ASBMB today

November 2011

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VOICES ON THE HILL

ADVOCACY TOOLKIT

LOOKING AHEAD

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American Society for Biochemistry and Molecular Biology

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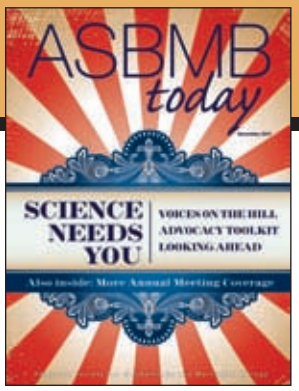

NOVEMBER 2011

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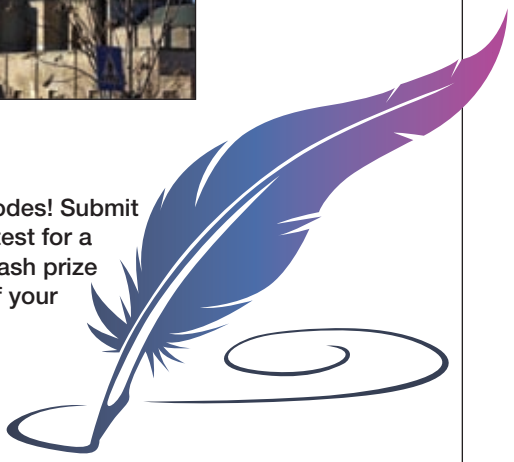

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Our new science writer, Rajendrani Mukhopadhyay, interviews Laurie Glimcher, left, the new dean of Weill Cornell Medical School. 12

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Check out our new series of blog reviews for readers who haven't yet explored all that the blogosphere has to offer when it comes to biochemistry and molecular biology. Contributor Aditi Das offers her recommendations for blogs useful in the classroom and lab. **www.asbmb.org/asbmbtoday**

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ASBMB Today

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2008 APEX AWARDS FOR PUBLICATION EXCELLENCE

president's message

A letter to the entering class

BY SUZANNE PFEFFER

What if every ASBMB member selected a mentee (a student, postdoc or junior faculty member) and gave him or her the gift of an ASBMB membership? I decided to do that for the 12 graduate students who began training this semester in the department of biochemistry at Stanford University. I don't expect many ASBMB members to gift 12 memberships in one year, but I cannot think of a better way to welcome young scientists into our discipline. I should have been doing this for years now, for all of my students, to help them understand from the outset that they are part of a much larger community of scientists. So with that, I share with you a letter to the entering class.

Dear First-Year Students,

I cannot think of a more exciting time to embark on a career in science. There are so many more tools available today than ever before, and our ability to study questions on a genomewide scale represents a major advance both in terms of the scope of the answers that can now be obtained and the systemwide complexity that we can now begin to explore.

You are now a professional researcher — getting paid to do experiments and make discoveries. The sooner you realize that students and postdocs make essentially all of the major discoveries, the sooner you will understand why coursework is an important starting point but not at all the point of graduate school. We need to teach you how to learn what you need to learn on your own. There simply is too much information and a broad swath of history that would take too much course time to explain. Discoveries won't happen if you aren't thinking hard about your science and spending a great deal of time doing experiments. You need to embrace your project as your own. The sooner you do this, the more successful you will be.

Some of you will be very lucky in graduate school: Your research project will yield ready answers, and your proteins will be well behaved. Others will have a more challenging time, and those of you in this latter category will learn another important lesson— that science is not always easy and success requires knowing when to keep trying and, just as importantly, when to change tack. I will worry about those of you who have easy success, because after you graduate and you face a tougher project (and it will be when and not if), you may not have acquired the skills needed to deal with that challenge. All of a sudden, science may not seem as much fun anymore. It is

those of us who have struggled who appreciate most the joys of discovery.

My wish for each of you is that you start graduate school with a project that is extremely likely to work. This will help you gain confidence in your experimental skills and teach you to trust your data— and the discoveries your data will reveal. Then, I hope you will pick a much bolder question— one that may not have been part of your research adviser's major grant proposal. All of us need to ask what is the most important experiment we can do or the most powerful approach we can take to address this specific question. Every molecule and process can be described and characterized, but only scientists who focus on the most significant questions will make the critical breakthroughs we all seek. The most important thing we can teach you is how to pick an important question and how to address it using a variety of approaches that will enable you to tackle whatever question you select.

Years ago, it was common for labs to study a single protein. Students could be assured that the lab knew how to purify that protein and how to handle it. Today it is more common for labs to study many different proteins, each with its own characteristics. When projects are selected, a student may wish for one protein and then realize that his or her exciting-sounding protein turns out to be impossible to work with. We can't know for sure what to expect until we try a project, but one way to ensure more rapid success is to team up with another lab member on an already moving project. This kind of teamwork makes a project go faster. Individuals can have their own parts of the project but share common reagents and help troubleshoot when something isn't working. For an adviser, this scenario is doubly reassuring, because multiple lab members can carry out complementary experiments and duplicate each other's findings at the same time.

In graduate school, I hope you will learn the value and power of collaboration beyond your own lab. The best scientists use multidisciplinary approaches to tackle a question, and by collaborating you can use multiple approaches and technologies to obtain a much richer and deeper answer. I can think of three times in my own lab when sending a student to another lab for a week (to David Lambright's lab in Worcester, Mass., and Francis Barr's lab in Munich, Germany) or a year (to Axel Brunger's lab at Stanford University) moved their projects forward in a quantum way. Don't be shy to collaborate. All of us are better scientists when we work together.

We (the faculty) have an obligation to prepare you for the wide variety of careers that your training will qualify you for. The ASBMB will offer four career workshops in the next 12 months (in San Francisco, Pittsburgh, Dallas and Raleigh-Durham) to connect alumni representing a number of career choices with students like you, who are considering all of their options. We offer four workshops every year in cities across the U.S. (Let us know if you would like to help plan one in your area.)

The ASBMB exists to support the pursuit of biochemistry and molecular biology. We publish three excellent journals (Journal of Biological Chemistry, Journal of Lipid Research and Molecular and Cellular Proteomics), we organize meetings large and small, we provide student and postdoc travel awards to help you participate in our meetings, and we devote a large amount of resources toward advocating for wise science policy and strong and stable science funding. Membership offers access and supports these activities, plus significant page charge discounts when you are ready to publish your research findings. Finally, membership includes a subscription to ASBMB Today, which I hope you will enjoy, starting with this issue. Welcome to the world of biochemistry and molecular biology; welcome to the ASBMB.

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

Advocacy resources at your fingertips

BY JULIE MCCLURE

Over the summer, the Office of Public Affairs revamped the ASBMB advocacy website to make it even more accessible and helpful to our members who are looking to break into the world of science advocacy. Here's a breakdown of some of the items you'll find:

Home page: Science policy issues arise almost daily. The "Latest News" section gives quick synopses of recent news items and links to more detailed stories reported by other news organizations that are followed by people interested in science policy. Occasionally, the "Breaking News" link is activated. This section broadcasts high-profile stories that are unfolding in real time and may need immediate action from the research community. The "From the Policy Blog" section lists the most recent posts from the ASBMB Policy Blotter, the official blog of ASBMB, where we report on the latest policy issues that affect our members. The home page also includes a listing of detailed policy articles written for ASBMB Today.

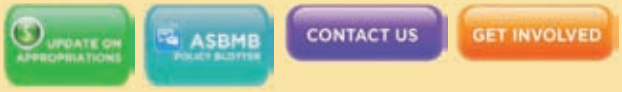
Those who are interested in becoming more deeply involved in science policy can click on the "Getting Involved" button to sign up for the Local Advocates Network. By joining the LAN, you receive the ASBMB Advocate, a monthly science policy e-newsletter from the Office of Public Affairs, and updates on science policy issues that are happening in your area. You also can subscribe to the ASBMB Policy Blotter RSS feed to be updated on issues like the congressional appropriations process; National Institutes of Health and National Science Foundation organization; and science, technology, engineering and math education and training issues. Finally, use the "Update on Appropriations" icon to track the status of funding bills in the congressional appropriations process.

About the PAAC: Find out about the members of the Public Affairs Advisory Committee and explore the various ways in which the committee works to represent you.

Advocacy toolkit: This resource has instructions for identifying and contacting your member(s) of Congress and provides sample scripts you can use to voice your opinion by email or phone. If you are interested in meeting directly with your representative, the toolkit explains how to orchestrate face-to-face interactions in your home district ("Hosting a Meeting" section) or in Washington, D.C. ("Congressional Visits Guide"). When preparing for a meeting, be sure to use documents from the "Congressional Meeting Materials" link and watch the "Meeting with your Congressman" video to see how a meeting should and should not be conducted. Moreover, you can find congressional biographies that provide information on members' backgrounds and voting records on science-related issues.

Visit the redesigned site

www.asbmb.org/Advocacy/advocacyhome.aspx



Position statements and correspondence: Read ASBMB's formal position statements on issues such as human embryonic stem cell research and maintenance of proper NIH grant portfolio balance as well as press releases detailing the official ASBMB response to news items that affect researchers. ASBMB is also part of multiple science coalitions and organizations that release statements and letters in response to legislative or administrative issues.

Events: The major advocacy event hosted by ASBMB is our biannual Hill Day, when members are brought to Washington to meet with lawmakers and to advocate for basic research. Learn what Hill Day is all about by browsing photos and participant interviews from past years. Upcoming events include the PAAC-hosted science policy seminar at the annual Experimental Biology meeting.

Related sites: Check out this extensive list of websites that cover the science policy spectrum, from legislative and government agencies to fellow scientific societies, coalition partners and organizations.

Julie McClure (jmcclure@asbmb.org) is a science policy fellow at ASBMB.

Translational-center plans move forward

BY JENNIFER A. HOBIN

The proposed National Center for Advancing Translational Sciences is one step closer to becoming a reality. This fall, the U.S. Senate Appropriations Committee approved its fiscal 2012 spending bill for the departments of Labor, Health and Human Services, and Education, which authorized the creation of NCATS as part of a broader restructuring of the National Institutes of Health that includes the termination of the National Center for Research Resources.

The bill also appropriates $20 million to activate the Cures Acceleration Network, a new NIH program to be housed in NCATS. CAN, which was authorized but not funded in the healthcare reform bill signed into law in March 2010, will make grants to biotech companies, universities and patient-advocacy groups to develop what the bill's authors dubbed "high-need cures," and it will help facilitate Food and Drug Administration review for these therapeutics. Thus far, the draft House appropriations bill contains no provisions for NCATS but provides funding for CAN and the NIH Clinical and Translational Science Award program, which would move from NCRR to the new center if it is established.

Final congressional approval of NCATS could come later this year if lawmakers approve a fiscal 2012 bill providing funding for the NIH.

Despite the uncertain funding situation, NIH has been pressing ahead with plans for the translational research center. NIH's advisory committee to the director's NCATS working group released a report Sept. 21 noting seven areas "ideally suited for NCATS activities":

1. supporting and enabling high-risk, high-reward projects for transforming, improving and accelerating the process of discovery, development and post-market research for diagnostics, therapeutics and devices;
2. galvanizing and supporting new partnerships among the regulatory, academic, public, private and nonprofit sectors to address challenges in translational sciences;
3. collaborating with the FDA on studies aimed at informing and improving the regulatory approval process;
4. encouraging collection and analysis of data about failed projects to facilitate the open exchange of information regarding scope, methods, analysis, results and lessons learned from research in the precompetitive space;
5. harnessing the power of the CTSA program by affording individual CTSAs flexibility in cultivating strengths and encouraging formation of a national CTSA consortium;
6. promoting training in translational science by catalyzing novel training mechanisms, providing incentives for physician-scientists to seek cross-training in human biology and drug discovery, and exploring cross-training of physicians and scientists between industry, academia and government labs; and
7. reviewing administrative processes at the NIH and NCATS to identify and overcome roadblocks to rapid and effective funding, management and termination of projects.

The report also identified areas ripe for innovation and inclusion in the NCATS portfolio. They include:

- target validation for rare and common diseases;
- understanding and modeling drug toxicity;
- systems pharmacology and how pharmacological agents affect cellular networks and contribute to pathology;
- biomarkers and disease phenotyping;
- new uses for established compounds;
- imaging technologies;
- developing more effective ways to incorporate FDA-approved medical products into patient care; and
- opportunities to collaborate with entities experimenting with the chemical space, including clean/green chemistry, inorganic chemistry and combinatorial chemistry.

The report emphasized that NCATS should not duplicate translational research efforts of other NIH institutes and centers or industry and that projects should be supported only until they attract commercial investment.

The working group also provided advice on choosing a director for the center, noting that he or she should have "a unique blend of expertise and experience that transcends a single field or discipline" and should ideally "be experienced in both academia and the private sector." NIH has formed a search committee but will not bring on a director until the center is established and funded.

Find out more about the NCATS working group and read its full report at http://bit.ly/mX1JXR.

Jennifer A. Hobin (jhobin@faseb.org) is associate director of scientific affairs for the FASEB Office of Public Affairs.

Members make their case for science on Capitol Hill

BY JULIE McCLURE

The 2011 American Society for Biochemistry and Molecular Biology fall Hill Day hosted nine investigators who live or work in the districts of representatives from the U.S. House Appropriations Subcommittee on Labor, Health and Human Services, and Education, which allocates funding for the National Institutes of Health. The invited researchers, along with seven members of the Public Affairs Advisory Committee, met with more than 40 congressional offices to advocate for biomedical research.

Gerald Shadel
Yale University School of Medicine

Gerald Shadel's research focuses on mechanisms that govern expression and maintenance of mitochondrial DNA, the requisite signaling pathways involved in regulating these processes, and how associated defects are involved in human disease and aging.

Malcolm Snead
University of Southern California

Malcolm Snead studies the control of biomineralization using structural biology approaches and interventional changes in gene structure via modifying the mouse genome.

Mark Quinn
Montana State University

Mark Quinn's research is focused on understanding microbicidal mechanisms utilized by innate immune cells in defense of the host against pathogens, specifically investigating the molecular and biochemical basis of phagocyte oxygen radical production as well as the role of phagocyte-generated oxidants in the tissue damage associated with inflammatory diseases in humans and livestock.

Kathleen Collins
University of California, Berkeley

Kathleen Collins studies functional complexes of RNA and proteins to understand their distinct assembly requirements and their innovations of activity. Much of the lab effort is focused on telomerase, an enzyme required for chromosome end maintenance and implicated in human disease.

Wayne Frasch
Arizona State University

Wayne Frasch studies ATP synthetase, the enzyme required by virtually every living organism to catalyze the conversion of energy from food or light into ATP.

Laszlo Prokai
University of North Texas Health Science Center

Laszlo Prokai uses mass spectrometry to identify novel proteins associated with aging and neurodegeneration. His broad interests are biological phenomena that can be explained with, elucidated through and made useful by the principles of chemistry.

Bernard Roizman
University of Chicago

Bernard Roizman studies the mechanism through which the herpes virus infects a cell.

Xian Luo
Loma Linda University

Xian Luo's focus is on cellular and molecular mechanisms of radiotherapy-induced normal tissue reactions.

Michal Laniado-Schwartzman
New York Medical College

Michal Laniado-Schwartzman's research consists of two projects focused on the role of lipid autacoids, more specifically, cytochrome-P450-derived eicosanoids, in the regulation of inflammation and vascular function in the areas of the cardiovascular system and vision.

PAAC Members who attended

Richard Eckert
University of Maryland

Mark Lively
Wake Forest University

Bettie Sue Masters
University of Texas Health Science Center at San Antonio

Lee Gehrke
Harvard University/Massachusetts Institute of Technology

John Kyriakis
Tufts Medical Center

William Merrick
Case Western University

Ronald Bach
Minneapolis VA Medical Center

"I had an amazing day visiting with my congressional representatives… I was amazed at the process and how willing every office was to listen to our comments about the importance of biomedical research and NIH funding. I was pleased to hear the support for NIH evident across the many offices we visited, regardless of political party."

—*Mark Quinn, Montana State University*

"I learned that constituent voices do get heard, but only if we ask to be heard."

—*Kathleen Collins, University of California, Berkeley*

"I must say that this visit exceeded my expectations in terms of what I learned and what we achieved… We were welcomed and received the highest respect… I truly believe that this forum is well worth our time and effort and appreciated the bipartisan positive feedback regarding the NIH budget. Also, I felt that from both sides of the aisle there was a great appreciation for biomedical research and understanding that support for NIH is conducive to economic growth and job creation."

—*Michal Laniado-Schwartzman, New York Medical College*

"The fascinating experience… made me realize that, as scientists, we must all speak out and reach out to politicians, who would actually later recollect what we shared with them when… appropriations are examined. Believe or not, our real-life stories are important for making progress with discovery in scientific research, especially when NIH funding is being cut… And if we do not express the need for such fiscal support and the importance of those considerations repeatedly, politicians may not realize and prioritize these needs."

—*Xian Luo, Loma Linda University*

"Two important aspects of these exchanges… were 1) the opportunity to clarify the difference between basic and translational research and the critical need to fund both going forward and 2) their recognition of the enormous social and economic impact of funding science in the U.S. and insight into… measures that could provide more bang for the taxpayer scientific buck, such as lowering the regulatory burden on scientists.

—*Gerald Shadel, Yale University School of Medicine*

"The Hill Day was a great experience that gave me the opportunity to convey to lawmakers our society's message with my personalized touch and ask for their support of biomedical research and related matters important to the scientists in our country."

—*Laszlo Prokai, University of North Texas Health Science Center*

Maternity planning for postdocs

BY KATHLEEN FLINT EHM

Planning to start a family can be a challenge for early career researchers, who often wonder when the "best" time might be. During graduate school? While on the tenure track? After tenure? Those considering the postdoctoral years can be constrained by multiple short-term appointments and the general uncertainty of a job market that offers no guarantees of stable, long-term employment.

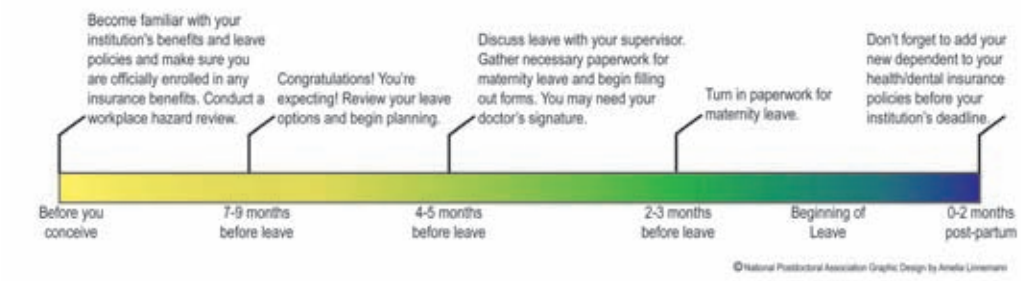
Recent focus groups conducted by the National Postdoctoral Association spotlighted these concerns among current and former postdoc women. A key concern expressed by participants was how to balance the "postdoc clock" versus the biological clock. One postdoc characterized the uncertainty this way: "You know, having a baby during grad school: maybe not the best idea. Having your baby while you're tenure-track: maybe not the best idea. So does that mean that I have to get pregnant right now because my postdoc is 24 months long, and that's it?"

Underscoring this uncertainty is the fact that postdocs often experience a lack of defined status at their institutions, or, as described by focus-group participants, a feeling of being "in limbo." As neither students nor faculty members, postdocs can feel isolated at institutions that lack infrastructure to support their positions, such as family-responsive policies like paid maternity leave. Most postdocs cobble together combinations of annual leave, partially paid disability insurance and unpaid leave. Moreover, the details of how such benefits apply to postdocs can be confusing due to the variety of postdoc employment classifications and funding sources.

To demystify the process of maternity planning, the National Postdoctoral Association recently published "A Postdoc's Guide to Pregnancy and Maternity Leave" (www.nationalpostdoc.org/publications/563-maternity-guide). It provides an overview of planning issues for women who are pregnant or considering becoming pregnant during their postdoc and for their partners, including safety during pregnancy, understanding paid- and unpaid-leave options, and advice for keeping research going during pregnancy and leave. Below are some highlights from the guide.

Pregnancy safety

Postdoc women considering pregnancy should think about requesting an evaluation of workplace hazards to those of child-bearing age prior to conception. Such an evaluation can allow a postdoc to identify hazards without declaring a pregnancy earlier than needed.



Basic right to maternity leave

Under Title IX, women at federally funded institutions, including postdoc women, should be entitled to take, at the minimum, job-protected, unpaid leave for a "reasonable" amount of time. In practice, the details of how leave is taken, for how long and how it might be paid depend solely upon an institution's policies. Postdocs should talk to their institutions' postdoc and/or human-resources offices about their options.

Keeping your research going

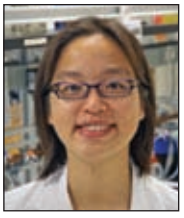
Postdocs planning family leave should begin making arrangements early for needed research accommodations. A written research plan can help lay out milestones and expectations for this period and provide a mechanism for discussing leave with a postdoctoral supervisor or collaborators who may be able to help keep a project going.

Kathleen Flint Ehm is the NPA ADVANCE project manager at the National Postdoctoral Association. NPA ADVANCE is supported by the National Science Foundation. Any opinions, findings, and conclusions or recommendations expressed in this material are those of the author and do not necessarily reflect the views of the NSF.

asbmb member update


CERIONE


HONKANEN


HAMMOND


WEIBEL


BASS


CLEMONS

Cerione, Honkanen win NIH awards for transformative work

Richard A. Cerione of Cornell University and Richard E. Honkanen at the University of South Alabama School of Medicine were among the 2011 recipients of the Common Fund's NIH Director's Transformative Research Award. The initiative, previously the Transformative Research Project, supports unconventional and innovative research projects that potentially could create or overturn fundamental paradigms. These projects tend to be inherently risky and may not fare well in conventional NIH review. The initiative supports research projects rather than individuals. Cerione is part of a team that got the award for the project "Succinylation and malonylation as novel protein modifications in cancer." Honkanen received his award for his "Methods to enable cholesterol catabolism in human monocyte derived macrophages" project.

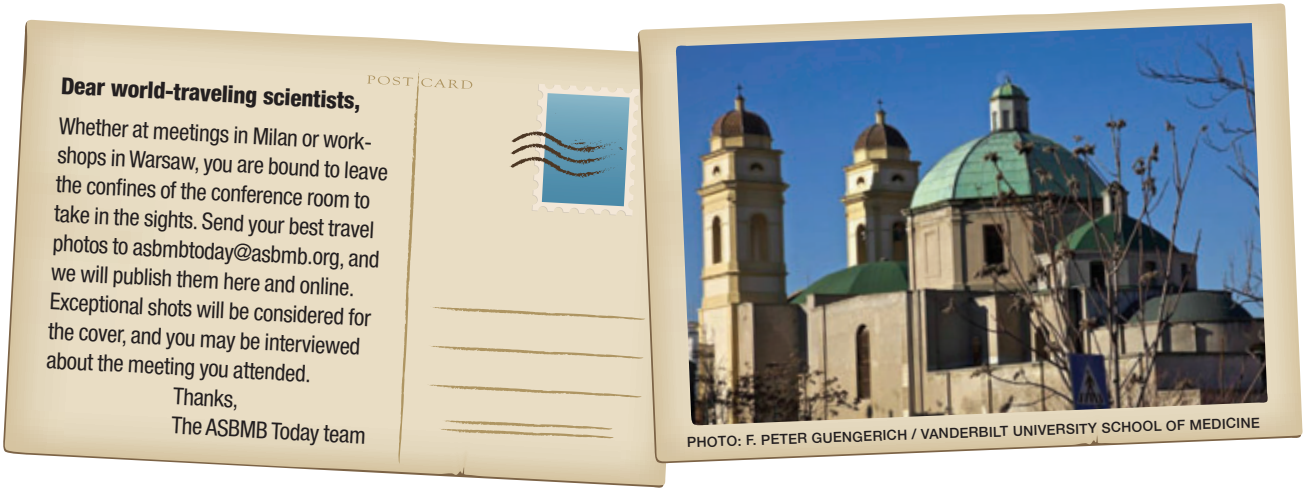
Hammond, Weibel among winners of NIH innovator prizes

Ming C. Hammond, the Chevron professor of chemistry at the University of California, Berkeley, and Douglas B. Weibel, an assistant professor of biochemistry and biomedical engineering at the University of Wisconsin, Madison, each received an NIH Director's New Innovator award. The awards aim to stimulate cutting-edge research done by exceptional new investigators. The program is different from traditional NIH grants, because it supports new investigators who have highly innovative and unusually creative research ideas but may lack the preliminary data required for an R01 grant. Hammond won hers for a project called "A chemical biology approach to tagging RNAs in live cells." Weibel received his award for the project "Revisiting the bacterial cell wall as a target for new antibiotics.

Bass, Clemons get NIH 'Pioneer' awards for their proposals

Brenda L. Bass at the University of Utah and William M. Clemons at the California Institute of Technology received the National Institutes of Health Director's Pioneer Award for 2011. The Pioneer Awards are designed to support individual scientists of exceptional creativity who propose pioneering and potentially transforming approaches to major challenges in biomedical and behavioral research. Bass received her award for her proposal titled "Cellular double-stranded RNA as a signal of stress, immunity, and aging." Clemons' project will focus on novel approaches to study membrane proteins.

Please submit member-related news and accolades to asbmbtoday@asbmb.org.



The church of Sant'Anna in Cagliari, Sardinia, Italy. Taken by Journal of Biological Chemistry Associate Editor Fred Guengerich while he was a visiting professor at the University of Cagliari in February. The quarter of Stampace is the oldest quarter of Cagliari and known as the Quarter of the Seven Churches, because each street has its own house of worship.

Scarpa retires and Nakamura steps in at NIH Center for Scientific Review

BY RAJENDRANI MUKHOPADHYAY

Antonio Scarpa retired in September as the director of the Center for Scientific Review at the National Institutes of Health. Scarpa, who was appointed to the position in 2005 by then-NIH Director Elias Zerhouni, played a key role in helping NIH develop and implement the first major changes to its peer-review system in 65 years. CSR receives all and reviews most of the more than 80,000 grant application submitted to the NIH every year.

Antonio Scarpa

"My six years at CSR were exhilarating," Scarpa said in a statement announcing his retirement. "I was privileged to serve in a period of unprecedented changes and opportunities in peer review. Thanks to a dedicated staff and reviewers, CSR excelled during this time, reviewing 50 percent more applications in addition to 40,000 applications for federal stimulus funds two years ago. This was only possible due to a shared passion and unfailing commitment to the quality and efficiency of peer review."

Scarpa spearheaded efforts to shorten applications, implement new scoring schemes and accelerate review cycles. He also reorganized CSR's review groups into five divisions to maximize efficiency and make sure the study sections covered evolving fields of research.

In an interview with Nature News after his retirement was announced, Scarpa said that he thought the changes he implemented were successful. He explained that as a result of shortening grant applications from 25 to 12 pages, peer reviewers were able to focus on the impact and significance of the proposed research. "Peer review is simple — I think it should ask only two questions. First: Is it worth doing? That is impact and significance. If the answer is yes, then you ask the second question: Can they do it? In the past we were asking those questions in reverse," he said, adding that peer reviewers soon saw the benefits of the changes. "People can see that focusing on impact and significance is probably the way to go."

Current NIH Director Francis S. Collins has appointed Richard Nakamura to take the helm of the CSR after Scarpa's departure. Nakamura had a 35-year tenure at the National Institute of Mental Health, where he served as both scientific director and deputy director. He also served as acting director from 2001 to 2002. Nakamura's expertise covers several areas, including cognitive and comparative neuroscience, science policy and funding, and ethics in science. He has 30 peer-reviewed scientific journal articles, most related to neurocognition in primates. He is a fellow of the American Association for the Advancement of Science and has won leadership awards from the Federation of Behavioral Psychological and Cognitive Sciences and the International Society for Behavioral Neuroscience. "I look forward to working with the many dedicated individuals engaged in this great enterprise," Nakamura said in a statement that announced his appointment. "It's a privilege to help NIH identify research with the most promise for making our world more healthy and productive."

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

NIH news

Visit asbmb.org/asbmbtoday regularly to get updates on the latest happenings at the National Institutes of Health and other relevant federal agencies. Here are highlights of the online coverage we're offering this month. Visit our homepage for details:

- Knockout Mouse Project enters second phase of phenotyping
- Junior investigators skip postdoctoral training under new program
- NIH, DARPA and FDA team up for novel chip technology, drug safety

BMB blogs in brief

This month marks the launch of an occasional series of blog reviews for readers who haven't yet explored the reportage and commentary that the blogosphere has to offer when it comes to biochemistry and molecular biology. ASBMB Today contributor Aditi Das is on the hunt for blogs that might be of use in the classroom and lab and will share her recommendations with readers in the coming months. In her first post, Das reviews "A Blog around the Clock" by Bora Zivkovic, a science blogging pioneer who today runs Scientific American's blogging network. Visit www.asbmb.org/asbmbtoday to find out more.

'Enzyme Purification Blues'

You've probably found yourself, at some point or other in your research life, waiting for an experiment to come to fruition and asking yourself, "How long do I have to wait?"

Stephen W. Ragsdale of the University of Michigan Medical School poses that very question in his tongue-in-cheek song "Enzyme Purification Blues," which was recently uploaded to the American Society for Biochemistry and Molecular Biology's YouTube channel.

The song is based on the tune "How Long Blues" made famous in 1928 by performer Leroy Carr and briefly chronicles the ups and downs of Ragsdale's experience with the enzyme Hydrogenase.

Visit our YouTube channel, www.youtube.com/user/ASBMBio, to have a listen.

Laurie Glimcher: New dean for Weill Cornell Medical School

BY RAJENDRANI MUKHOPADHYAY

On Jan. 1, Laurie Glimcher of Harvard Medical School and Harvard School of Public Health will become the first woman to serve as dean of Weill Cornell Medical College in Manhattan. Glimcher is a practicing physician and has an impressive track record in biomedical research. Her laboratory exploits biochemical and genetic tools to elucidate the molecular pathways involved in lymphocyte development and activation in the immune system. In recent years, Glimcher's research interests have expanded into skeletal biology. She also has experience in the pharmaceutical industry and sits on the board of Bristol-Myers Squibb and has collaborated with Merck Co.

The awards Glimcher has won over the years include the FASEB Excellence in Science Award (2000), the American Society of Clinical Investigation Outstanding Investigator Award (2001) and the American College of Rheumatology Distinguished Investigator Award (2006). She is a fellow of the American Academy of Arts and Sciences and belongs to the National Academy of Sciences and the Institute of Medicine of the National Academy of Sciences. Glimcher is also a member and past president of the American Association of Immunologists.

ASBMB Today spoke with Glimcher to find out about her goals for Weill Cornell Medical College, her vision for the future of the biomedical research enterprise, her management style, and her ideas to help women take on more prominent roles in science and medicine. Below are edited excerpts from the interview:

Q: *What made you decide it was time to make a career move?*

GLIMCHER: I was ready to spend more of my energy and effort in thinking about the health of biomedical research in this country. As a physician-scientist, I thought leading an academic medical institution, which was involved in basic biomedical research and translation of the research into the clinic, was the ideal place. This job came up, and I was asked to put in my CV. I spent a lot of time interviewing and thinking about [the job] and decided it was exactly what I was looking for.

Q: *What are some of the opportunities you see for WCMC?*

GLIMCHER: I want a place that is committed both to the basic biomedical sciences and the translation of discovery into the clinical care delivered to patients. WCMC is perfectly positioned to be on the forefront of academic medicine thanks to the fantastic work of the current dean, Antonio Grotto; Sanford Weill, who is the chair of the board of overseers; the board of overseers; and the president of Cornell, David Skorton. A new research building, for which Tony Gotto, Sandy Weill and the others have raised $1.3 billion so far, is going up with the intent of making it into a first-rate biomedical research center. It has one of the best hospitals in New York City, outstanding medical education, an excellent graduate student program and, clearly, a history of greatness in the biomedical sciences. My feeling is that with this brand-new research building under construction, WCMC is poised for pre-eminence in the biomedical sciences, which it has already achieved in clinical medicine.

WCMC has several key advantages. It's got strong ties to other New York City institutions. It has the tri-institutional graduate-student program, which it shares with Rockefeller [University] and with [Memorial Sloan-Kettering Cancer Center]. There are collaborations that are already ongoing between these three, but I think there could be more opportunities for collaboration in interdisciplinary science.

Another key connection is WCMC's close alliance

Laurie Glimcher will be the first female dean in the 114 years of Weill Cornell Medical Center's existence.

with its outstanding parent university, whose president, David Skorton, is a physician-scientist. One of Cornell University's strategic goals is to increase faculty excellence. I share President Skorton's belief that this is the central mission of the next dean. WCMC is a part of Cornell University, and I look forward to strengthening that bond through shared interests and interactions among the current and to-be-recruited biomedical scientists. I think it's an enormous opportunity for enhanced collaboration between the parent university and the medical school.

Q: *What are some of the challenges you anticipate?*

GLIMCHER: A big challenge for all American biomedical research institutions is funding. The [National Institutes of Health], I am sure I don't have to tell you, has tightened its belt and is going to tighten it further. It's a big challenge for all of us to support ourselves in this current financially constrained environment. We have to be thinking creatively about how to support biomedical research by private foundations, philanthropy and appropriate partnering with the private sector. WCMC has academic excellence and an attractive location, and I think it's going to be possible to recruit first-rate senior and junior faculty in a variety of disciplines. I also think its relatively small size makes it a perfect laboratory for developing innovative approaches to medical education, translational research, clinical care and academia-private sector collaborations.

Q: *What steps will you take to foster more collaboration between academia and industry and between physicians and researchers?*

GLIMCHER: I think the dean needs to be deeply involved in both basic biomedical research and clinical translational research. It's a real opportunity to strengthen research in both and to get the clinicians collaborating with the scientists. There is also NewYork-Presbyterian Hospital, of course, and I'm very eager to maintain and expand the excellent relationship that the current dean has established between the medical college and the hospital.

I really believe that the private sector is essential to translational research. We have to leverage the talents of everybody but always, always, always shine a bright light on any potential conflict of interest. There is an

old saying, "Sunlight is the best disinfectant." You have got to keep everything above board, open and transparent.

We had a wonderful collaboration with Merck for three years. We serendipitously had isolated a new gene that controls adult bone mass. We established a real partnership with [Merck]. It wasn't as if they wrote us a check and said good-bye. We met with Merck project leaders and scientists on a monthly basis to review our joint progress. We helped design a high-throughput drug screen that Merck scientists could use to screen their chemical libraries. They identified some compounds, and we looked at them in cultures of osteoblasts to see if they actually activated osteoblasts. Their funding allowed me to establish a presence in the field of skeletal biology, which I had never been in before. I built a team of really superb postdocs who had come to me originally to work in immunology and instead became skeletal biologists. This is a field that is underpopulated and ripe for expansion and recruitment of bright young scientists. This funding [from Merck] allowed me to make good progress, but it also allowed me to train some talented young people for the field. I could have never done that with NIH funding alone.

Q: *In an environment of financial belt-tightening, how will you identify research directions?*

GLIMCHER: First of all, I'm going to be doing a lot of fundraising. We will have some resources, but there is always a need for more.

But you're right, it's a small place. We can't do everything and need to focus. One area WCMC has chosen to focus on is neurodegenerative diseases. WCMC received a wonderful gift from one of the members of the board of overseers, Robert Appel, to fund a center for neurodegenerative disease. WCMC recruited Steven Paul from Eli Lilly [and Co.] to head it. The intent is to do more recruiting in that area. Neurodegenerative diseases are going to take down our health-care system if we can't figure out how to deal with them. As the population ages, we're going to have many millions of people over the age of 80 who have Alzheimer's or Parkinson's disease. It's our responsibility as biomedical scientists and physicians to figure out how to tackle these diseases. Another area of huge unmet medical need is metabolic syndromes: the triad of obesity, diabetes and cardiovascular disease. These diseases are going to be an enormous drain on our health-care system.

I am very interested in skeletal biology. Before I joined this field, I had no idea that osteoporosis is the most common disease worldwide. One out of two women over the age of 50 have osteoporosis or will develop osteoporosis, and it's one out of five for men. There's major mortality from fractures. The numbers are startling: 25 percent of individuals who sustain a fracture are dead within a year. The Hospital for Special Surgery is closely aligned with Weill Cornell. They are interested in expanding their biomedical research, and I think this is a wonderful opportunity to do that.

Q: *How do you describe your leadership style?*

GLIMCHER: I have developed my leadership and management style both from my many years of supervising a large lab and my years on corporate boards. My own management style is very relaxed. My door is always open. If postdocs and graduate students get a result they are excited about or have a question, they are welcome to pop their heads in. If somebody wants to meet with me, they don't have to go to my secretary and say "I need to arrange a meeting with Laurie" and be told "That will be four days from now." Absolutely not. If they need to speak to me, I will find time to speak to them right away. Period.

I have no problems with making tough decisions, but I think one always has to be respectful of one's colleagues. That's not just the people who are your peers or your superiors but, most important, the people who report to you. I judge myself and other people by the quality of their interactions with individuals below them in the pecking order.

I make the decision I think is right and best for the institution. Then I explain why I made that decision to people who might not agree. That's going to be really important as dean, because you can't always get everyone on board. You can't get consensus all the time, but people have to understand how you reached a decision.

Glimcher with her three children in 2008.

Q: ***You are only the second woman to be named dean for a major medical school. The first was Nancy Andrews for Duke University School of Medicine in 2007. What needs to be done for female scientists and physicians to take on more prominent roles?***

GLIMCHER: It is a tough problem. You have biology intersecting with a time when you need to be devoted to your career. It's not easy, and I know that. I've lived through it with three kids. I remember when I was a postdoc at the NIH. The guys — at least some of them, not all — would sit around, schmooze and talk science. They didn't have to think about picking up a child at day care. I barely ever saw the cafeteria at NIH. I would make lunch and bring it in a paper bag. I didn't have time to have coffee and chat with the other postdocs. I had to work, work, work, because I had to pick up my daughter at 5 o'clock from day care! When I was home while she was still awake, I spent time with her, but I would be up late working. I didn't want to spend my entire weekend in the lab. Yes, I would go into the lab for a few hours [on weekends] but couldn't and didn't want to do that all the time. This became even more challenging with the arrival of two more children over the next several years.

Ideally, postdocs who are primary caregivers should have access to another pair of hands to help level the playing field. I'm not saying they shouldn't do the experiments themselves, and of course they should direct the research. But, realistically, they may not be able to put in the long hours during the week and weekend that their peers can. I started a program when I was president of the AAI, the PCTAS program at [the National Institute of Allergy and Infectious Diseases], which stands for Primary Caregiver Technical Assistance Supplements. It provided technician salaries. It was a small program. I wish it had more funding, but I did get a number of letters from young women who said it made a real difference in their careers for them to have a technician.

Q: ***You have received numerous awards. Which one makes you most proud?***

GLIMCHER: The award that I'm the most proud of is the American Association of Immunologists' Excellence in Mentoring award [in 2008]. That, to me, is the major task of the senior scientist. It's to train the next generation. I think it's a huge responsibility. It's going to be one of my emphases as dean to make sure the mentoring programs at WCMC are as good as they should be.

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Goodbye, Beaumont House

BY RALPH A. BRADSHAW

Colorful fish on the tiles and 50 volumes of the Journal of Biological Chemistry to peruse (while otherwise occupied) in an upper floor bathroom, a winding grand entrance hall and staircase, elegant marble fireplaces (and a decorative half-round window) in some of the offices and meeting rooms, and beautiful gardens and grounds, gloriously in bloom with dogwood and azaleas… all this is a part of Beaumont House, the mansion and grounds that were the home of the American Society for Biochemistry and Molecular Biology for over 50 years and that I visited on the last Saturday in April. In the following week, the moving vans rolled up to the front door, and the society decamped for more modern digs a few miles farther north on Rockville Pike, leaving the only permanent home it had ever known.

As Barbara Gordon, executive director and by far the member of the ASBMB staff with the most memories (she started with the society in 1972), took me on a poignant tour of some of the more obscure corners of the building, I was struck by the many meetings and activities of historical interest that had transpired there and the myriad scientists of renown who had been involved with them. During the society's occupancy, biochemistry and later molecular biology experienced nearly exponential growth, becoming arguably the central sciences of biological research (1).

Beaumont House was also the home of the Journal of Biological Chemistry during all those years, and it enjoyed the same growth and expansion as the society. Indeed, it was, in the end, a need for more room that really necessitated the move to a space designed for modern office practices and needs. Nostalgia aside, the old house and outbuildings were built for residential purposes, and converting them to office space had produced some interesting compromises

Beaumont House

that sadly no longer suited the society's needs. As we wandered down the narrow back staircase originally intended for use by servants or stuck our heads in various closets and crawl spaces, it was much easier to imagine it as a setting for some "dark and stormy night" thriller than the home of a learned society.

Professor R.H. Chittenden, the first president of the ASBMB, at the Beaumont Memorial at Lebanon, Conn. (Coleman's Photo Service, New Haven.) p. 83, History of the American Physiological Society: The Third Quarter Century 1937-1962, by Wallace O. Fen. 1963. PHOTO COURTESY OF THE AMERICAN PHYSIOLOGICAL SOCIETY

The Acquisition of the Hawley Estate by APS

The Hawley mansion was the centerpiece of a nearly 40-acre estate located on Rockville Pike less than a mile north of the National Institutes of Health campus in Bethesda, Md. It was designed by Irwin S. Porter and erected in 1929. The purchase of the Hawley estate and its conversion to a campus home for societies with biological and biomedical interests were mainly due to the efforts of Milton O. Lee, an individual prominent in the history of both the American Physiological Society and the Federation of American Societies for Experimental Biology (2).

Lee was hired by APS in 1947 as the managing editor of publications and as executive officer of that society. At the same time, APS and the federation moved their offices into space at the National Academy Building on Constitution Avenue at no cost, due largely to the generosity of Detlev Bronk, president of the academy and a member of APS. As a result, Lee also became executive secretary of FASEB.

However, the academy soon decided to collect rent ($12,000/year), and this concerned both organizations. Accordingly, the APS formed a Committee on Society Headquarters and began to look for a permanent home elsewhere. It apparently was the intention of the committee to locate the offices in central Washington (convenient to Union Station and eventually National — now Reagan — Airport), but it was largely stymied by limited options and high prices.

However, after Lee and members of the committee viewed the Hawley estate in Bethesda, a 38-acre property with a fieldstone mansion and outbuildings, the possibilities were clearly evident to most. Ultimately, it was bought outright by the APS at a price of $225,000, with most of the money coming from the APS publication reserves.

A part of the land was then sold to the state (for widening Rockville Pike) and to a developer, who used the land to build residential housing. Subsequently, the APS Board of Publication Trustees sold the remaining 12 acres and buildings to the federation and loaned it money to close the deal. It cost the federation, then composed of only six societies, $100,000, which was raised from its reserve fund and a mortgage from the Riggs National Bank of Washington. K.K. Chen, then president of the federation, also raised more than $24,000 from industry and a few private donors who assisted in the purchase and in the renovations that followed. The APS and federation took occupancy in August 1954. The first federation board meeting was held there in January the next year.

Online exclusive

They say family makes a house a home. But what can be said for a house converted into a workplace? In a series of interviews with longtime ASBMB employees it was revealed that, in fact, quite a bit can be said! Visit our website, www.asbmb.org/asbmbtoday, to read online-only Q&As with ASBMB veterans Jeanne Gladfelter, Joan Cuthbert, Ed Marklin, Ned Maher and Barbara Gordon and former staffers Muriel "Mickey" Korn and Chuck Hancock. Have a thing or two to say about the ASBMB's old stomping grounds? Join the discussion by leaving a comment online or by sending a missive to asbmbtoday@asbmb.org for publication on our new Open Channels page.


Gladfelter


Cuthbert


Marklin


Maher


Gordon


Korn


Hancock

The eponymous William Beaumont

The name of the building was changed soon after to Beaumont House for physician and pioneering physiologist and biochemist William Beaumont (3). Beaumont was born in Connecticut in 1785 and received medical training as an apprentice in Vermont. It was while serving in the army at Fort Mackinac that he was serendipitously called on to treat a trapper, Alexis St. Martin, who had suffered a shotgun wound in the stomach.

To the surprise of Beaumont, St. Martin survived his injuries but with a fistula in his stomach that never completely healed. Beaumont seized on this opportunity to conduct a series of experiments over several years on digestion and the nature of gastric juices, which established that this process was basically chemical, not mechanical. Beaumont died in 1853 and is buried in St. Louis; St. Martin lived until 1880.

Hanging in the conference room of Beaumont House in what was once the living room is an oil sketch by Dean Cornwell of Beaumont treating St. Martin. The original, larger painting is on permanent display at a museum devoted to Beaumont on Mackinac Island. Cornwell's rendition has looked down on many a meeting as the plans and aspirations of the society were discussed and re-discussed in this room for 50-odd years.

Enter the ASBC

During the fall of 1953, as the APS committee was considering possible locations for the moving of its headquarters, Phil Handler and D. Wright Wilson, secretary and president of the American Society of Biological Chemists at that time, exchanged several letters about the possibilities for the ASBC in these matters. In a letter dated Nov. 2, 1953, Wilson noted, "I believe last year [1952] the Federation was talking about buying property." He went on to say, "I think probably the Biochemists will be up against a proposition in the near future because I doubt if Universities will agree to donate space for the Journal's Publication Department." He raised the possibility that the ASBC might wish to consider being financially involved in the Hawley deal.

Handler replied that he had just discussed the Hawley estate purchase with Milton Lee, who wanted to know his opinion. Handler noted that he had expressed personal interest but thought that as long as Rudolf Anderson was the managing editor of the JBC, "we … should not want to make a change." However, he also said that after Anderson, a "permanent editorial office might be a valuable thing to have."

Not stated in these remarks was the totally autocratic control that Anderson exercised over the journal and its finances and his unwillingness to consider any change in the way they were managed. Thus, it was the location of the journal activities at Yale University and Anderson's position as managing editor that effectively kept the ASBC from being more directly involved in the purchase of the Hawley estate. However, these events undoubtedly contributed to bringing the Anderson editorship to an end a couple of years later.

In 1955, the ASBC Council, noting the purchase and occupancy of Beaumont House by APS and the federation was complete, resolved to explore the transfer of its pertinent documents and materials to a fireproof vault to be housed in the new federation headquarters (1). The next year, the ASBC Council, now wrestling more directly with the complicated problems engendered by the finances of the journal on the one

hand and those of the society on the other and confronted with the realization that "the burden of this office [Secretary] has grown to such an extent that the Society no longer has the right to impose upon one of its members to the extent now demanded," resolved that when a new managing editor was appointed, the headquarters of the society should be located at Beaumont House, including the publication activities, and that "the possibility should be explored of a combined Managing Editor and Executive Secretary" (1).

Indeed, Anderson retired in 1958, and John Edsall of Harvard University became editor of the journal. Edsall made it quite clear that he didn't care for the business end of running the JBC, and Bob Harte was hired shortly thereafter as the first executive officer and managing editor of the journal in part to relieve Edsall of those chores. With those changes, the society set up its permanent office at Beaumont House. When it first moved in, it shared the space with the federation as well as other societies, but this changed quickly when it became clear that more space would be needed to meet the growing demands on the federation facilities.

Thus, the Milton O. Lee building was erected and opened in 1962. Eventually, the ASBC became the sole occupant of the original buildings, as all other FASEB and non-FASEB societies relocated to the more recently constructed buildings on the FASEB grounds, a trend that continued into the next century.

The Beaumont House is now more than 80 years old, and it is beginning to show its age. Although solidly built, chipping paint, water stains and other signs that some serious maintenance and even some restoration is sorely needed are all too evident. Indeed, there were carpenters and painters banging and scraping away as we took our stroll through the halls of Beaumont House one last time. At the risk of being overly palaeolatric, it has served the ASBC (and ASBMB) well, and one can only hope the next tenants will grow and prosper during their residency as the society did.

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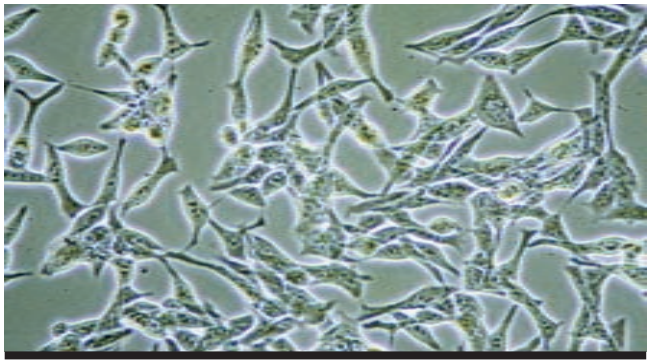

Organelle dynamics

BY BEN GLICK AND DAVID CHAN

It has become increasingly clear that eukaryotic cells have highly dynamic organelles. The four exciting sessions in the 2012 annual meeting's organelle dynamics theme will highlight state-of-the-art approaches aimed at understanding how the dynamic behavior of organelles is linked to their functions. These sessions will focus on mitochondrial dynamics, organelle quality control, the organization of the secretory pathway and endomembrane system dynamics.

Mitochondrial dynamics

The first session will feature the mitochondrion as an organelle whose dynamic properties are central for its function. Jodi Nunnari (University of California, Davis) will discuss how the fusion and fission of mitochondria are regulated. Her group has developed in vitro assays that allow for the identification of regulatory factors.

David Chan (California Institute of Technology) is examining how the dynamic behavior of mitochondria regulates their function. Dysfunction of mitochondrial dynamics is associated with neurodegenerative disease. His group has developed mouse models to investigate the link between mitochondrial dynamics and cell physiology.

Hiromi Sesaki (Johns Hopkins University School of Medicine) will discuss the molecular mechanisms and physiological functions of mitochondrial fusion and fission.

Organelle quality control

The second session will focus on how cells ensure organellar integrity. Tamotsu Yoshimori (Osaka University) will discuss the longstanding debate concerning the origin of autophagosomes, which are unique, ad-hoc organelles that form transiently. Recent results indicate the endoplasmic reticulum and mitochondria are involved in autophagosome biogenesis. Yoshimori also will describe how autophagosomes form to combat intracellular bacteria.

Thomas Langer (University of Cologne) is exploring how mitochondrial proteases control mitochondrial dynamics. The processing and stability of the dynamin-like GTPase OPA1 is emerging as a central mechanism to monitor mitochondrial integrity. Using yeast and mice, Langer's group examines the relevance of stress-induced degradation of OPA1 for mitochondrial quality control and neuronal survival.

Gia Voeltz (University of Colorado–Boulder) will describe mechanisms regulating the three-dimensional structure of the endoplasmic reticulum. She'll focus on how three factors — membrane shaping proteins, cytoskeletal dynamics and interactions with other organelles — work together to distribute the endoplasmic reticulum in the cytoplasm and generate the complexity of ER functional domains.

Organization of the secretory pathway

The third session will focus on how compartments of the secretory pathway are generated and maintained. Ben Glick (University of Chicago) will describe how the ER export domains known as transitional ER sites are established within the rough ER. Transitional ER sites are defined by a dynamic balance between growth and export-mediated shrinkage. His group is studying how a protein called Sec16 controls tER dynamics by regulating ER export.

Nava Segev (University of Illinois at Chicago) studies molecular switches and cascades regulating protein traffic in yeast. She focuses on the roles and interactions of small GTPases of the conserved Ypt/Rab family, which regulates multiple steps of transport in the secretory and endocytic pathways. Her group is investigating how various Ypt/Rab GTPases cooperate to specify compartment identity and turnover.

Adam Linstedt (Carnegie Mellon University) studies the mammalian secretory pathway with an emphasis on the Golgi apparatus. His work includes structure-function studies of tethering proteins, which have multiple roles in the capture of transport vesicles and the establishment of Golgi structure.

Endomembrane system dynamics

The fourth session will focus on how compartments of the secretory and endocytic pathways communicate and change. Christian Ungermann (University of Osnabrück in Germany) studies membrane dynamics of endosomes and lysosomes (or vacuoles in yeast). He'll cover how Rab GTPases work with large tethering complexes to

regulate membrane fusion and endosome maturation.

Jon Audhya (University of Wisconsin, Madison) will describe the development of C. elegans as a model system to study how membrane trafficking and organelle dynamics are modulated during development, cell proliferation and cell differentiation. His lab studies the ESCRT complex, which promotes membrane fission reactions at late endosomes and other cellular locations.

Catherine Rabouille (Hubrecht Institute) will describe how her group has developed Drosophila as a powerful model system for studying the cell biology of the secretory pathway. Her work includes studies of ER export and Golgi organization as well as unconventional secretion mechanisms that bypass the traditional secretory pathway.

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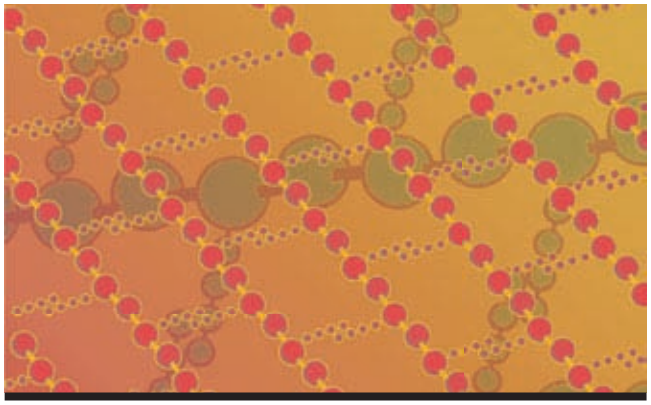

Sugar fix

The diverse biological roles of glycoconjugates

BY KAREN COLLEY AND ANANT K. MENON

Glycoconjugates play critical roles in recognition, adhesion, protein stability and function. Alterations in glycosylation frequently lead to disease. The four sessions in the glycobiology theme focus on the role of glycoconjugates in pathogenesis, signaling, development, metabolism and disease. They also address novel metabolic routes of glycoconjugate assembly.

Pathogenesis

Glycoconjugates often provide the key interface between a microbial pathogen and a host cell and are, therefore, excellent targets for the development of therapeutics. The first session, "Glycoconjugates in Pathogen Invasion and Virulence," features three talks that focus on the surface glycoconjugates of bacteria and a protozoan parasite.

Malcolm McConville (University of Melbourne) will highlight recent advances in our understanding of cell-wall assembly in mycobacteria. The cell walls of these important pathogens are composed of several classes of glycolipids, and a number of novel proteins have been shown to regulate their assembly and transport across the cell membrane.

Lora Hooper (University of Texas Southwestern Medical Center at Dallas) will present her work on the innate immune mechanisms that promote symbiotic relationships with the vast communities of bacteria that inhabit the intestine. She will focus on the role of a secreted carbohydrate-binding protein in maintaining the mutually beneficial nature of these host-microbial interactions.

Igor Almeida (University of Texas at El Paso) has identified glycoconjugates of the Chagas-disease-causing parasite Trypanosoma cruzi that are virulence factors. He will describe recent efforts to use these glycoconjugates as targets for vaccine development.

Signaling and development

The second session, "Role of Glycoconjugates in Signaling and Development," further highlights the diverse roles of glycoconjugates. David Levin (Boston University Goldman School of Dental Medicine) will present on cell-wall-integrity signaling mechanisms that enable yeast cells to respond to cell-wall stress.

Hannes Buelow (Albert Einstein College of Medicine) will describe his studies of the role of heparan sulfate proteoglycans in axon guidance and nervous-system development in the model organism Caenorhabditis elegans.

Thomas Biederer (Yale University) will talk about his work on the SynCAM family of adhesion molecules and the role that glycans play in regulating adhesion mediated by these proteins and subsequent synapse development.

Glycoconjugate assembly

Although the assembly of glycoconjugates from activated monosaccharides is generally understood, there remain numerous gaps in our knowledge. In the third session, "Novel Metabolic Routes of Glycoconjugate Assembly,"

Karen Colley (University of Illinois College of Medicine) will discuss the biosynthesis of polysialic acid, a unique anti-adhesive glycoconjugate found on only a few proteins that play roles in development and function of the nervous and immune systems. She'll offer new data that show how these proteins are selected for polysialylation.

Debra Mohnen (University of Georgia) will discuss the assembly of pectin, a major plant cell-wall polysaccharide, which functions in plant growth, development, and response to pathogens and symbionts and has diverse positive effects on human health. She will describe new results describing novel mechanisms that regulate pectin synthesis and cell-wall assembly.

A key feature of the assembly of many glycoconjugates is the transbilayer movement of lipid biosynthetic intermediates. Anant Menon (Weill Cornell Medical College) will discuss recent efforts to identify the enigmatic flippases required for moving these complex glycolipid structures across the membrane bilayer.

Glycoconjugates in metabolism and disease

In the final session, "Role of Glycoconjugates in Metabolism and Disease," Jeff Esko (University of California, San Diego) will discuss his work on endothelial cell receptors and their interaction with heparan sulfate with respect to innate immunity.

John Hanover (National Institutes of Health) will describe his group's studies on the role of nutrient-driven O-GlcNAc in regulating gene expression by modulating higher-order chromatin structure and the multifaceted histone code. His results suggest that O-GlcNAc directly regulates RNA polymerase II and may contribute to transgenerational epigenetic reprogramming.

Lance Wells (University of Georgia) will speak on the role of O-mannosylation in congenital muscular dystrophy, cancer metastasis and arenavirus entry into cells. He will present data that highlight the novel protein substrates for O-mannosylation, as well as the enzymes and the novel glycans they synthesize that are disrupted in various pathophysiologies.

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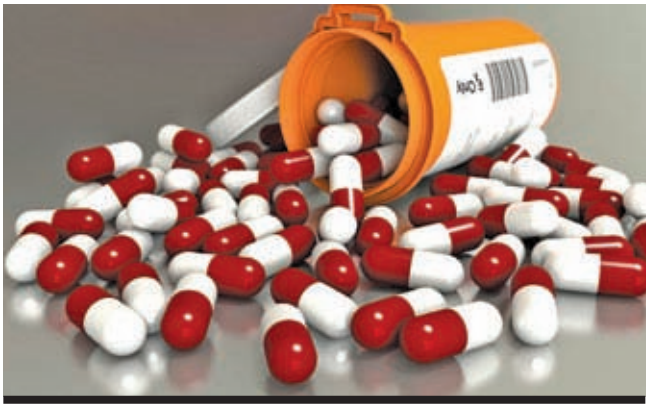

'Developing' drugs

If only it were that easy

BY RANDALL KING AND PETER K. JACKSON

In the context of the early embryo or a growing child, the term "development" implies a set of stereotyped transitions from one well-defined stage to another until adulthood is achieved. In this context, the term "drug development" is an oxymoron, as most drug-discovery projects never reach maturity. This is especially true for complex diseases such as cancer, as the diversity of disease mechanisms can make development of effective therapies challenging. Despite these hurdles, exciting progress is being made. In this symposium, we explore some recent advances in the development of cancer therapies. The sessions will discuss the full developmental spectrum of drug-discovery projects — from new technologies for target discovery to compounds making their ways into the clinic.

Killing cancer cells

The first session, "Drug Development and Apoptosis: Linking Tumor Regression to Cell Death," will feature Junying Yuan (Harvard Medical School), who will describe recent work in developing small-molecule inhibitors targeting autophagy, an important catabolic mechanism that mediates the turnover of misfolded proteins and damaged intracellular organelles. The inhibitors have revealed an important tumor-suppressor mechanism that is regulated by autophagy and the possibility of inhibiting autophagy to treat cancer.

The BCL-2 family of apoptotic proteins regulates the critical balance between cellular life and death. Loren Walensky (Dana Farber Cancer Institute) will discuss his laboratory's progress in dissecting the BCL-2 family interaction network using a novel pharmacological

strategy, stabilized alpha-Helices of BCL-2 domains.

Vishva Dixit (Genentech) will discuss the state of drug development in apoptosis with a focus on IAP and BCL-2 inhibitors. He also will discuss recent progress on the molecular basis of necrosis. While the players that mediate apoptosis are well defined, little is known about what mediates necrosis, except for the recent dramatic discovery of the involvement of the RIP3 kinase.

Targeting each person's cancer

The molecular heterogeneity of cancer poses great challenges for drug development, yet it also affords new opportunities for developing highly targeted therapies. In the second session, "Targeted Cancer Drug Development: Defining Molecular Profiles of Sensitivity," Alan Ashworth (Institute of Cancer Research) will discuss harnessing genetic dependencies in cancer therapy. Many tumours harbour defects in their ability to maintain genomic integrity. His lab used a synthetic lethal approach to target the defect in DNA repair by homologous recombination in tumours with a BRCA1 or BRCA2 mutation. This strategy using PARP inhibitors is showing considerable promise in the clinic. Here, he will describe the approach as well as recent work defining determinants of sensitivity and resistance to PARP inhibitors.

Neil Rosen (Memorial Sloan-Kettering Cancer Center) will discuss molecularly targeted therapies for cancer. Among these targets, the Raf kinase is activated by mutation in several tumors, and inhibitors of B-Raf show great promise in treatment of tumors that harbor activating mutations, such as melanoma. However, in tumors with wild-type Raf genes, the effects of Raf inhibitors are complex, as they perturb feedback mechanisms in the MAP kinase pathway and can induce proliferative responses. Explaining these results requires careful molecular analysis of the dynamic behavior of the pathway in tumor models, which will be the topic of the presentation.

It has been known for many years that metabolism is perturbed in cancer cells. Recently, mutations in components of metabolic pathways have been identified that provide exciting new opportunities for drug development. Scott Biller (Agios Pharmaceuticals) will discuss how metabolism informs cancer drug discovery.

Finding new molecules and targets

Many exciting new technologies are being developed to identify new drug targets for cancer and other diseases. In the third session, "New Methodologies for Target Discovery and Target Validation," William Hahn (Dana-Farber Cancer Institute) will discuss how functional genomic approaches now enable the interrogation of gene function at scale and how the integration of functional approaches with other high-throughput technologies permits the identification and validation of cancer targets.

Cancers can show a high degree of cellular heterogeneity within tumors. Peter Jackson (Genentech) will discuss proteomic network building to discover new disease genes and drug targets.

Finally, the ubiquitin-proteasome system represents an exciting new opportunity for drug development, as inhibitors of the proteasome are in the clinic. Randall King (Harvard Medical School) will discuss the use of phenotypic screening to discover new inhibitors of ubiquitin ligases and their potential role as novel antimitotic agents.

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Systems biology

Biochemical networks in space and time

BY STEVEN ALTSCHULER AND ALEXANDER HOFFMANN

With DNA sequencing costs falling faster than Moore's law, the challenge is less to discover what is in the genome but how the biological molecules interact to produce biological function. Molecular interactions are often multivalent to produce complex networks. Biochemical networks operate in time to determine cellular responses to environmental changes and in space within and across boundaries and organelles, and they are

subject to the physical laws that apply to all molecules, including the fundamental stochasticity of molecular interactions and chemical reactions. Given data quantities and the potential for complexity that exceed even well-honed, intuitive reasoning, a hallmark of the systems biology approach is to combine experiment and modeling to formulate and test hypotheses. The sessions below were designed to highlight approaches that derive and reveal behaviors of complex networks on molecular, time and distance scales.

Network assembly

The first session will address novel approaches that allow for assembly of large network models containing many components. Trey Ideker (University of California, San Diego) will describe strategies to combine high-throughput genetic and physical interaction data sets as well as recent work revealing how some aspects of networks change in response to DNA damage and how others do not.

Nevan Krogan (University of California, San Francisco) will describe approaches and insights gained from characterizing the physical interaction network within mammalian cells and how intruding pathogen proteins harness and manipulate it.

Martha Bulyk (Harvard University) will report on innovative high-throughput approaches to understanding the gene regulatory network in quantitative terms, such as interaction affinities between DNA binding proteins and their diverse cognate sequences.

Networks and time

The second session will highlight recent studies of kinetically controlled network behavior. Peter Sorger (Massachusetts Institute of Technology/Harvard University) will discuss insights gained from quantitatively measuring and modeling the activities of signal transducers that respond to death-inducing stimuli.

Alexander Hoffmann (University of California, San Diego) will report on recent work in applying parallel and experimental and kinetic modeling studies to the pathogen-responsive signal regulatory network and gene regulatory network to develop a "virtual cell" capable of predicting responses to pathogen exposure.

Karla Neugebauer (Max Planck Institute of Molecular Cell Biology and Genetics in Dresden) will address the role of kinetics in cotranscriptional splicing as a means to regulate the generation of alternate mature mRNAs. Thus, a key step in regulating gene expression may be understood only by integrating the biochemical processes of transcription and splicing that were previously studied separately.

Networks and space

The third session will focus on how signal-transduction networks give rise to behaviors in both space and time. Lani Wu (University of Texas Southwestern Medical Center at Dallas) will address the question of how human neutrophils rapidly respond to environmental changes yet ignore irrelevant fluctuations.

Orion Weiner (University of California, San Francisco) will discuss signal-transduction networks in chemotaxing neutrophils and how altering cell geometries can help to identify or rule out mechanisms underlying spatial organization of the signaling components.

Victor Sourjik (Ruprecht-Karls-Universitat Heidelberg) will discuss the assembly and dynamics of signal processing complexes used by bacteria to extract and respond to weak signals from noisy environments.

Networks and noise

The final session will focus on core design principles by which biological networks can reliably give rise to cellular behaviors despite — or because of — the presence of biochemical noise. Steve Altschuler (University of Texas Southwestern Medical Center at Dallas) will discuss how simple positive feedback circuits that lie at the heart of many pattern-forming networks can make use of biochemical noise to create cell polarity and how noise can be used as a biomarker to discriminate different mechanisms of redundancy in protein interaction networks.

Jeff Hasty (University of California, San Diego) will describe how synthetically designed biological circuits, lab-on-a-chip microfluidic devices and mathematical modeling can be brought together to understand the complexities of gene-regulatory networks in single cells.

Chris Voigt (University of California, San Francisco) will present recent work on developing a platform for designing biological networks that enable cells to be programmed to perform reliably complex, coordinated tasks.

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Chemical biology and biocatalysis

BY PHILIP A. COLE AND JASON K. SELLO

While it long has been appreciated that chemistry and biology are linked inextricably, scientists working today at the intersection between these disciplines are providing molecular resolution descriptions of complex biological phenomena and generating new tools that will transform the way we live. The symposium "Chemical Biology and Biocatalysis" at the 2012 ASBMB annual meeting highlights the work of prominent scientists whose work defines how chemical intuition and chemical tools can inform studies and applications of biological systems.

In a session titled "Metabolomics," geneticist Michael Snyder will describe how a comprehensive, mass-spectrometry-based approach has revealed new insights into metabolite-protein interactions. This work is an extension of his groundbreaking work in high-throughput transcriptomics. Chemist Alan Saghatelian will discuss progress in the cataloging of metabolites and pathways. His group recently has identified monoalkylglycerol ethers as natural adipocyte differentiation factors and has explored the identification of endogenous ligands of nuclear hormone receptors using a systems approach. Plant biochemist Anne Osbourn will talk about her work on biosynthetic pathways of natural products in oats and rice. Her studies have uncovered how the complex and biomedically important small molecules often isolated from plants can be stitched together.

In "Chemistry and the Service of Medicine" pharmacologist Phil Cole will describe acyltransferases as possible targets in cancer and metabolism. Using rational design principles, his group has obtained preclinical data that show selective synthetic agents can be identified for this difficult-to-inhibit enzyme family. Chemist Gabriella Chiosis will highlight the potential of protein chaperones, including heat-shock protein 90, as targets with significant clinical promise for the treatment of a variety of cancers. Her small-molecule inhibitors of chaperones are proving valuable tools for the exploration of this anticancer landscape. Chemist David Spiegel will describe his unorthodox approach to generating immune response to cancer or infectious targets. By creating bivalent high-affinity ligands that interact with specific receptors found in neoplasms or pathogens on the one hand and immune complexes on the other, he is recruiting the immune response to specific cell types.

In "Metabolic Engineering: From Antibiotics to Biofuels," biochemist Michael Thomas will present his studies of enzymes called polyketide synthases, which catalyze the biosynthesis of pharmacologically important antibiotics. His discoveries of noncanonical mechanisms of polyketide synthase catalysis inform the engineering of non-natural enzymes for drug synthesis. In a complementary talk, Christina Smolke will discuss her groundbreaking work in the engineering of yeast to produce new variants of compounds normally produced by plants. These compounds, known as alkaloids, have potential to treat malaria and other maladies. Finally, Jason Sello will discuss his work on engineering soil-dwelling Streptomyces bacteria to convert plant biomass into high-value chemicals and fuels.

In the "Frontiers in Enzymology" session, biochemist Henning Lin, a leader in the field of post-translational modifications, will describe the molecular mechanisms by which dipthamide, the target of the diphtheria toxin, is biosynthesized. Structural biologist Chuan He will provide a molecular-resolution exposé of enzymes that use peculiar catalytic logic to repair DNA damage. The studies of Lin and He are characterized by ingenious integration of methods from chemistry and biology. Enzymologist David Cane has provided new insights into mechanistic enzymology via his mining of newly available microbial genome sequences. His analysis of novel and peculiar terpene synthases has provided new insights into startlingly sophisticated bond formations and skeletal rearrangements in the biosynthesis of medicinally and ecologically important metabolites.


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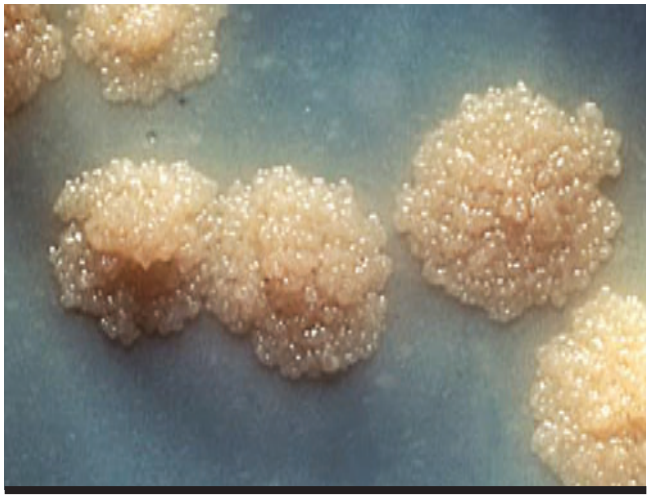

Targeting tuberculosis

What we know about the molecular details of the host-pathogen relationship and how the bacterium is affected by our attempts to stop its spread

BY SQUIRE J. BOOKER AND CLIFTON E. BARRY III

Tuberculosis kills between 2 million and 3 million people each year and continues to be a major global health concern. Mycobacterium tuberculosis, the etiologic agent responsible, is an obligate human pathogen that has infected mankind since the dawn of time. The emergence of highly drug-resistant forms of the disease threatens to completely undermine disease-control efforts and even may be shifting the fundamental pathobiology of the host-pathogen relationship.

The community of scientists engaged in studying this deadly disease has made dramatic advances in understanding the biology and biochemistry of this deadly pathogen, but many important details are only now starting to be appreciated. These three symposia in the tuberculosis theme will bring together diverse speakers struggling to understand the molecular details of the host-pathogen relationship and how the bacterium may be adapting to human attempts to bring the disease under control. The subjects were chosen so that the three symposia build upon each other by providing state-of-the-art lectures covering our understanding of the in vivo biochemistry, how it drives the host-pathogen relationship and how this relationship may be changing as new strains of the bacterium adjust.

In vivo biochemistry of the pathogen

The first session, chaired by Squire J. Booker (The Pennsylvania State University), will provide an overview of the adaptations that M. tuberculosis makes to survive in the challenging environment of the human lung. The bacterium faces many obstacles to replication in the face of the human immune response, obstacles that have driven unusual and distinct biochemical adaptations.

A lecture by Valerie Mizrahi (University of Cape Town), titled "Mechanisms of DNA Repair and Mutagenesis in M. Tuberculosis," will describe her laboratory's contributions to the understanding of the complex systems of DNA repair that have evolved in response to the need to maintain the integrity of this molecule in the face of both the organism's exceedingly long generation time and the continuous oxidative and nitrosative stress challenges mounted by the host immune system.

William R. Jacobs (Albert Einstein College of Medicine) will describe his lab's efforts to understand the biochemical details of cell-envelope construction — essential for understanding the mechanism of antitubercular drugs and in the construction of new vaccines. Jacobs' group made a particularly important contribution to understanding transport of one of the most important of the disaccharides used in cell wall biogenesis, trehalose.

Natasha Nesbitt (State University of New York, Stony Brook) will present a lecture titled "Cholesterol Metabolism in Mycobacterium Tuberculosis: Chewing through the Fat." She will describe her work with Nicole Sampson on cholesterol utilization in M. tuberculosis, which is important because, in the intracellular environment of the host, M. tuberculosis shifts from a carbohydrate-based metabolism to a lipid-based metabolism. Moreover, it can utilize cholesterol as its sole carbon source in culture.

Biochemical mediators of the host-pathogen interaction

The second session, chaired by Clifton E. Barry III (National Institutes of Health), will feature a lecture from Carolyn Bertozzi (University of California at Berkeley) titled "Chemical Approaches for Probing Mycobacterial Metabolites." Bertozzi will describe her lab's chemistry-driven approach to understanding microbial metabolism and adaptation of that metabolism to the host environment.

Sonia Flores (University of Colorado Denver) will give

a talk titled "Vitamin D-Dependent Innate Antibacterial Responses on Tuberculous and Non-tuberculous Mycobacteria."

The session will end with a lecture from Mary Jackson (Colorado State University-Fort Collins) titled "Biogenesis of Mycobacterial Cell Envelope Glycoconjugates," in which she will elaborate on her lab's longstanding interest in the biogenesis of one class of the most important mediators of the host-pathogen relationship.

Relationship of host and pathogen

The final session will be chaired by Jackson and will feature a lecture from Barry. In "Molecular Mechanisms of the Evolution of Drug Resistance in TB," Barry will describe his lab's attempts to understand the molecular evolution of resistance and subsequent fitness adaptations in highly drug-resistant clinical isolates.

Miriam Braunstein (University of North Carolina at Chapel Hill School of Medicine) will deliver a lecture titled "Protein Export via the Accessory Sec System of Mycobacterium tuberculosis." She will describe her lab's elaboration of the mechanisms of protein secretion developed by M. tuberculosis to enable survival in the macrophage phagosome.

Finally, Sarah Fortune (Harvard School of Public Health) will deliver a lecture titled "On the Clock: Diversity through Growth and Division in Mycobacteria," describing her lab's attempts to probe adaptation of extant strains of M. tuberculosis using next-generation sequencing approaches to identify and understand polymorphisms that are geographically or pathogenically unique.

The three symposia also will include presentations chosen from submitted abstracts and will be complemented by related poster sessions. These symposia will present a unique opportunity for investigators interested in the biochemistry and detailed molecular mechanisms underlying the pathogenesis of this important disease to be exposed to an exciting selection of some of the most important recent developments in this area.

Squire J. Booker (sjb14@psu.edu) is an associate professor of chemistry and associate professor of biochemistry and molecular biology at The Pennsylvania State University. Clifton E. Barry III (clifton_barry@nih.gov) is a senior investigator and chief of the tuberculosis research section at the National Institute of Allergy and Infectious Diseases.

Education and professional development

Maximizing competitiveness during challenging times

BY SUZANNE E. BARBOUR AND PETER J. KENNELLY

Although the economy shows some signs of recovery, today's college graduates continue to face a challenging job market. Similarly, institutions of higher learning face the challenge of maintaining economic viability while continuing to deliver comprehensive instruction using state-of-the-art technologies.

At the faculty level, diminishing resources and increasing time commitments have redefined the three major missions of academia: scholarship, teaching and service. Finally, the emergence of strong economies and research infrastructure in other countries challenges U.S. scientists to remain competitive and develop collaborations on a global scale. Recognizing these challenges, the 2012 education and professional development theme is focused on increasing competitiveness at the global, institutional and individual levels.

Outreach and research

The program is organized into six sessions. On Saturday, April 21, the activities will focus on education and outreach in coordination with the 16th annual undergraduate poster session, sponsored by the Undergraduate Affiliate Network. After the poster session, students will be invited to a speed-dating-like session with representatives from various career paths called "Finding Your Perfect Career Match."

Undergraduate research experiences provide a unique means for developing the technical and critical-thinking skills that allow graduates to be competitive in the job market. As such, Sunday morning's session, "Maximizing Institutional Effectiveness," will focus on approaches to bolstering undergraduate research/research training. Peter J. Kennelly (Virginia Polytechnic Institute and State University) will approach the issue from the perspective of a research-intensive institution. Next, Joseph Provost (Minnesota State University Moorhead) will discuss this issue from the perspective of a primarily undergraduate institution. Finally, Cecile Andraos-Selim (Hampton University) will discuss the unique challenges to undergraduate research/research training at a minority-serving institution.

Talks for teachers

On Sunday afternoon, the emphasis will shift to the classroom with a session titled "Maximizing Teaching Effectiveness." In the first talk, Paul Craig (Rochester Institute of Technology) will discuss cutting-edge instructional technologies in a presentation titled "Effective Use of Electronic Teaching Tools and Resources." Dennis Wykoff (Villanova University) will discuss the unique challenges facing today's junior faculty in his talk, "Effective Teaching and Mentoring While Publishing and (Hopefully) Having a Life." In the last talk, Neena Grover (Colorado College) will describe the Undergraduate Affiliate Network as a means to promote science education and outreach.

On Monday morning, the focus will be on maximizing marketability through development of survival skills for careers in academia and industry. Judith Bond (The Pennsylvania State University College of Medicine) will discuss strategies to develop administrative and organizational skills. Her talk will be followed by Martin Rosenberg (Promega Corp.), who will focus on opportunities in the private sector and the skill sets required to be competitive for securing those opportunities. The last talk will focus on the interface between technology and networking. Lisa Balbes (Balbes Consultants) will give a talk titled "Effective use of Social Networking for Career Development," which will focus on the advantages and potential pitfalls of this emerging means for connecting with potential employers.

A competitive world

The Monday afternoon session broadens the theme to take on a global perspective. In the first talk, Anthony James (University of California-Irvine) will present his work on malaria as a model for developing collaborations on an international scale. Estralita Martin (San Diego State University) will use the second talk to discuss cultural competency, an emerging concept that is of growing importance as our classrooms and laboratories become more diverse. In the last talk, Shirish Shenolikar will discuss his experiences at Duke and the National University of Singapore Medical School and how they can be a model for understanding the unique challenges to science and science education in emerging countries.

We realize that these presentations address only a subset of the challenges facing scientists and science educators in the 21st century. However, we hope that attendees will come away from these sessions with a renewed sense of confidence that they can and will be competitive during these challenging times.

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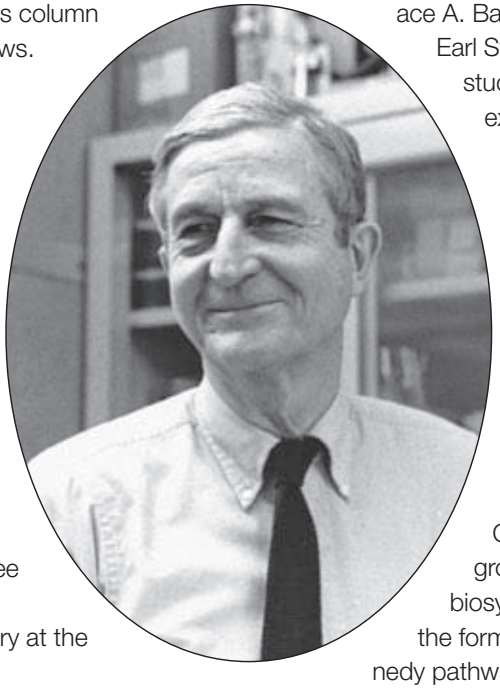
Eugene P. Kennedy (1919 – 2011)

BY DANIEL RABEN



It is unfortunate that sometimes this column must communicate unwanted news. Such is the case now, when I must share the sad news that the lipid community has lost another icon. Eugene Patrick Kennedy passed away Sept. 22. It's unlikely that there's anyone working in the lipid field today who doesn't know of his work. The Kennedy pathway for the synthesis of some of the major phosphoglycerides remains one of the hallmarks of lipid biochemistry.

Kennedy was born in 1919 in Chicago. He enrolled at De Paul University in 1937 to pursue a degree in chemistry and in 1941 began his graduate studies in organic chemistry at the University of Chicago (1).

To pay for school, Kennedy worked during those war years at the meatpacking facility Armour and Co. to obtain pure bovine serum albumin, which at the time was thought to be useful for treating shock in wounded soldiers. The effort was abandoned by 1942, at which time the Red Cross began collecting blood from human volunteers. Kennedy transferred to Armour's new Fort Worth location in 1942 to focus on fractionation of human blood. He worked there until 1945.

The experience sparked an interest in biochemistry, which Kennedy continued to pursue upon returning to the University of Chicago. It was then that Kennedy started working with a new assistant professor in the department of biochemistry, Albert Lehninger, and developed an interest in lipid biochemistry. Despite some reservations (1), Kennedy began to study fatty-acid oxidation for his thesis work in 1947. It was during this work that Kennedy made one of his seminal discoveries that, in addition to oxidative phosphorylation, fatty acid oxidation and the reactions of the Krebs cycle occurred in the mitochondria.

After completing his graduate work, Kennedy went to the University of California, Berkeley, to study with Horace A. Barker. It was there that he, along with Earl Stadtman, who was then a graduate student, studied the ability of soluble extracts of Clostridium kluyveri cells to produce short-chain fatty acids from ethyl alcohol.

In 1950 Kennedy did a brief stint with Fritz Lipmann at Harvard Medical School to work on mitochondrial energetics.

He re-joined the University of Chicago a year later after obtaining a joint appointment in the department of biochemistry and the Ben May Laboratory for Cancer Research and began his groundbreaking work on phospholipid biosynthesis. That work eventually led to the formulation of the now famous Kennedy pathway, which remains true to this day.

It should be no surprise that Kennedy was selected to become a Hamilton Kuhn professor and head of the department of biological chemistry at Harvard Medical School in 1959. He continued his research on phospholipid biosynthesis and outlined a detailed picture of phosphoglyceride and triacylglycerol biosynthesis. But his contributions are not limited to these discoveries. Kennedy went on to make significant discoveries regarding the biogenesis and function of membranes, translocation of phospholipids, periplasmic glucans and cell signaling in bacteria.

Kennedy served on the editorial board and as an associate editor for the Journal of Biological Chemistry. He was also the president of the American Society of Biological Chemists in 1970. He received numerous awards and honors throughout his career, including election to the National Academy of Sciences (1964), the Gairdner Foundation International Award (1976), the University of Chicago Distinguished Service Award (1966), the Boehringer Ingelheim Heinrich Wieland Prize (1986) and the Pasano Award (senior laureate, 1986).

We tell our graduate and post-doctorial students that the job of a scientist is to discover new knowledge and

make significant contributions to his or her field of study. Kennedy has set a very high bar indeed — one that we all should strive to achieve. His accomplishments go well beyond what can included in a brief outline of his work. Kennedy will be missed, but his work always will remain influential.

Daniel Raben (draben@jhmi.edu) is director of the ASBMB Lipid Division and a professor in the department of biological chemistry at the Johns Hopkins University School of Medicine.

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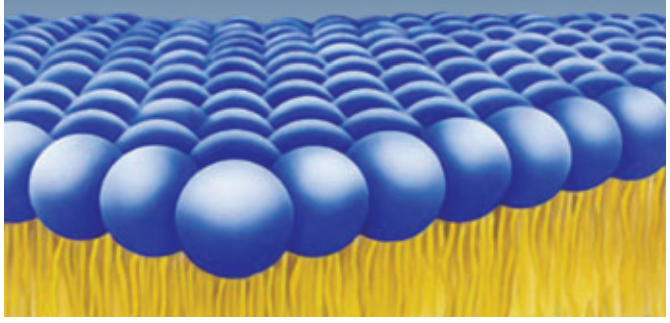

MCP **MOLECULAR AND CELLULAR PROTEOMICS**

Proteomic, metabolic basis for anxiety and depression

BY RAJENDRANI MUKHOPADHYAY

Psychiatric disorders, such as anxiety and depression, have complicated molecular foundations that involve dysfunctional neural circuits.

"The characterization of these altered networks and neural circuits will be critical to get a better understanding of psychiatric disorders and, in turn, make it possible to define targets for the development of more specific medicines," explains Chris Turck of the Max Planck Institute of Psychiatry in Germany. He adds there presently aren't any biomarkers for psychiatric illnesses that could help with accurate diagnosis, tracking treatment efficacy in various types of psychiatric patients, and improving drug development efforts.

To address this issue, Turck and colleagues recently compared the proteins and small molecules expressed in two mouse models to identify potential biomarkers. Their results were published in Molecular and Cellular Proteomics. One mouse strain was selectively bred to be a high-anxiety model while the other was a low-anxiety model.

For the proteomic analysis, Turck and colleagues fed a diet that was laced with a stable isotope to these mice. After the animals' phenotypes had been determined by exposing them to assays to assess anxiety and depression characteristics, the researchers analyzed brain sections and plasma molecules from the mice that were now labeled with the stable isotope by quantitative mass spectrometry.

Turck and colleagues identified a number of proteins and small molecules that belonged to several metabolic, signaling and neural pathways. For example, the researchers found that some proteins and metabolites of the phosphatidylinositol signaling pathway had altered expression levels in the high-anxiety mouse model.

The group has also extended the stable-isotope metabolic labeling method to protein turnover analysis, which will provide more information about the pathways affected in anxiety and depression. Ultimately, the researchers want to use several molecules in clinical diagnostic assays instead of a single biomarker, because an individual molecule may not be specific and sensitive enough to accurately monitor a disease.

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JLR **THE JOURNAL OF LIPID RESEARCH**

Thematic review series highlights lipid droplet research

BY MARY L. CHANG

Lipid droplets are functionally important in the human body. The components contained within lipid droplets in liver cells can be turned into lipoproteins. Lipid droplets of epithelial cells of the mammary gland figure into the nutritional value of breast milk. On an immune system level, it is hypothesized that lipid droplets play a role in macrophage function during phagocytosis. Even hormones and transcription factors may get their start from what is enclosed in these interesting and biologically vital units.

When lipid droplets accumulate in an excessive way, common diseases such as atherosclerosis, diabetes and metabolic syndrome can occur. Lipid droplets are even implicated in the pathogenesis of bacteria and viruses such as hepatitis C, which infects approximately 3 percent of the world's population.

The November issue of the Journal of Lipid Research marks the start of a new thematic review series on this very topic, titled "From Lipid Droplet Storage and Metabolism: from Yeast to Man." The series is being coordinated by Karen Reue of the David Geffen School of Medicine at the University of California, Los Angeles.

Reue, a recognized expert in the field, also penned a special editorial for the issue that serves as a great introduction to the series. In the editorial, Reue explains why lipid droplet research is so hot right now: There has been increased recognition that lipid droplets are implicated in health and disease.

The series is unique in that it will explore lipid droplet biology and metabolism from an evolutionary point of view, examining the topic in yeast, nematodes, plants, fruit flies and mammals.

"GPIHBP1, an endothelial cell transporter for lipoprotein lipase," the first review in the series by JLR Associate Editor Stephen G. Young of UCLA and colleagues, discusses what is known about GPIHBP1, a protein that has been shown to be involved with the transport of lipids and a facilitator of lipoprotein lipase, an enzyme that makes components of lipids available for other uses in the body.

Mary L. Chang (mchang@asbmb.org) is managing editor of the Journal of Lipid Research and coordinating journal manager of Molecular and Cellular Proteomics.

jbc THE JOURNAL OF BIOLOGICAL CHEMISTRY

Formation of radical for DNA generation

BY RAJENDRANI MUKHOPADHYAY

Ribonucleotide reductases are essential in all living organisms, because they supply the raw material for DNA synthesis. The class IA ribonucleotide reductases are iron-dependent enzymes that create deoxyribonucleotides from ribonucleotides. In humans, the enzymes are successful targets of several chemotherapy drugs, such as gemcitabine and clofarabine. The enzymes have two homodimeric subunits, α2 and β2. The β2 subunit contains a di-iron cluster that generates a tyrosyl radical that is essential in making deoxyribonucleotides. The cluster in the resting state is a diferric-tyrosyl radical, $Fe3^{+}$-Y·. The tyrosyl radical has a fleeting existence in humans, hanging around for only 20 minutes. Some chemotherapy drugs target this radical to destroy it and inactivate the enzyme. But as Mingxia Huang at the University of Colorado School of Medicine and JoAnne Stubbe at the Massachusetts Institute of Technology explain, the biosynthesis of the cluster and its maintenance "in an active form inside the cell has been a major unsolved problem." In a recent Journal of Biological Chemistry "Paper of the Week" the duo led a team to explore how this important iron center is formed in the β2 subunit of yeast. The investigators suggest that there are two proteins involved in the process: Grx3/Grx4, a protein complex that may contribute in some way to iron delivery, and Dre2/Tah18, which may provide the reducing equivalents. The investigators explain that understanding how the $Fe3^{+}$-Y· cluster forms and finding out whether there is a pathway to regenerate the radical may provide new cancer therapeutic strategies.

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Tabor investigator chosen at lipids meeting in Italy

BY ANGELA HOPP

HERBERT TABOR YOUNG INVESTIGATOR AWARD

Alessandra Ferrari was named a Journal of Biological Chemistry/Herbert Tabor Young Investigator Award winner at the 52nd International Conference on the Bioscience of Lipids, which was held in late summer in Warsaw, Poland. JBC Associate Editor George Carman attended the conference and presented Ferrari with her prize.

Ferrari, 25, received her master's degree in pharmaceutical biotechnology in the spring from the University of Milan (in Italian, Università degli Studi di Milano), where she works under the supervision of Maurizio Crestani.

She and colleagues study the transcriptional and epigenetic mechanisms involved in the regulation of energy metabolism with a focus on the role of histone deacetylases and nuclear receptors in the metabolic regulation of adipose tissues, liver and skeletal muscles under both normal and disease states.

In her free time, Ferrari enjoys travel, music and photography.

Angela Hopp (ahopp@asbmb.org) is a science writer and handles public relations for ASBMB.

Changing how we view and evaluate student gains in understanding

BY J. ELLIS BELL

A revolution is under way in educating students in the molecular life sciences. For a number of years, there has been a series of reports and white papers talking about how the education of students in the life sciences needs to be revamped for the 21st century. The most recent, released earlier this year, is "Vision and Change in Undergraduate Biology Education: A Call to Action"(1), a report of a national discussion by the American Association for the Advancement of Science with support from the National Science Foundation. The report is centered on several basic premises represented by the first three chapters: undergraduate biology education for all students, cultivating biological literacy, and student-centered undergraduate biology education. It concludes with two important chapters about implementation of the ideas in the report.

The principal focus of the second chapter is the need for education to focus on core concepts of the biological sciences and core competencies and disciplinary practice rather than simply breadth of knowledge. The chapter, in part, emphasizes understanding what students have mastered and suggests that three questions (2-4) should be considered in course or program design:

1. What knowledge and skills are relevant to the subject area? What should students know and be able to do at the end of the unit or course?
2. What do proficiency and mastery in the subject area at this level in the curriculum (e.g., an introductory course or capstone seminar) look like?
3. What evidence would I accept that a student has achieved proficiency or mastery across the relevant content and skills identified in item 1? What evidence would convince my colleagues?

On curricula and accreditation

These questions helped inform the Research Coordination Networks — Undergraduate Biology Education project "Promoting Concept-Driven Teaching Strategies in Biochemistry and Molecular Biology through Concept Assessments," which the American Society for Biochemistry and Molecular Biology received funding from NSF to implement (5). Now in its second year, the project is at the center of many of the society's undergraduate-education initiatives, dovetailing with the work of the Education and Professional Development Committee on both accreditation and revision of its curricula recommendations (6).

Two key features of the project involve developing a consensus concerning:

1. the foundational concepts from biology, chemistry, mathematics and physics that underpin the molecular life sciences as well as unique foundational concepts of the molecular life sciences and the requisite skills and competencies that a student graduating with a degree in biochemistry and molecular biology should have, and
2. developing appropriate assessment tools that can be used both formatively and summatively to determine whether a student has benefitted from his or her education, whether in a given class or from the curriculum as a whole.

On student assessments

One of the goals of the Vision and Change initiative is to move students away from rote memorization of facts and toward a deeper understanding of the concepts and processes of science to better prepare them for the many challenges they face in the future. Many would argue, and I have myself (7,8), that this means changing the way we educate students, but often missed in the discussion is the reality that it also means changing the way we assess student outcomes.

In addition to using validated assessment approaches and instruments, I believe we need to completely rethink when and how frequently we assess student outcomes. If we are interested in students acquiring long-term conceptual understandings

of material and competency with skills, it makes no sense to focus our grade giving on frequent quizzes and tests (although students love those because they know exactly when to study — i.e., the night before — and what to memorize), as these foster exactly the wrong type of learning.

It is far better to use a variety of forms of continual assessment that build to give a picture not only of what a student really understands (summative assessment) but also of where an instructor may be failing to get the message across (formative assessment) over time to not only re-emphasize key points but also try other strategies. Of course, in a curriculum that really works, topics and skills can, in true Aristotelian fashion (9), be introduced, developed in detail and reiterated, all with appropriate assessment. I suspect that one of the hidden premises of Vision and Change is that by focusing on foundational concepts and skills, we should be able to carve out time in a course or curriculum to allow students to master material and not simply memorize.

Quick recap

The first year of the ASBMB's RCN-UBE project involved both regional and national gatherings and focused on initiating network-building and discussion of the foundational concepts and competencies of the molecular life sciences. The first year's activities culminated with a workshop and core working-group meeting held in conjunction with the meeting titled "Student-Centered Education in the Molecular Life Sciences II" sponsored by the society and held at the University of Richmond in July.

After the meeting, the working group met for another day and a half to assess progress and plan the project's second-year activities. The working group consists of the primary investigators and co-PIs of the grant and 12 other members: Joe Provost, Ann Wright, Kristin Fox, Ben Caldwell, Terry Platt, Cynthia Peterson, Peter Kennelly, John Tansey, Teaster Baird, Brenda Kelly, Jason Sello and Takita Sumter. All were chosen to represent different interests and geographical diversity.

Looking ahead

During the coming year, five physical meetings and one virtual meeting are planned together with a symposium and workshop at the 2012 ASBMB annual meeting in San Diego.

Regional RCN-UBE workshops will be held at Moravian College in Pennsylvania, at Northeastern University in Massachusetts, at Hope College in Holland, Mich., and in the San Diego and Knoxville, Tenn., areas over the next six months or so. A virtual meeting will be held in May.

At the ASBMB annual meeting in April, there will be a symposium the morning of April 24 featuring talks on "Defining Foundational Principles and Concepts," "Developing Assessments for Foundational Concepts," and "Helping Students to Access and Assess Knowledge" as well as short talks selected from submitted abstracts. The symposium will be followed in the afternoon by an RCN-UBE working group meeting and workshop (open to anyone) that will focus in more detail on assessment-tool development.

A call to action

So, in the immortal words of Bob Dylan (10), "Come gather 'round, people" — after all, the project is all about network building for a common cause — "for the times they are a-changin'."

Vision and Change is a call to action, and we need everyone interested in student-centered education in the molecular life sciences to join the discussion. If you are planning to be at the ASBMB annual meeting in San Diego, submit an abstract on your ideas of how to assess student understanding and take the opportunity to get involved in the RCN-UBE project.

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

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LETTER TO THE EDITOR

The Toxic Professor Syndrome

Dear Editor,

The article of professors Hannun and Raben (August issue) with the above title brings to mind Jevons' remark that asking researchers about the research funding system is like asking birds about aerodynamics (1). Given the goal that Hannun and Raben aver — namely the enhancement through research of "our understanding of human health and disease" — they might have begun by admitting, at least as a theoretical possibility, that the present system is precisely tuned to that goal, with the existential problems to which they refer as an unavoidable consequence. And they might have demonstrated a knowledge of at least some of the existing literature on the topic, where some of the specific solutions that they hope for are already on the table (1–3). Decades ago, the first priority of the National Institutes of Health should have been the establishment of an Institute for the History of Science with the mandate of investigating how past discoveries were made and how the discovery process might be optimized. Surrounding that very large institute would be the much smaller, less richly staffed institutes dedicated to cancer, infectious diseases and other biomedical subjects. Over the years, the latter institutes would probably have grown and the former would possibly have shrunk. Perhaps there would then be no "current crisis… of epidemic proportions" with pious calls for us only now to begin "serious study and analysis."

Donald R. Forsdyke
Queen's University, Kingston, Canada,
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Response:

We were pleased to see Dr. Forsdyke's response to our article on the "Toxic Professor Syndrome." Our primary goal in writing the article was to raise an awareness of this critical issue. Despite the fact that this issue has prevailed for some time, as Dr. Forsdyke notes, there has been very little formal discussion and even less movement to address the growing crises we all recognize. To bring new attention to this issue, we believed that posing the problem in terms of a biomedical phenomenon would help raise awareness. It appears this goal has been met, and we thank Dr. Forsdyke for helping to continue the discussion. We welcome all input, as not addressing this issue promises to seriously, and perhaps irreparably, damage the basic science research enterprise.

Yusuf Hannun and Daniel Raben

READER COMMENTS ONLINE

President's Message, "Awards in biochemistry," October 2011

Interesting commentary. Of course the one group that is not merely underrepresented, but essentially excluded from awards is industrial scientists.

—BOB COPELAND

I agree... that awards should be made to deserving individuals who are not previous recipient of awards, thus recognition is brought to diverse group of scientists. Additionally, I suggest the number of supporting letters for the nomination may be reduced to five to six letters. —VIJAY KALRA

Retrospective, "Chris Raetz," October 2011

Thanks for this very personal remembrance.

—DENNIS VANCE

Tabor award, "Harvard med school investigator recognized," September 2011

As a recently retired AP biology and biotechnology teacher, I am fascinated more each day of the elegant way in which regulatory proteins play an essential role in our everyday lives. More high school students need to be exposed to the wonderful world of cell communication at its best. I applaud Amy Walker for her well-deserved award, which comes with tremendous dedication and persistence.

—C. FORD MORISHITA-MILWAUKIE

Corrections

The name of the National Postdoctoral Association's annual observance in recognition of postdoctoral scholars was erroneously reported in the September issue due to an editing error. It is called National Postdoctoral Appreciation Week.

Journal of Biological Chemistry/Herbert Tabor Award winner Amy Walker received her award at the Gordon Research Conference on Molecular and Cellular Biology of Lipids. The September issue erroneously reported that she received her award at a separate event.

We sincerely regret the errors.

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