'affinity group sites' will make browsing more efficient and possibly foster collaboration**

BY ANGELA HOPP

The Journal of Biological Chemistry in late November launched a new platform that aggregate the journal's new and archived content in four areas of study. The "affinity group sites," which are publicly available but essentially still in a testing phase, represent just one of the innova-

nect people with the information that most interests them."

The deployment of the affinity group sites comes just a few months after the JBC redesigned its online editorial board directory to organize reviewing editors according to affinity groups so that they can be identified easily by prospective and current authors. Fedor said the new content sites were a natural next step after publicly categorizing reviewing editors by their shared expertise.

The JBC has 22 affinity groups representing each of the journal's table-of-contents categories, and the first four group webpages that aggregate journal content are the ones for RNA, signal transduction, gene regulation and enzymology. Other affinity group sites are in the pipeline.

Fedor said one advantage of providing a one-stop shop for articles about a certain area of study is that readers won't have to wade through the large number of articles the JBC publishes daily to find the most relevant ones.

"The collections could make people aware of material that they didn't know to look for but that we were able to identify as being related to the subject they're interested in," Fedor said. "So I think it could very well put people in touch with salient information before they even know that they're interested in it. And,

in that way, it could build bridges across different focused areas within a group." By presenting current research articles together with Minireviews, Classics and Reflections by leading scientists on similar subjects, affinity sites provide a rich context for understanding cutting-edge research.

Fedor emphasized that information consumers today expect content providers to customize information to their wants and needs, and she said the JBC consistently has been a leader in harnessing technology to satisfy those wants and needs.

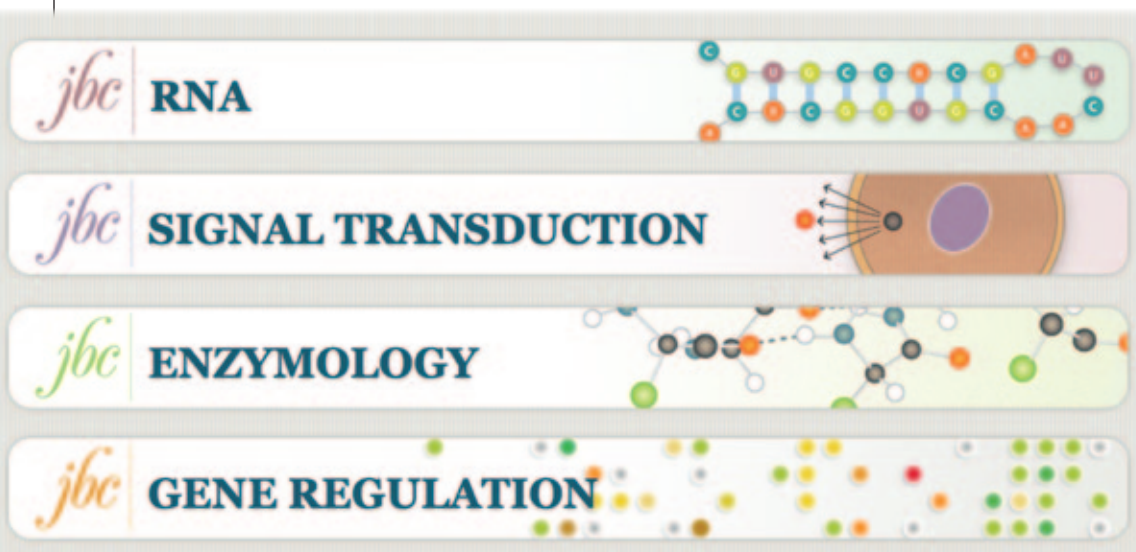
"This is our experiment in tailoring scientific communication to the people who can best make use of the information," Fedor said. "With the JBC being published only online starting in 2012, I think the affinity sites illustrate how we'll be taking advantage of the opportunities now available to scientific communication since it has broken free from the conventional paper format." ❧❧❧

tions the journal will be implementing in 2012, the first year the journal will be published only online.

JBC Editor-in-Chief Marty Fedor said she hopes the four new affinity group sites will offer content that is both specific to an individual reader's interests and complementary to those interests.

"One of the big challenges with scientific communication these days is that it has become like drinking from a fire hose: There is just a flood of information, and no one diving into that stream can easily sort out what of that information is of special interest to them," Fedor said. "The affinity group sites are designed to collect the information related to a particular area and present it in a way that it can be easily accessed by anyone in the field — from those who are conducting research to students who are just dipping into it for the first time."

A major advantage of publishing in the JBC, Fedor said, is that the journal captures information from the wide array of subjects in biological chemistry and reaches a broad audience. But, she added, "We need to find ways to con-





# Giving junior lipid scientists a turn at the podium

## *The Southeast Regional Lipid Conference*

BY BINKS WATTENBERG

**G**reat ideas stand the test of time, and so it is with a meeting conceived over 45 years ago in Tennessee. The concept was to create a high-quality, focused and accessible conference that emphasized participation of students and postdocs and in doing so encouraged entire labs to attend, mingle and form long-lasting relationships. The enduring success of this meeting, the Southeast Regional Lipid Conference (SERLC), is a testament to this model, and we would do well to emulate this format in other disciplines.

In 1966, Fred Snyder of Oak Ridge Associated Universities Medical Division and John Coniglio of Vanderbilt University, pioneers in the fields of ether-linked lipids and fatty-acid metabolism, respectively, realized that within driving distance of eastern Tennessee were a number of labs with strong lipid-research programs. They devised a small, informal meeting with the expressed purpose

of giving junior lab members a place to present their work and hobnob with leaders in the field. For 45 years, through epic changes in the science, this meeting has flourished and yet retained its original intimate character. The original meeting had about 40 participants. Over time, the meeting has expanded moderately. Recent meetings have had about 120 participants.

This meeting may be small, but its quality, convenience and informal format draws keynote speakers from the upper echelons of lipid biochemistry. In its early years, speakers included such pillars of the field as P. Roy Vagelos, Konrad Bloch, Bob Bell, Bill Lennarz, Dan Lane, Konrad Sandhoff, Bill Lands and Ralph Snyderman, to name just a few. More recent speakers (pillars-in-waiting) have included Judy Storch, John Exton, Dennis Vance, Wim van Blitterswijk, Bob Dickson, Mike Frohman, Bill Smith, Claudia Kent, Ed Dennis, Fred

Maxfield, Jim Hurley, Bob Michell, Tim Hla, Alex Brown, Gordon Mills and Charles Serhan.

A majority of the attendees have been participating for years, some since the earliest stages of their careers. With the exception of two keynote speakers, the talks at the meetings are exclusively from graduate students and postdocs. Session chairs are drawn from the ranks of postdocs and junior faculty. Candidates for the conference chair are chosen from participating junior faculty by a more senior steering committee. In this way, the meeting provides the



High Hampton Inn PHOTO COURTESY OF LARRY DANIEL, WAKE FOREST UNIVERSITY BAPTIST MEDICAL CENTER





PHOTO COURTESY OF DAVID KUSEL, THERMO FISHER SCIENTIFIC

opportunity not just to give talks and present posters but also to train young researchers in the vagaries of meeting organization. True to its name, this is a regional meeting that includes laboratories from Georgia, Kentucky, Tennessee, Maryland, North and South Carolina, and Virginia. As the lipid cognoscenti know, this region encompasses some of the lipid powerhouses in the country, including those at Medical University of South Carolina, Virginia Commonwealth University and the Georgia Institute of Technology, among many others. Avanti Lipid Award recipients Yusuf Hannun and Sarah Spiegel are longtime participants, as are lipid mass spectroscopists at Georgia Tech Al Merrill and Cameron Sullards, who have pioneered and perfected analytical technologies that have reinvigorated the field. Members of other key labs, too numerous to mention, also are regular attendees. The strength of the meeting has pulled in participants from as far away as Washington state and California, and interlopers from Michigan, Indiana, Pennsylvania, Ohio and other states are not uncommon.

For the first 14 years, the meeting bounced around sites in Tennessee, North Carolina and Georgia. In 1980,

it finally settled at the ideal site. The High Hampton Inn is a rustic 80-year-old resort in Cashiers, N.C., near the Great Smoky Mountains National Park. The lodge is a prototypical example of the timbered mountain retreat of its era and has been beautifully maintained. The setting is breathtaking, close beside a lake and the peaks of the Blue Ridge Mountains. This is a wonderful destination, with amenities for hikes, golf, fishing and just plain hanging out in front of one of the roaring fireplaces during breaks in the meeting. The meeting is usually scheduled for early November, when the mountain air is crisp.

A key to the success of this meeting is that it is short and inexpensive. The cost of the meeting to participants is minimal, supported by generous contributions of suppliers well known to the lipid research community. And because the meeting site is within driving distance of most of the participating labs, transportation costs are low. Recognizing participants' time constraints, especially amid the proliferation of meetings, the conference is relatively compact, scheduled from Wednesday evening to Friday morning. Mealtimes are fueled by an extravagant Southern-tinged buffet served by the historic High Hampton staff. The evening poster sessions, lubricated by a well-stocked bar, are historic in their own way, especially after the postdocs and students have put their mentors to bed. Tradition dictates that the final evening is dominated by a local clogging group, enticing meeting participants to stomp their way to salvation accompanied by the tight harmonies of an exceptional local bluegrass quartet.

The atmosphere at this meeting harks back to an earlier time in science, when personal relationships — usually collaborative, occasionally combative — fueled advances in the field. It is no accident that the idea to form a Lipid Research Division within ASBMB came from conversations at the bar during this meeting. This meeting fosters the tradition of developing young scientists as an integral part of the scientific mission. The success of this junior scientist-centric format is mirrored in other similar meetings, such as the biennial International Charleston Ceramide Conference and recently established Gordon Research Seminar. Not coincidentally, the cross-fertilization that follows from the focus on junior scientists benefits the principal investigators and enriches the field as a whole. ∞∞∞



Binks Wattenberg (b0watt01@louisville.edu) is an associate professor in the departments of medicine, biochemistry and molecular biology and pharmacology and toxicology at the University of Louisville School of Medicine.

## Careers at the chalkboard, the bench and the conference table

### *Viewpoints on professorships at teaching-intensive schools*

BY SYDELLA BLATCH

**H**ave you ever envied a professor with a “teaching” job? It sure sounds relaxing to have only to teach some classes. How nice it must be not to worry about grants, publications or troubleshooting difficult experiments. Most of these positions have the classic triad of teaching, research and service. I call them student-centered professorships, because this underlies almost everything we do. For me, it is a stimulating, engaging, fascinating and rewarding career — and exhausting!

#### **At the chalkboard:**

##### **What is involved and how to prepare**

Teaching is the largest aspect of the job, typically covering 60 to 80 percent of the responsibilities. This includes basic, class-related duties: creating and delivering lectures; teaching labs; writing exams and assignments; grading; offering office hours and tutoring; and communicating with students, parents and other school faculty and staff members. Most teaching-intensive faculty jobs are at primarily undergraduate institutions, so there are few graduate students to teach labs or grade papers for you.

Teaching is as complex as any other field. And there is another layer of work: researching and trying innovative teaching techniques, creating new courses, and managing courses taught by multiple people. Often, students want to form connections with you; sometimes they just come to your office to chat. Or maybe they want your advice. Like it or not, you are an automatic role model. As a woman or minority, you may be an even larger role model, because these are still atypical images of scientists or professors.

How can you prepare for the teaching aspect of a student-centered professorship? The absolute best preparation is teaching your own college-level course as an adjunct professor or instructor. Some assistant professor jobs require this. But if it is not required, it is likely that a couple dozen of the 100 or so other applicants to the position will have this experience. Other options



The author, Sydella Blatch, right, mentoring one of her summer research students, Pipan Lee.

might include teaching assistantships, guest lecturing in an undergraduate course (few principal investigators would turn down such an offer), teaching MCAT/GRE prep courses, or volunteering to teach a weekly journal club. These other experiences will make you a more competitive applicant for adjunct jobs.

#### **At the bench:**

##### **What is involved and how to prepare**

Most professors at primarily undergraduate institutions have not left the bench. Research might make up between 15 and 35 percent of our responsibilities, and it is accomplished with a small number of undergraduates who work part time during the semester. Some may be able to work for only one semester, and they may have differing levels of undergraduate education. We still have to publish and secure external funding, but, of course, we do not have the time or facilities of research-intensive institutions, so the number of publications and the amount of funding we have to secure is less.



Poster presenters at Stevenson University.

How do you prepare for teaching-intensive research? Like teaching, our research is student centered. Your research must be broken into many small questions that can be answered in one semester by a part-time worker with little or no prior training and without many of the facilities or staff members available to graduate students or postdocs.

**At the conference table:  
What is involved and how to prepare**

Conference tables? Yes, for a variety of reasons, we periodically sit down together in various subsets at a big, oval table. Most of this falls under what I used to call service, but the term is too limited to capture it all. This aspect of your work may make up 5 to 25 percent of your responsibilities and usually involves advising a few dozen students in the major; mentoring individual students; participating in department, school, committee and university wide meetings, events and ceremonies; faculty governance; moderating student organizations; participating in recruitment events or community service; helping with assessment; and other department-necessitated tasks. As a graduate student, I always had the sense that service was somehow evil, but I find it gives me a chance to learn about disparate things and to interact with all kinds of people. If you like student-centered activities, you most likely will enjoy this conference-table work, too.

Do you even need to prepare for service? Service at primarily undergraduate institutions often boils down to the role faculty members play in running the entire university; it is an important part of the job. If a search committee thinks an applicant would not do well in service work, the applicant might be viewed as unorganized, not caring about the university as a whole or not functioning well in teams. These kinds of skills are critical for successfully conducting all the other aspects of student-centered professorships. To stand out in this arena, become a

leader in some way (such as starting or leading a journal club), stay organized with materials and how you store and present information, and communicate respectfully and courteously with everyone. Again, these skills are the same ones that great teachers need as well.

**Go forth**

If you are looking into a student-centered faculty career, read! Research it! There are articles from websites such as the Chronicle for Higher Education and career-development sessions at most scientific conferences. The bottom line is that you should look into the requirements now so you can get qualified. A second-rate research university applicant is usually not a first-rate teaching applicant.

If you are mentoring someone looking into these jobs, be supportive. This career path is one of many that are fulfilling and important. If you are not aware of the qualifications your students will need, encourage them to find out what those qualifications are. They might have to take steps to prepare for an independent position that are different from those taken by trainees seeking research-based positions. Remember that you are probably not losing a research colleague. These jobs are not second-rate for those of us who worked very hard to get here and love it! ∞∞∞



Sydella Blatch (sblatch@stevenson.edu) is an assistant professor of biology at Stevenson University.

**For more information**

For the full-length version of this article, please go to ASBMB Today online at [www.asbmb.org/asbmbtoday](http://www.asbmb.org/asbmbtoday).





## The NSF's two-criteria review

### *Broader impacts are here to stay*

BY JOSEPH PROVOST

**P**reliminary data? Check. Budget worked out and passed through institutional review? Check. Fantastic (and transformative) hypothesis with strong experimental design? Seems like it. Broader impacts? Huh? What's that? Never mind; I'll write up some outreach bit and worry about it later.

Although the National Science Foundation's two-merit-review criteria have been around for nearly 15

years, this scene continues to be played in the office of many a well-meaning proposal writer. It doesn't take long to find articles or faculty opposing this system; however, the criteria are here to stay, and, in fact, criterion two, "broader impacts," is changing.

At a recent national meeting, I met with a number of scientists and asked what they knew about broader impacts and how they incorporated them into their proposals. Surprisingly, only a few seemed to understand what the two-merit-criteria system was all about. Some got upset about having to consider diluting their time with another activity. In 1977, the NSF began requiring two components in all proposals. Since 2002, both criteria must be addressed in a proposal or the work will not be reviewed. The first criterion, "intellectual merit," is the discipline-specific review of the proposed work. The second, "broader impacts," has increased in importance and is better understood by the general community. This second criterion was developed in response to the Clinton administration's requirement of accountability and fits the NSF's goal to integrate research and education throughout its programs. The current definition of broader impacts requires the proposal writer to work outside of a strictly scientific aim and to align some part of his or her project with a greater societal need. What is hard for some to come to terms with is that this criterion typically is best met neither by the impact of the research results nor by the training of graduate students and postdocs. Both criteria are part of the review process and incorporated in funding decisions, and, as a result, broader impacts must be taken quite seriously.

In 2010, the National Science Board and the NSF initiated a review of both criteria and in the summer of 2011 requested feedback from the stakeholders. The resulting assessment was that "the two review criteria of intellectual merit and broader impacts are in fact the right criteria for evaluating NSF proposals, but that revisions are needed to clarify the intent of the criteria, and to highlight the connections to NSF's core principles" (1). Part of the upcoming changes to the review criteria will



Joseph Provost mentors undergraduate Lisa Magstadt while conducting research funded by the NSF.





research collaborator, include letters of support from your institution to help with your activity. If you are planning to work with a regional school, get a supporting letter from a teacher, principal or counselor showing real commitment. If your broader impact activity is to create a new course to expand scientific understanding, then include how it will be incorporated into your institution's curriculum. Provide evidence of support from your departmental chair or dean for the class and, if needed, resources to sustain the activity beyond funding the research. Many universities have existing outreach programs you can build upon.

include gauging how a proposal reflects one or more of the national goals as defined by the America COMPETES Reauthorization Act of 2010 (2). This U.S. House resolution states that the NSF must include broader impacts as a review criterion to achieve a range of national goals (see box).

How might we best meet these needs? One way not to do it is to tack on some activity or presentation to a K-12 class not related in any way to your proposed work. Another way to diminish a proposal is to focus on only the research results. If the results of your research meet one of the criterion, then relate how this happens. To create a stronger, broader impact takes time, just like creating a well-supported hypothesis and scientific approach. Make a coherent plan that incorporates some facet of your science into the activity. Find support for your activity and, just as you would when finding a

Next, assess how you will evaluate these goals. If your activities include students or other participants, does your budget reflect your commitment? Statements about including teachers and undergraduates or increasing access for students without a budget to support their work over a summer are a red flag for some reviewers. Most importantly, take time to think about what you want to do, find support and don't be afraid to ask a program director for guidance and insight. Ask early and ask often. He or she will be very interested in helping you work through the current and pending changes to the broader-impacts criteria.

It is critical for us to become accountable to our funders by meeting the public need. The private and public sectors are simply running short on STEM-trained workers. What is worse is that this challenge to America's competitiveness has grown over the past five years. Who better to build this workforce and change the nature of how science is perceived by our society than our own community? ☺☺☺

### Eight national goals to enhance American competitiveness

- Increased economic competitiveness
- Development of a globally competitive science, engineering, technology and math workforce
- Increased STEM participation of women and minorities
- Increased partnerships between academia and industry
- Improved pre-K-12 STEM education and teacher development
- Improved undergraduate STEM education
- Increased public scientific literacy
- Increased national security



Joseph Provost (joseph.provost@ndsu.edu) is at the Center for Biopharmaceutical Research and Production at North Dakota State University and serves on the ASBMB Education and Professional Development Committee.

#### REFERENCES

1. NSB/NSF seeks input on proposed merit review criteria revision and principles. [www.nsf.gov/nsb/publications/2011/06\\_mrtrf.jsp](http://www.nsf.gov/nsb/publications/2011/06_mrtrf.jsp)
2. America COMPETES Reauthorization Act of 2010. [www.nsf.gov/statistics/about/BILLS-111hr5116enr.pdf](http://www.nsf.gov/statistics/about/BILLS-111hr5116enr.pdf)

# Learning military lingo

## Emily Heuring reflects on her career at the Institute for Defense Analyses

BY EMILY HEURING

**S**even years ago, I took a giant leap from the comfort and routine of an academic environment at the Johns Hopkins University School of Medicine to the realm of military acquisition. My Ph.D. thesis work was in understanding the molecular mechanisms of how the simian version of HIV-AIDS affected the primate central nervous system. But it quickly became apparent that bench work was not for me.

As a person who likes instant gratification for hard work, I knew working for months on a single experiment just wasn't my cup of tea. So I decided to take a nontraditional career path shortly after starting graduate school. I wanted to use my training in molecular biology and virology to help nonspecialists, particularly government policymakers, understand difficult scientific concepts. I looked for positions in the Washington, D.C., area. After replying to a job posting in the Washington Post, I got a call from the Institute for Defense Analyses in Alexandria, Va.

IDA is a nonprofit that provides the government, mainly the U.S. Department of Defense, with unbiased and not financially motivated technical analyses of a variety of subjects. To do this, IDA employs people from a wide range of backgrounds, including physical, life and computer scientists and former members of the military.

At IDA, I provide technical exper-



Emily Heuring left the bench for a career that would help policymakers understand scientific concepts. Her work at the Institute for Defense Analyses is usually an office job, but it has taken her to operational test events in the field. Above, adventure-seeking Heuring is shown in Ecuador last year with her now-husband, Terry.

tise for the evaluation of chemical and biological defense programs within the DOD. Over the years, I have analyzed data and written reports about a variety of chemical and biological defense systems, including detectors for biological agent aerosols and chemical vapors, polymerase chain-reaction machines for medical diagnostics, and systems mounted on armored vehicles.

For the most part, my job is a desk job, and I spend most of my time

reading and writing reports, listening to teleconferences and attending meetings. However, one of the perks is attending operational test events in the field. These events are held at military test ranges all over the country and are intended to test systems in the most realistic environments possible. Because testing of chemical and biological defense systems with actual agents, such as nerve gas or anthrax, is restricted to laboratory environments, we evaluate the performance of

detectors during operational test events using benign stimulants that present the detectors with as realistic a challenge as possible without harming the environment or the system operators.

During operational testing, military personnel operate the systems in the same way they would operate them in the field. By observing the operational test and evaluating the data from the test, I can discern whether these detection systems actually work the way they should and how easily military personnel can use them.

When I first came to IDA, I had no experience in the military. Just learning how the bureaucracy associated with a DOD-acquisition program worked, not to mention the volumes of acronyms associated with programs, took me several months. At the beginning, I sat through many meetings with no idea of what was being

discussed because I wasn't up to speed with DOD lingo. Another problem I had to overcome was being unfamiliar with the ranks and insignias of the various military officers and enlisted personnel. Nothing is more insulting to a colonel than being mistaken for a major! With time and patient mentoring from other IDA research staff members, I got comfortable with my role and responsibilities at IDA as well as military culture and language.

My work at IDA is extremely satisfying, because people with Ph.D.s in technical areas are held in special regard. If I offer an opinion or a point of view, people listen. While they may not always agree with what I have to say, they understand that I don't have a dog in the fight and that I'm really just trying to help the program. My input also is valued highly by my DOD sponsor as well as my colleagues

at IDA. I feel the work I do on a daily basis has an impact, most notably in ensuring that the soldiers, sailors, airmen and marines get systems that work reliably and provide them with accurate information.

My advice to any scientist seeking an alternative career is to not be afraid to do something outside of your comfort zone. Joining an organization that worked with the military was probably the last thing I thought I would end up doing when I started graduate school. However, looking back now after seven years, I'm happy to say that in making my giant leap from the bench to the world of military acquisition, I landed on my feet and am now marching along happily. ∞∞∞

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Emily Heuring (eoverhol@ida.org) is a research staff member at the Institute for Defense Analyses in Alexandria, Va.

## Textbook usage survey for members

The ASBMB Education and Professional Development Committee is interested in which textbooks ASBMB members use in biochemistry and molecular biology courses.

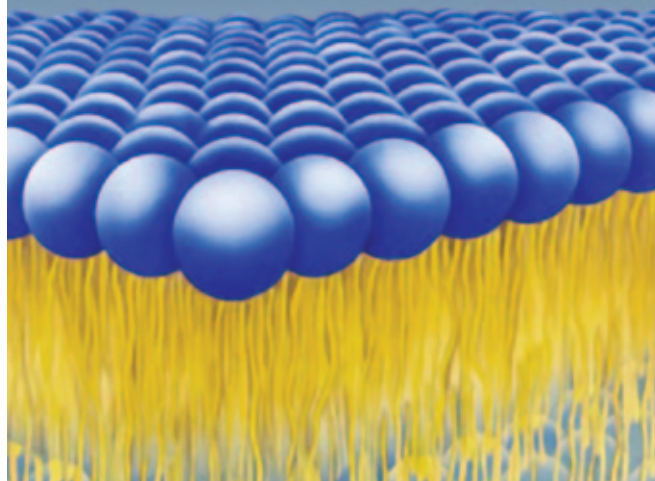
Please take a moment to complete a short textbook survey at [www.surveymonkey.com/s/H5Y3ZNY](http://www.surveymonkey.com/s/H5Y3ZNY).

Aggregate results will be posted on the ASBMB website. We appreciate your input and hope this information will be useful to our members.

Please complete the survey for a single course. If you are involved with multiple courses, please complete a separate survey for each one.



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Enrico di Cera, *Saint Louis University School of Medicine*  
**Granlibakken Resort and Conference Center**  
(Tahoe City, CA)

March 1, 2012: Early Registration & Abstract Submission

**JUNE 27-29**

## **Mitochondria: Energy, Signals and Systems**

Laurie S. Kaguni, *Michigan State University and*  
Howard T. Jacobs, *University of Tampere, Finland*  
**Kellogg Hotel and Conference Center**  
**Michigan State University**  
(East Lansing, MI)

March 15, 2012: Early Registration & Abstract Submission

**SEPTEMBER 4-9**

## **Frontiers in Lipid Biology**

Joint meeting with: **International Conference on the  
Bioscience of Lipids and Canadian Lipoprotein Conference**

Dennis Vance, *University of Alberta,*  
*Canada Organizing Committee:*  
Bill Dowhan, *University of Texas, Houston;*  
Fritz Spencer, *University of Graz, Austria;*  
Rene Jacobs, *University of Alberta;*  
Richard Lehner, *University of Alberta;*  
Spencer Proctor, *University of Alberta;*  
Simonetta Sipione, *University of Alberta;*  
Jean Vance, *University of Alberta;*  
Dawei Zhang, *University of Alberta*

**The Banff Center (Banff, Alberta CANADA)**

June 1, 2012: Early Registration & Abstract Submission

**OCTOBER 4-8**

## **Transcriptional Regulation: Chromatin and RNA Polymerase II**

Raymond Trievel, *University of Michigan and*  
Ali Shilatifard, *Stowers Institute for Medical Research*  
**Snowbird Ski and Summer Resort**  
(Snowbird, UT)

February 1, 2012: Platform Lecture Abstract Deadline  
August 1, 2012: Early Registration Deadline

**OCTOBER 11-14**

## **Post Translational Modifications: Detection and Physiological Role**

Gerald W. Hart, *Johns Hopkins University*  
*School of Medicine*  
Lauren E. Ball, *Medical University of South Carolina*  
**Granlibakken Resort and Conference Center**  
(Tahoe City, CA)

August 1, 2012: Early Registration & Abstract Submission

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## LETTER TO THE EDITOR

### Glimcher Q&A

#### To the Editor

In skimming your article on Laurie Glimcher in ASBMB Today, I noticed the statement that she was the second dean of a major medical school after Nancy Andrews at Duke. I wanted to point out that Leah Lowenstein was dean at Jefferson Medical College in 1982 (25 years earlier).

*Peter E. Prevelige Jr.*

University of Alabama at Birmingham

## READER COMMENTS ONLINE

### “Five years of giving rural students second chances,” December 2011

*As an individual growing up and attending school from grade 1 through 12 with Billy Hudson in Grapevine, Ark., I am very proud of him and his work. The article is very interesting but does not give him any more credit for helping others than he deserves. I have always loved him like a brother, and he will always remain my lifelong friend.* — SHELBA FIELDING BRADFORD

## SNEAK PEEK

### iPad apps to kick your work into high gear

On the ASBMB Today website this month, contributor Angela Alexander, a postdoc at the University of Texas MD Anderson Cancer Center in Houston, offers reviews of her favorite iPad apps. Below are some excerpts. Read more of Alexander's reviews at [www.asbmb.org/asbmbtoday](http://www.asbmb.org/asbmbtoday) and follow her on Twitter at [www.twitter.com/thecancergeek](http://www.twitter.com/thecancergeek).

#### Portable filing system



**Evernote:** This amazing free app helps you “remember everything.” It lets you capture notes on your phone, laptop, desktop or iPad (of course) and have them automatically synced to all devices. Notes can be text,

pictures, webpages, audio — your imagination is the limit! Get the app at <http://bit.ly/seVgIV>.

#### Get organized



**Agenda:** The built-in calendar app on your iPad is fine, but I like the look and feel of Agenda for iOS much better. It's been described as elegant and intuitive, and I'd add “pretty powerful,” too.

Get your calendars from wherever they currently may be hosted (Google, MS Exchange, Mobile Me or just start fresh), and see all of them color-coded in daily, weekly, monthly or yearly view. Get the app at <http://bit.ly/sjwOSc>.

#### Read up!



#### iAnnotate PDF!

Read, search, annotate and share PDFs. For example, mark up those journal articles with notes about all their flaws or about things to look up later. You can also sign all the necessary forms

and other annoying paperwork you'll receive in graduate school and beyond. It's Dropbox-friendly too! However, you'll want a stylus for this app. Get it at <http://bit.ly/vMCQfU>.

#### At the bench



**Promega:** I've tried out many life science companies' free apps, and I have to say Promega's comes out on top for usefulness. It includes lots of information about general molecular and cell biology protocols, including videos and

animations, some useful calculators (conversions galore!), a restriction enzyme tool and, in case you need anything else, quick links for contacting Promega by various methods. Get the app at <http://bit.ly/uPt0vO>.

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