BIOTECH IN THE SUNSHINE STATE

ASBMB today

December 2009

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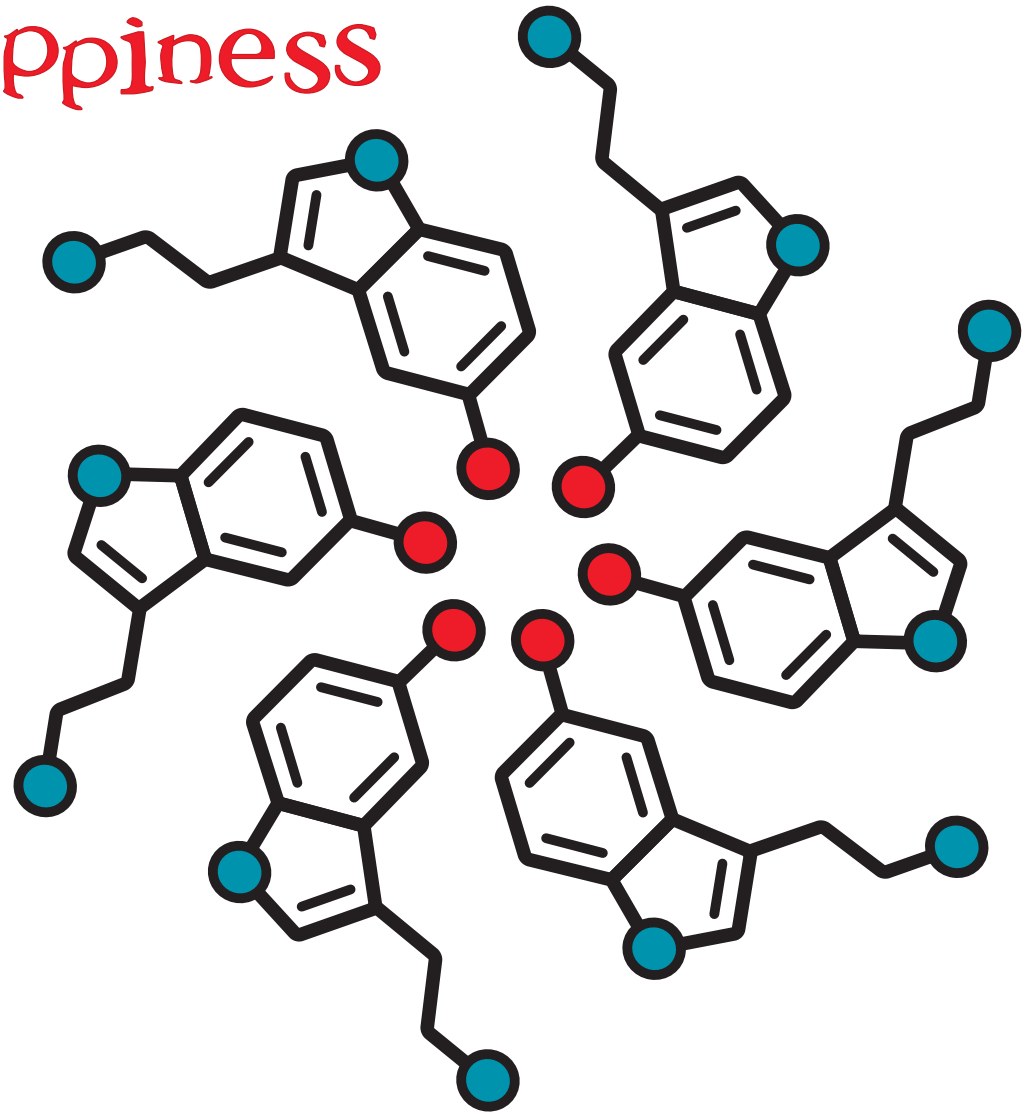

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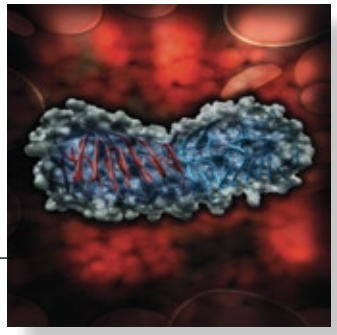

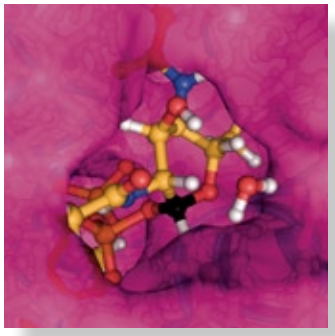

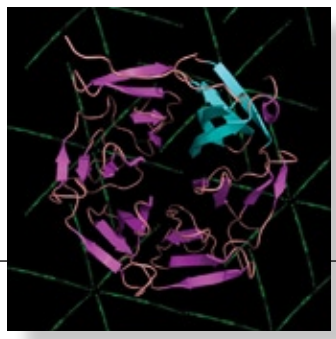

2011

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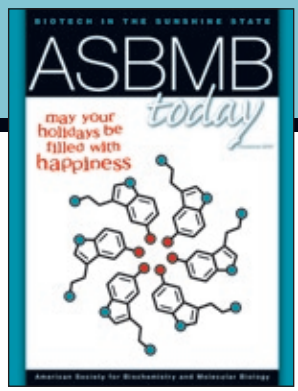

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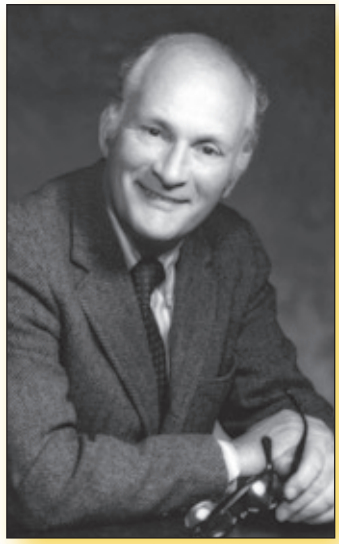

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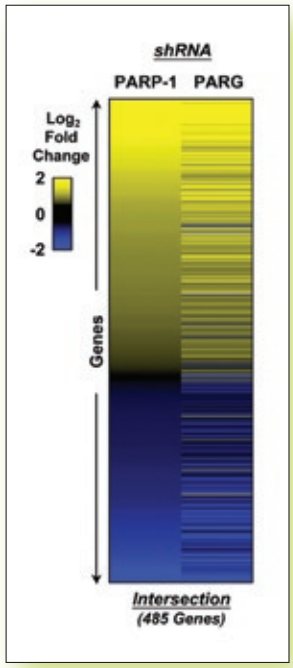

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Check out the latest ASBMB podcast, in which Journal of Biological Chemistry Associate Editor James N. Siedow interviews author Ludger Beerhues about metabolic engineering in plants.

To hear this and other podcasts, go to www.asbmb.org/Interactive.aspx

ASBMB today

A monthly publication of
The American Society for
Biochemistry and Molecular Biology

letters to the editor

Scaring off Young Scientists

Dear Greg,

I would like to thank you for the thoughtful editorial you wrote for the September issue of ASBMB Today. The sentiments you express regarding our generation, our students and our junior faculty are exact.

There is one thing you allude to but do not further pursue: "I've taught college freshmen for almost 30 years…"

At Concordia University, McGill University, the University of Toronto, the University of British Columbia…wherever I turn, there is a disdain for teaching undergraduates. Young colleagues are hired and very quickly learn that if they are to be successful, they had better learn to sit at their computers and write grant applications, fill out the 1 million forms demanded by the university administration and do as little teaching as possible. Teaching counts for zero here. If you are a disaster at it, it will weigh against you, but the idea that you might actually enjoy trying to help undergraduates learn is viewed as a waste of good research time.

In many ways, my junior colleagues have a rough and unsatisfying time. They literally spend most of their time writing grant applications and filling out forms. They talk about money and the new equipment it will buy. They rarely go into the lab after their first year. They do not cry over an experiment that gave the "wrong" results, and they do not cry when the data finally begin to make sense.

Worst of all, their older colleagues almost never ask them what is good in their labs, in their classes and in their lives. It's our generation that has created this situation, and I've yet to figure out how to right the wrong.

Best regards,
Jack Kornblatt
Concordia University

Hi Greg,

I enjoyed your article in the September issue of ASBMB Today. You touched on a number of themes and pet peeves that have bothered me over the years (e.g., whining about what lousy jobs we have when we actually have great jobs; demanding that young people publish in Nature and Cell when most of their senior colleagues don't).

I have feared for some time that we are scaring off a generation of young scientists who just can't see the logic of living a monastic life until they're nearly 40 years old, only to be told they didn't make tenure so they are out of a job. I have firsthand experience with this. My son got his Ph.D. in chemical biology from the University of California, San Francisco, in 2005 and then did a postdoctoral fellowship in neuroscience at the Massachusetts Institute of Technology. During the course of his postdoc, he decided he'd had enough of academics. However, he still loved science and wanted to make a more global contribution. So, he resigned from his postdoc this past May and started a Web site designed to help young people become better scientists.

The site (www.benchfly.com) provides user-generated videos to share key features of experimental techniques that make it easier to do science. It also has multiple career features to help students and postdocs navigate the political and financial waters in which they find themselves. He recently launched the site, and I think he's got a good idea that is packaged with humor and practicality. Hopefully, this will provide him with an opportunity to have an impact on young people that he won't be having through the traditional laboratory/classroom route. In fact, part of the reason he started this site was that he saw so many of his colleagues turning off to careers in science.

When I read your article, I thought about Alan and thought you might

enjoy taking a look at the site. I'll declare my conflict-of-interest as his major (sole) investor!

Anyway, thanks for writing the article. It struck a chord.

Best regards,
Lawrence J. Marnett
Vanderbilt Institute
of Chemical Biology

Training the Next Generation

Greg,

Kudos for your column in the October issue of ASBMB Today. For someone of your stature to write 2.5 pages on science education issues marks a major step forward for the American Society for Biochemistry and Molecular Biology. We've come to expect columns about God, tales of your training background or ideas for the next research challenge and how to attack it, so this was a nice change of pace.

It may be a symptom of my advancing years, but the issue of training the next generation has become very important to me. I attended the ASBMB-sponsored Colorado College conference, "Student-Centered Education in the Molecular Life Sciences," for two reasons: First, I had a renewal application due for our Howard Hughes Medical Institute Science for Life Program for undergraduate research and education, and, second, because I promised myself that I would attend one conference per year that was not entirely focused on my personal research interests. While the plenary lectures were interesting, the best part of the conference was the morning and afternoon workshops that explored new approaches to teaching topics in biochemistry and molecular biology. For me, these were real eye-openers, and they fulfilled my goal of coming back with new ideas.

It's only a small point, but I want to mention that our HHMI program here is designed to get early undergraduates into research laboratories of all kinds as soon as possible. We believe that many freshmen coming out of high school today are prepared to handle complex research questions and to utilize challenging laboratory techniques with a minimal amount of training by graduate students, postdoctoral fellows and faculty mentors. I find over and over that the details of chemistry and biology related to the projects under way in my own laboratory are not difficult for these young students to master. Thus, the age-old bias of faculty in general, and especially senior faculty, to avoid undergraduates in their labs "until after they've had two semesters of organic chemistry" no longer holds true. The advantage of having students start early in the research laboratory is that frequently they are able to accomplish more than enough to merit getting their names on at least one publication from the lab, which helps them in all future steps in their careers.

Best wishes and keep the hits coming,
Ben Dunn
University of Florida

Dear Greg,

I was pleased to read your President's Message this month ("A Teachable Moment"), which described the findings and directives of the Teagle working group and proposed a role for the American Society for Biochemistry and Molecular Biology in the revitalization of biochemistry and molecular biology education. I was especially struck by your observation that "there's a disconnect between what we believe and what we are doing" with regard to the importance of skills in BMB education.

I would like to propose that one of the most powerful changes we could make as a society to help improve student preparation in speaking, writing, teamwork and other skills is to change how each of us views ourselves as teachers in these areas. As a group, scientists who teach at colleges and universities tend to regard the teaching of these essential professional skills as someone else's domain. For example, few of us received formal training in English composition and, therefore, we are most comfortable leaving the teaching of writing to our colleagues in the humanities. Yet, what many of us fail to recognize is that most of us who have reached the position of professor know a lot about what it takes to be a good writer, speaker or team player in the sciences.

Once we realize that having these skills is a small step from being able to teach these skills to our students, our outlook on what is possible in the science classroom becomes radically different. Seeing ourselves as experts not only in our area of scientific interest but also in scientific writing, speaking, etc., empowers us to consider how to blend the teaching of content and the teaching of skills so that learning of both happens simultaneously.

Thanks for your interest and creative perspective on teaching. Improving student learning in BMB is the only guaranteed way to ensure a bright and productive future for our field.

Jenny Loertscher
Seattle University

Advice and Dissent*

BY GREGORY A. PETSKO

Former U.S. President George W. Bush was not a man given to irony. Yet, when asked where he got his information, he replied, "The best way to get the news is from objective sources. And the most objective sources I have are people on my staff."

Sadly, for the United States and for the world, he was not being ironic — he actually believed what he said. The notion that people close to the king typically try to remain close to the king by telling the king what he wants to hear does not seem to have occurred to that remarkably unreflective man.

Woe betide the courtier who troubles his or her monarch with unpleasant realities. David Nutt must now understand this principle better than anyone. Until a few weeks ago he was the chairman of the U.K.'s Advisory Council on the Misuse of Drugs — an independent expert body that provides scientific advice to the British government on drug-related issues, including recommendations on how to classify the dangers of cannabis (marijuana), Ecstasy and other drugs of abuse. On Oct. 30, he was summarily fired from his position by British Home Secretary Alan Johnson for giving the government advice and then criticizing it for not taking it.

That advice concerned the thorny issue of reclassification, of cannabis in particular. Few subjects illustrate the divide between conservatives and liberals more starkly than drugs, and cannabis is the drug that provokes the most heated debate. People may argue about whether all drugs should be legalized, but they generally agree that heroin and cocaine are dangerous substances that can have severe psychotropic effects. Cannabis, however, is viewed so differently by liberals and conservatives that one's opinion on its harmful effects could serve as a shibboleth for distinguishing the two philosophies. Most liberals consider marijuana a relatively harmless recreational drug, along the lines of alcohol but less addictive and not socially damaging, whereas most conservatives regard it as a tool of the devil — a drug that, in addition to producing all manner of terrible side-effects, is guaranteed to lead its user down a slippery slope to even more dangerous drugs.

In Britain, cannabis originally was classified in 1971 in The Misuse of Drugs Act as a Class B drug. The category was created specifically for cannabis and some other drugs (such as amphetamines), as a compromise between those who thought cannabis was as dangerous as heroin (Class A) and those who thought it was a "soft" drug like the benzodiazepines (Class C). After several abortive attempts to reclassify it as Class C, marijuana officially was downgraded in 2004. Nutt's ACMD was the group that made the recommendation for that downgrading. (These classifications can have significant consequences: If cannabis is a Class B drug, people convicted of possessing it can face up to five years in prison.) However, in 2008, then-Home Secretary Jacqui Smith rejected the advice from the ACMD to keep cannabis at Class C and moved it back to Class B, despite the council's extensive review of evidence concerning its long-term effects, including any link to mental illness.

Nutt reacted angrily to this decision and earlier this year publicly accused ministers of "devaluing and distorting" the scientific evidence over illicit drugs by their decision to reclassify cannabis to Class B against the advice of the ACMD. In deciding to speak out, he was probably also stung by the government's decision, in February, to veto another ACMD recommendation, after a review of 4,000 papers on the subject, that the drug Ecstasy be downgraded from Class A. This public criticism prompted his dismissal from his post as head of the committee, a government action that has ignited a firestorm of editorials and comment, including predictable references to the Catholic Church's prosecution of Galileo in 1633. (For a set of links, see www.guardian.co.uk/uk/david-nutt.)

No one questions the government's legal right to sack someone they appoint; the issue is the cause. It can't be a question of competence: David Nutt is certainly well qualified. A professor at both the University of Bristol and Imperial College London, he is a specialist in the psychopharmacology of depression, addiction, insomnia and other psychiatric disorders. The stated reason for his dismissal was that, by going public with his dissent, he

made it impossible for the government to send a clear and consistent message about drugs to the public.

A number of people agreed with that decision. In an opinion piece in The Telegraph on Nov. 7, Alasdair Palmer wrote, "Prof Nutt isn't a martyr to science who lost his job merely for confronting the government with incontestable facts. He was sacked because, as Mr. Johnson insisted, 'he cannot be both a government adviser and a campaigner against government policy.'" He goes on to say that "Prof Nutt's views on policy matters… are not straightforward inferences from the scientific facts… The harm that cannabis can cause in teenage brains is a good reason for, as the government says, 'erring on the side of caution' and classifying cannabis as a Class B drug, with heavy penalties for those convicted of possession. The science does not force you to that conclusion — but then it does not force you to the conclusion that cannabis should be downgraded to Class C."

But many scientists were appalled by the government's actions. Two members of the ACMD resigned in protest, raising the possibility that the committee would no longer have enough expertise to do its job. And, one week after Nutt's dismissal, more than 20 academics, including Martin Rees, president of the Royal Society, sent to the government a set of guidelines that the academics say "would enhance confidence in the scientific advisory system and help government to secure essential advice." The guidelines assert that "disagreement with government policy and the public articulation and discussion of relevant evidence and issues by members of advisory committees cannot be grounds for criticism or dismissal." When scientific advice is rejected, they said, the reasons should be described explicitly and publicly.

Ironically, Nutt's sacking took place just days after the British government had issued a statement about the importance of independence in scientific advice that said, in part, that scientists should not be criticized for publishing scientific papers or making statements as professionals, independent of their role as government advisers. So why was David Nutt sacked, really?

My guess is that it had relatively little to do with the issue of scientific independence and a lot more to do with the peculiar nature of drugs as a political and social lightning rod. Few issues, short of abortion, raise the moral outrage of the Right as reliably as a suggestion that we should go softer on those who use certain drugs. Governments advocate such positions at their peril. Facing a hostile electorate because of the financial crisis, together with a strong challenge from a reinvigorated Conservative Party, the Labour government of Gordon Brown probably felt it could ill afford to be seen as being anything but hard-line on any drug issue at this time. Not firing Nutt, they may have thought, would send a mixed message to the voters about their confidence in their drug policy.

Regardless of the underlying motives, this case should have a powerful resonance in the United States. For eight of the past nine years, the American government deliberately misrepresented and ignored scientific advice whenever that advice contradicted the ideology of those in power. It routinely put poorly qualified scientists and even nonscientists in "scientific" advisory positions, so long as they passed the litmus test of political and religious attitudes. It edited scientific data and conclusions out of reports and persecuted government scientists who questioned its policies. So bad was the situation that, when

he was elected, President Barack Obama felt the need to address this problem publicly in both his inaugural address (saying, "We will restore science to its rightful place,") and in a speech he gave before the National Academy of Sciences on April 27 (saying, "[W]e have watched as scientific integrity has been undermined and scientific research politicized in an effort to advance predetermined ideological agendas").

Ignoring and marginalizing science has a long, sorry history in the United States. One of the main reasons for the failure to develop a firm policy on the climate

> **"...the American government deliberately misrepresented and ignored scientific advice whenever that advice contradicted the ideology of those in power."**

crisis can be seen in the persistent tendency of several administrations to find that handful of scientists who disagreed with the majority opinion and only listen to them. Confronted with scientific evidence that one of his cherished beliefs was simply not supported by the facts, President Ronald Reagan would simply dismiss it by saying, "Oh, I don't think that's true." The Eisenhower and Truman administrations stocked their scientific advisory boards with physicists who shared their militaristic, Cold War anticommunist philosophy and in some cases persecuted those (J. Robert Oppenheimer, for example) who begged to differ.

The tension between scientific advice and policy advice remains strong. I believe that it is the function of a scientific adviser to any government to provide advice purely on scientific matters. Your job, in other words, is to tell your bosses what the data say. If the data are relatively unambiguous and there is good consensus on their interpretation, that needs to be said. If there are reasonable opposing conclusions that are supported by reliable measurements, it is important to see that those views are aired. But a scientist has to be careful about advocating a particular policy in response to the science. If science can say that there is a probability that a particular policy would have severe negative consequences, it is essential that governments be told that. But in general, policy is a matter not for scientific advisers but for politicians.

Politicians, we are constantly told, acquire and retain power by deceit and salesmanship, and frequently are contemptuous of the people they profess to serve. But, true as that cliché might be (and happily there are some notable exceptions), it is their job to get something done, and frequently getting something done requires making compromises that appall or offend scientists. A good politician usually keeps his or her options open. I agree completely with the guidelines proposed by the 20 academicians in Britain, which state that scientific advisers should not be dismissed for public criticism of policy decisions, but I would issue a caution to those who contemplate doing so.

Scientific advisers should be free to air their views — and not just on matters of science. But they need to understand the consequences. Politicians are naturally suspicious of anyone with an agenda, and, not being reluctant to spin the facts if it serves their purpose, they are quick to believe that others will do so as well. If scientific advisers seem to be advocating particular policies, their scientific objectivity will come into question, regardless of the solidity of their conclusions. David Nutt was right to criticize a policy decision that he felt went against the science. But it led to his being removed from a position where he might have been able to influence such policies in the future. If we want governments to learn to trust scientific advice, we have to ensure that such advice is seen to be objective, as well as actually being so. In his position, would I have done what Nutt did? Probably, but with one significant difference: I would have resigned before going public with my criticism, thereby establishing the separation between my duties as a scientific adviser and my duty as a concerned scientist to speak out about a flawed policy. I also think the Labour government overreacted and in so doing turned a debate about drug safety into one about the independence of scientific advice and the limits of dissent. Instead of looking tough on drugs, they came across as being afraid of the truth.

Yet, we cannot give the advice that governments need to hear if we are seen as just another political faction with its own (usually liberal) agenda. The great strength of science is that its conclusions are evidence-based. Scientific advice, like Caesar's wife, must be above suspicion. If we seem to stray from that, we lose.

*This article originally appeared in *Genome Biology* (2009) 10, 113 and was reprinted with permission from BioMed Central.

New Advocacy and Policy Resources

BY CARRIE D. WOLINETZ*

In an ongoing effort to engage scientists in advocacy for research funding and science policy and to provide innovative new tools for our member societies, the Federation of American Societies for Experimental Biology has rolled out several new electronic resources.

NSF Clearinghouse

The National Science Foundation Advocacy Clearinghouse is a comprehensive resource developed for the NSF advocacy community, policymakers and members of the public interested in supporting NSF and its pioneering scientific research and education programs.

The site contains links to data, policy reports, NSF-funded scientific breakthroughs, advocacy tools and relevant government and nonprofit information.

"We hope that this new resource will inspire and help the many friends of NSF in their efforts to tell the story of this remarkable driver of progress," said FASEB President Mark O. Lively.

Congressional Visit Toolbox

The Congressional Visit Toolbox is an online resource aimed at empowering, training and equipping scientists to build relationships with their elected representatives in Congress. The toolbox contains everything needed to plan and conduct a congressional visit, including templates for meeting requests and follow-up letters, printable state-specific "leave-behind" materials and customizable talking points on the importance of biomedical research. Training materials, such as a slideshow tutorial on advocacy and a video of congressional visit role-playing, are also linked to the site.

The launch of the toolbox comes at a time when science advocacy is critical. "With the recent investments in biomedical research through the American Recovery and Reinvestment Act set to expire next year, and future funding for the National Institutes of Health and other science agencies uncertain, scientists have an important role to play by directly contacting their legislators to talk about their concerns and priorities," said Lively. "Hopefully, the toolbox will provide scientists with all they need to convey their messages effectively, whether they are new to biomedical science advocacy or longtime leaders in the field."

To field-test the toolbox, several members of the FASEB board of directors and Science Policy Committee conducted visits with their elected officials over the August recess. Larry J. Suva, director of the Center for Orthopaedic Research at the University of Arkansas for Medical Sciences, did a test run in his home state and remarked, "The templates for leave-behind information and introductory remarks for setting the stage were invaluable. I was well prepared, and it showed."

Updated Training Data

FASEB also has updated its compilation of survey data on education and employment in the biological and medical sciences.

Recent data from national surveys indicate that the number of graduate students in the biological and medical sciences continues to grow and that the postdoctoral population is also growing. However, for both graduate students and postdocs, the growth rate has slowed for temporary residents. Among postdocs, the growth rate for U.S. citizens and permanent residents now exceeds that of temporary residents for the first time since the mid-1990s.

Carrie D. Wolinetz (cwolinetz@faseb.org) is director of scientific affairs and public relations for the Office of Public Affairs at FASEB.

Howard Garrison and Kimberly McGuire of FASEB's Office of Public Affairs also contributed to this article.

For more information

- The NSF Clearinghouse can be found at www.NSFadvocacy.org.
- The Congressional Visit Toolbox is available at http://bit.ly/3V5Dzr.
- FASEB's compilation of education and employment data is at http://bit.ly/EJSaN.

The More Things Change… Appropriations Bills Still Hanging Fire

BY PETER FARNHAM

Despite solid majorities in both the U.S. House and Senate and a president sympathetic to the majority's legislative agenda, congressional Democrats still remain unable to agree on several major appropriations bills, including those that fund the two main federal research agencies — the National Institutes of Health and the National Science Foundation — in which the American Society for Biochemistry and Molecular Biology is most interested. This continues a trend going back to at least the Reagan administration, in which action on most appropriations bills is not completed by the start of the new fiscal year, and the remaining bills get lumped together at the end of the fiscal year in continuing resolutions before some agreement is finally reached, months after the legislation was supposed to have been approved. The trend has continued no matter which party is in power. And, so far in the first year of the Obama administration, it shows no signs of abating.

At this point, only four of the 12 regular appropriations bills have been signed into law, although another one is on the president's desk awaiting his signature. Two bills are in conference. The House has completed consideration of all 12 bills, the Senate only seven. Unfortunately, two of the bills in which action is incomplete are the commerce, justice, and science appropriations bill, which funds a host of science agencies, including the NSF, NASA and others, and the labor, health and human services, and education appropriations bill, which funds the NIH.

Since fiscal 2010 started on Oct. 1, the government has been running on a series of continuing resolutions that fund the government at current levels (that is, last year's levels) for varying lengths of time. The latest continuing resolution runs out Dec. 18, thus signaling the possibility of another delayed congressional recess. Although the Senate leadership has indicated it would like to pass the remaining appropriations bills individually, it is becoming increasingly likely that a so-called "minibus" will emerge, rolling the remaining bills into one package. ("Minibus" is a policy wonk play on words, taking off on an "omnibus" continuing resolution, which rolls *all* appropriations bills into one package.)

The National Institutes of Health

The NIH is funded at differing levels in the House and Senate versions of the legislation. The House-passed version funds the NIH at $31.26 billion, $854 million more than funding in fiscal 2009 (not counting the stimulus funding provided earlier this year). The Senate Appropriations Committee has approved the L/HHS bill as well, but it funds NIH at $500 million lower than the House has provided — at only $30.76 billion, a $364 million increase. The stimulus money ($10 billion over two years) is accounted for separately, but, if added in, it boosts both totals by $5 billion each for 2010. This money must be spent by the end of fiscal 2010, Sept. 30.

ASBMB, along with the rest of the biomedical community, has been considering what level of funding to request for fiscal 2011. Pretty much everyone in the biomedical research community is coalescing around a figure somewhere in the range of $35 billion. Those who have studied the numbers (ASBMB staff among them) believe that it would take a figure in that range to avoid a catastrophic dropoff in the number of competing grants that can be funded. However, no specific number is being promulgated at this time until the fiscal 2010 appropriations level has been settled. Unfortunately, we are hearing very downbeat assessments of the likelihood of an NIH request even approaching this level.

The president will be presenting his budget proposal for 2011 in early February, and Office of Management and Budget officials and others have informed us that we should not be optimistic about major increases in the coming year. An increase on the order of $5 billion to $6 billion more for NIH would use most of the additional funds expected to be available to the Department of Health and Human Services in next year's budget. The president is thus unlikely to put most available money into NIH and propose no increases in other programs in the bill.

It is also somewhat unusual that the Senate figure is significantly below that of the House. However, the Senate Appropriations Committee has indicated that the passage of the stimulus funding bill made a big difference in its funding levels for regular appropriations, since NIH

received so much stimulus funding and since most of it will be spent in 2010.

Unfortunately, NIH's stimulus funding also has caught the attention of Rep. Joe Barton, R-Texas, ranking minority member of the House Commerce Committee, which oversees NIH. He wrote to NIH Director Francis Collins on Sept. 24, asking for information on a number of NIH-funded grants, including one studying Thai "sex workers" and one on patterns of drug use in Brazilian "rave culture." He has also written to the Government Accountability Office asking that NIH's use of the $10 billion in stimulus money be examined. He wants to know if the process and criteria for funding grants under the stimulus program were different from the ways NIH usually funds grants and how many jobs were "created or maintained" (one of the objectives of the stimulus package).

On this note, President Obama indicated Sept. 30, during a visit to NIH, that more than $5 billion in NIH stimulus money had been awarded, funding 12,000 new grants and creating "tens of thousands of jobs conducting research, manufacturing and supplying medical equipment and building and modernizing laboratories and research facilities all across America."

National Science Foundation

The National Science Foundation bill has passed both houses of Congress, but a conference has yet to be called. The House has approved a funding level for NSF of $6.937 billion, a $447 million increase over 2009. The Senate level is $20 million less, at $6.917 billion. The Senate debated the bill for almost a month before passage. One item of contention was an amendment offered by U.S. Sen. Tom Coburn, R-Okla., to eliminate $9 million for funding of political science research. However, this was defeated, and the bill ended up passing the Senate handily.

Peter Farnham (pfarnham@asbmb.org) is director of public affairs at ASBMB.

A New Biochemistry

BY KYLE M. BROWN

Earlier this fall, the National Research Council released "A New Biology for the 21st Century," a report calling for a new national biology initiative. The report, authored by a committee of the nation's leading biologists, envisions a new interagency approach to biological research that would augment existing research programs and tackle societal problems related to food, the environment, energy and health.

New Prominence

With an array of established theories and techniques that will help address the New Biology initiative's societal challenges, biochemistry is likely to take on a central role in this initiative.

To guide the New Biology initiative's research program, the committee outlined four societal challenges involving food, the environment, energy and health. According to the report, the New Biology initiative investigators should be tasked with (1) adapting any food plant to any growing conditions, (2) diagnosing and repairing ecosystem damage, (3) expanding sustainable alternatives to fossil fuels and (4) achieving individualized health surveillance and care.

While biochemistry will be crucial in the creation of personalized medicine, its role will extend beyond human health. For example, adapting food plants to new growing conditions will require knowledge of the biochemical traits required for survival in different climates.

New Biochemists

As the New Biology initiative utilizes biochemistry to solve major societal problems, initially the ranks of biochemists are likely to expand from collaborations. Previously trained biologists, in fields not traditionally associated with biochemistry, will seek out collaborations with biochemists to tackle a problem.

But, the report underscores that "the emergence of the New Biology signals the need for changes in how scientists are educated and trained." It recommends "the creation and implementation of interdisciplinary curricula, graduate training programs and educator training." As biochemistry will be a central portion of the initiative, the development and implementation of interdisciplinary curricula is likely to expose even more biologists and scientists to the concepts and tools of biochemistry.

New Funding

The New Biology initiative will require a large investment of funding over a long period of time. Realistically, the report acknowledges that "the cost will be too large to be extracted from current research budgets." If Congress allocates new funding for the initiative, biochemistry will benefit from the rising tide.

More importantly, the New Biology initiative is likely to open new funding opportunities for the biochemistry community. Its interagency approach would ask the scientific community to re-examine its highly compartmentalized structure. Currently, 11 different federal agencies fund life sciences research, and each has its own rules about the types of research it will fund. That creates particular problems for researchers who perform interdisciplinary research that does not fit under any single agency's program. The New Biology initiative may help break down some of the traditional barriers while providing specific funding for interdisciplinary approaches.

New Challenges

While biochemistry, biology and society will benefit from the initiative, serious questions remain about putting this initiative into practice. The report states that "the committee does not provide a detailed plan for implementation," and with no details, policymakers are left with fundamental questions about what the New Biology initiative would look like. If it's not an agency, then what is it? Who, or what, should run it? How much money over how long? How should it allocate funding? To whom?

Calling for this bold new initiative, the NRC has taken the first step. To make the recommendations a reality, scientists and policymakers must work together.

Kyle M. Brown (kmbrown@asbmb.org) is an ASBMB science policy fellow.

For more information

- To view the National Research Council report, "A New Biology for the 21st Century," go to http://bit.ly/1OM8i0.
- For more science policy news, information and opinion, visit the ASBMB Policy Blotter at http://asbmbpolicy.wordpress.com.

asbmb member spotlight

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

Trievel Presented with Etter Award

Ray Trievel, associate professor of biological chemistry at the University of Michigan Medical School, has been named the recipient of the 2010 Etter Early Career Award from the American Crystallographic Association.

Trievel will receive his award next summer when he delivers a lecture at the ACA annual meeting in Chicago. The Etter award recognizes outstanding achievement and exceptional potential in crystallographic research demonstrated by a scientist at an early stage of his or her independent career. The award was established in 2002 to honor the memory of Margaret C. Etter, who was a major contributor to the field of organic solid-state chemistry.

Trievel studies the mechanisms by which protein modifications within the nucleus affect transcription and other genomic processes. His primary research goals are to elucidate the molecular mechanisms of enzymes that catalyze chromatin modifications and the specificities of effector proteins that recognize those modifications and transduce the information encoded by those marks. He also is developing biochemical assays and other reagents to facilitate high-throughput screening of small-molecule inhibitors against chromatin modifying enzymes.

Fuchs Garners L'Oréal-UNESCO Award

Elaine Fuchs, Rebecca C. Lancefield professor and head of the laboratory of mammalian cell biology and development at Rockefeller University, is the recipient of a 2010 L'Oréal-UNESCO Award in the Life Sciences. Fuchs is one of five scientists, representing five continents, who will be honored with the award this year.

The award, founded 12 years ago, recognizes female scientists who have made important contributions to science and who have been a source of support, motivation and inspiration for women in science. It is presented by the L'Oréal Corporate Foundation, based in France, and the United Nations Education, Scientific and Cultural Organization, which promotes cooperation, ethics and peace in science.

Fuchs, who also is an investigator at the Howard Hughes Medical Institute, is being recognized for her contributions to our knowledge of skin biology and skin stem cells. Her research centers on how skin stem cells self-renew, develop and maintain the epidermis and hair follicles and the molecular mechanisms that enable those cells to respond to various external cues, depart from their niche and accomplish those tasks.

Lefkowitz Wins Research Achievement Award

Robert J. Lefkowitz, James B. Duke professor of medicine and biochemistry at Duke University, is the recipient of a 2009 American Heart Association Research Achievement Award. He received the award for his research on G protein-coupled receptors, which transmit chemical signals that regulate physiological processes, such as heart rate and blood pressure.

Lefkowitz's work on G protein-coupled receptors, the largest and most pervasive family of cell receptors, began in 1982 with the identification of the gene for the β-adrenergic receptor, which helps regulate the body's fight-or-flight response by reacting to epinephrine. Shortly thereafter, he discovered seven additional adrenergic receptors. Those receptors — and all G-protein receptors — share a basic structure in which the molecule weaves its way back and forth seven times across a cell's membrane. When the portion of the molecule that lies outside the cell connects with the receptor's favored signaling molecule, the internal portions of the molecule can trigger the appropriate cellular response.

Lefkowitz is also a Howard Hughes Medical Institute investigator.

Three ASBMB Members Elected to IOM

CURRAN

GOLDBERG

PODOLSKY

Three American Society for Biochemistry and Molecular Biology members are among the 65 new members and five foreign associates elected to the Institute of Medicine this year. Election to the IOM is considered one of the highest honors in the fields of health and medicine.

The ASBMB members newly elected to the IOM are:

THOMAS CURRAN, deputy scientific director of Joseph Stokes Jr. Institute, Children's Hospital of Philadelphia, and professor of pathology, University of Pennsylvania.

ALFRED L. GOLDBERG, professor of cell biology, department of cell biology, Harvard Medical School.

DANIEL K. PODOLSKY, Philip O'Bryan Montgomery Jr. M.D. distinguished presidential chair in academic administration and Doris and Bryan Wildenthal distinguished chair in medical science, department of internal medicine, University of Texas Southwestern Medical Center at Dallas.

Retrospective: Mahlon Hoagland (1921–2009)

BY THORU PEDERSON

Mahlon Hoagland, who contributed two seminal discoveries to the field of gene information flow, died on Sept. 18, 2009, at his home in Thetford, Vt., three weeks before his 88th birthday. Working in a group headed by Paul Zamecnik at the Massachusetts General Hospital, Mahlon revealed the enzymatic activation of amino acids at their carboxyl termini by the formation of acyl anhydrides with adenylate (1, 2) and co-discovered, with Zamecnik, transfer RNA (3, 4).

Mahlon was the son of a leading behavioral neurophysiologist. A career in either biology or medicine seemed ordained when he entered Harvard University in 1941, transferring from Williams College. At Harvard, he was deeply impressed by Louis Fieser's organic chemistry course, recalling, "I was enthralled by his ability to breathe life into molecules" (5). When the war broke out, Harvard premedical students were fast-tracked. Mahlon was commissioned as a Navy midshipman and entered Harvard Medical School in 1943. Two years later, on a fateful morning at Boston's Children's Hospital, he contracted tuberculosis from a baby for whom he was caring. His infection progressed rapidly, and he ended up at Chelsea Naval Hospital, where he was discovered by a Harvard physician, Walter Burrage, who evacuated him to the Trudeau Institute in Lake Placid, N.Y., to "take the treatment," the term used in that era to indicate fresh air and rest.

Returning to Harvard Medical School in 1947 to repeat his fourth year, Mahlon found that his initial interest in surgery remained strong. However, his promised appointment as a surgical resident at Massachusetts General Hospital was rescinded by the chief, who didn't want a post-TB doctor rumbling around the wards. Mahlon applied for, and received, a surgical residency appointment at the Peter Bent Brigham Hospital but soon found that his tubercle infection had reactivated. Accordingly, he took a research post at Massachusetts General Hospital's Huntington Laboratory, headed by the physician-toxicologist Joseph Aub. One of Aub's many interests was beryllium toxicity, based on the problem of industrial exposure to the element (as beryllium oxide) in the phosphors used in the manufacture of fluorescent lamps. For the next three years, Mahlon worked on the induction of osteogenic sarcoma in animals exposed to beryllium as well as its effects on plant growth, becoming a recognized expert in this area of toxicology.

Although Mahlon was strongly influenced by Aub, it was another investigator he encountered in the group who made a deeper and more lasting impression on him — Paul Zamecnik. Zamecnik had joined Aub's group in 1938 and had been directing a comprehensive program on the control of liver growth viewed as an issue of protein synthesis. By the time Mahlon had completed his beryllium projects, he had received an American Cancer Society fellowship and, on Zamecnik's advice, joined Kaj Linderström-Lang at Copenhagen's Carlsberg Laboratory. There, he was significantly influenced both by Linderström-Lang and Herman Kalckar. Mahlon then returned to Massachusetts General, where, again on the advice of Zamecnik, he did a stint in the laboratory of Fritz Lipmann.

Lipmann had written a prophetic review in 1941 on the energetics of ATP activation as a general mechanism in biological chemistry. Mahlon's stint in the Lipmann lab exposed him to its gestalt and steered his attention to the possibility that covalent ATP activation might be involved in protein synthesis. This idea had not escaped Lipmann's ever-fertile mind, and the two groups found themselves in "comfortable competition" a few floors apart. But Mahlon got it first.

In addition to his glittering training with the Copenhagen and Boston leaders in biochemical energetics, Mahlon had another great advantage — a cell-free system that

the Zamecnik group had painstakingly developed, springing from an initial interest in protein turnover in normal liver and hepatomas and aided by key contributions by Philip Siekevitz, another member of the able team Zamecnik had assembled. The group also enjoyed a relatively unique trove: C^{14} amino acids from Robert Loftfield. Using a pyrophosphate exchange assay, Mahlon discovered amino acid activation (1, 2). Presciently, he and Zamecnik also observed that, once activated, the amino acid was not released from the catalytic activity (vide infra).

Only two years later, Mahlon found that the temporal and subcellular fraction pathways through which amino acids reached the ribosomes involved a "soluble" RNA (3, 4). This discovery was seeded by a puzzling result Zamecnik had obtained previously: that labeled amino acids became attached to a small amount of RNA in the system. Mahlon's experiments defined the temporal and enzymatic attachment of activated amino acids to this soluble RNA and led to the important deduction that the enzymes responsible for activating the amino acids catalyzed their linkage to the RNA (these enzymes later to be defined as the aminoacyl tRNA synthetases). Previously, in 1956, Francis Crick had predicted, in a privately circulated document, the existence of an "adaptor" that would have to be involved in translating the DNA code into protein. Mahlon later wrote, admiringly, that he had had an image arise in his mind, that of him and Zamecnik "slashing and sweating our way through a dense jungle, rewarded at last by the vision of a beautiful temple, looking up to see Francis, on gossamer wings of theory, gleefully pointing it out to us!" (6).

Having made two monumental discoveries while he was a "senior" postdoctoral fellow, Mahlon was on the recruitment hot list. Harvard Medical School bacteriologist Bernard Davis had followed Mahlon's career with increasing admiration and appointed him assistant professor in his department of microbiology. Mahlon undertook teaching for the first time, and, as he would recall later with a combination of humility and amusement, he was called into Davis' office after every lecture for an intense post-mortem. He set up his lab, attracted fine students and postdocs, but increasingly disliked the landscape and moved to Dartmouth College as chair of biochemistry. There, he turned his research to the control of protein synthesis in regenerating liver and also led efforts to integrate basic research findings into the medical school curriculum. In 1970, Mahlon was recruited to take over the Worcester Foundation for Biomedical Research, which had been founded in 1943 by his father and Gregory Pincus. He promptly added a program in cell biology and won a core grant from the National Cancer Institute, making that institution the first NCI-designated cancer center in Massachusetts.

At the Worcester Foundation, Mahlon turned his attention to writing and speaking to lay audiences about the importance of basic research. The terms "curiosity driven" and "unfettered" were among his favorites, and readers and audiences reacted warmly. They did so, in part, because Mahlon possessed an unassuming, modest style and an almost childlike excitement about the discovery process. In the mid-1970s, Mahlon catalyzed a group including James Watson, Arthur Kornberg, George Palade, Lewis Thomas and others to form the Delegation for Basic Biomedical Research. The group went to Washington and brought a new cogency to the view that fundamental research can predict no outcomes. The group was an overnight sensation and soon was widely imitated.

After retiring in 1985, Mahlon authored or co-authored six books that conveyed his unique talent for expressing science to a general readership. He was a longtime member of the American Society for Biochemistry and Molecular Biology, a member of the American Academy of Arts and Sciences and the U.S. National Academy of Sciences and received numerous other honors and awards, including the Franklin Medal (1976) and the 1982 and 1996 book awards from the American Medical Writers Association. He and Zamecnik were nominated for the Nobel Prize more than once.

Having made two seminal discoveries as a young investigator, Mahlon spent the last part of his career leading and reforming the Worcester Foundation and inspiring lay audiences to understand what makes science happen. It is a matter of subjectivity as to the arena in which he made his most enduring contribution: as a biochemist or as an eloquent statesman-spokesman for basic research. Maybe it's a tie. He was a gifted biochemist over short quanta of everlasting discoveries, a gracious, modest man and an eternal optimist for science.

We offer our deepest sympathy to Mahlon's family. Below are reflections by his colleagues.

To do my work, I climbed onto the shoulders of Mahlon Hoagland, who was a great trailblazer and who laid the foundation and basic framework for the grand world of aminoacyl tRNA synthetases. These ancient, universal proteins, which appeared at the base of the tree of life in conjunction with the development of the genetic code, embody so many mysteries yet to be solved. Little did

any of us know that Hoagland's early work would guide those like me into a land filled with surprise and meaning — from the role of tRNA synthetases in the evolution of the tree of life to their development of expanded functions that are critical for wellness and homeostasis and that have applications to human diseases.

Paul R. Schimmel
Ernest and Jean Hahn Professor
The Scripps Research Institute

I encountered and spoke with Mahlon occasionally during the '60s. What struck me most was the modesty and the quiet demeanor of such a highly accomplished scientist. The impression I got was of an urbane, sophisticated and broadly educated individual. Quite recently, in preparation for historical talks at some meetings, I have had the occasion to read and re-read some of Mahlon's classical papers and reviews, and one cannot but be impressed with the clarity and precision of his writings. In scientific publications and in books, Mahlon had the tremendous gift of taking the reader along with him and conveying the sense of excitement that he felt about science.

In describing experiments showing that aminoacyl sRNAs were the intermediates in protein synthesis, Mahlon writes, "It was night by the time the samples were dried, stacked and ready to move automatically under the counter tube. I still can clearly see the dark windows of the lab, smell the organic solvents, hear the buzzing of a defective fluorescent lamp in the next room. In front of me were the transfixing flashing lights of the Geiger counter as the samples began to be counted… Those little numbers caused a shiver to go down my spine: Amino acids had left the RNA and entered protein!" (7) As someone who started working with radio isotopes using what was likely the same type of gas flow counter that Mahlon was describing, I read these lines and could sense the excitement that he must have felt as he saw the flashing lights of the counter indicate to him that the number of counts in sRNA were going down and those in the protein were going up. This was scientific writing at its best, and Mahlon was a master at that.

Uttam L. RajBhandary
Lester Wolfe professor of molecular biology, The Massachusetts Institute of Technology

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Retrospective: Charles Tanford (1921–2009)

BY WALTER GRATZER

Charles Tanford was one of the leaders of that remarkable generation of physical chemists who were drawn to biology in the decade following World War II. Their incursion into biochemistry tilted the emphasis quite abruptly, away from metabolic processes and toward the structure and thermodynamics of macromolecules. From this sprang the effulgent new discipline of molecular biology, viewed with mistrust by many biochemists, for it was, in the words of Erwin Chargaff, no more than "biochemistry practiced without a license."

Tanford was also a part of the wave of Central European émigrés who so enriched the American academic scene in the 1930s. He was born to assimilated Jewish parents in Halle, Germany. In 1929, his father, Max Tannenbaum, foreseeing perhaps what was to happen five years later, pulled up his roots and took his family to London. The next year, he changed his name to Tanford, and Charles, age 8, was sent to the very reputable University College School. In 1939, Max made another far-reaching decision and dispatched his son to New York into the care of an aunt. Charles' mother and younger sister eventually followed.

Another relative, at Max's urging, got Tanford into New York University to study chemistry. On graduating, he was enrolled as a graduate student at Princeton University with the expectation that he would work with one of the leading theoretical chemists of the day, Henry Eyring. However, the war intervened, and Tanford was drafted and sent to Oak Ridge to assist in Harold Urey's program on the fractionation of uranium isotopes.

When the war was over, Tanford returned to Princeton, but Eyring imposed the condition that he must work with another professor, R. N. Pease, on combustion in gases. This was not what he wanted to study, but the work produced a Ph.D. and two papers on what became known as the Tanford-Pease theory; this enjoyed a brief vogue before being supplanted, according to Tanford, by more elegant formulations.

At this point, chance intervened to change the course of Tanford's life and career: Walter Kauzmann arrived at Princeton as an assistant professor and ignited Tanford's enduring fascination with proteins. Rejecting the temptations of a lucrative industrial job, Tanford applied instead for a place in Edwin Joseph Cohn's protein laboratory — the only one of its kind in the country, and, in its setting at Harvard Medical School, a curious anomaly. When Tanford arrived, the main concern of the laboratory was the rigorous analysis of proteins, in respect of molecular weight, size, charge and ion binding, and it had attracted a galère of distinguished chemists. The most important for Tanford was George Scatchard, for whom he developed a deep admiration and from whom he absorbed the finer points of solution thermodynamics.

After two years, and equipped with a grasp of the mainly hydrodynamic techniques then available for the study of proteins in solution, Tanford headed for his first faculty position in the chemistry department of the University of Iowa. There, he taught a course on the physical chemistry of polymers and discovered that no satisfactory textbooks were available. It was at this point that he resolved to write his own, an undertaking that was to occupy him intermittently for eight years and resulted in the book "Physical Chemistry of Macromolecules."

In the midst of all this, he took a sabbatical year with eminent theoretician J. G. Kirkwood at Yale University. There, he developed a theoretical treatment of the electrostatic characteristics of globular zwitterionic polyampholytes, based on evenly distributed discrete ionising groups, rather than on the familiar model of a uniformly charged surface. The outcome permitted a realistic interpretation of acid-base titration profiles of proteins, many of which Tanford and his students measured in the laboratory.

In 1960, Tanford moved to a professorial chair in the department of biochemistry at Duke University Medical Center, where he remained for 28 years. He will perhaps be best remembered for his work on protein stability and the hydrophobic effect. This became central to the way in which the structure of globular proteins is perceived. He himself always emphasized the debt he owed to Kauzmann, who, if not the originator of the concept, clarified it and brought it to the attention of protein chemists. Kauzmann planted the seeds in Tanford's mind during their conversations at Princeton, and the notion that the folded state is imposed on globular proteins by the instability of the unfolded chain in water, rather than the energy of interaction in the globule, came to him as an epiphany. It led to a series of classical studies on protein unfolding by nonaqueous solvents, and especially by urea and guanidinium chloride, and on the free energies of transfer of model hydrophobic compounds from water to such media.

Throughout this period, Tanford made forays into more functional aspects of protein chemistry. Notable among these was his work on antibodies. Rival models of immunoglobulin G were in circulation. Antibodies of this kind were known to be divalent, but the disposition of the antigen-binding sites was a matter of controversy. By a tour de force of hydrodynamic analysis and inference, Tanford and his colleagues defined the lineaments of the molecule. Moreover, they separated the light and heavy chains of an antibody, denatured, refolded and reunited them, and showed that the antigenic specificity was recovered. This eliminated in one stroke Linus Pauling's "template" theory of antigenic specificity, which was based on transitions between conformational states of the protein.

Around this time, Tanford embarked on his last major undertaking, this time in association with Jacqueline Reynolds, a professor in the department of anatomy at Duke University. Together, they took a daring plunge into what were then the turbid waters of membrane chemistry. Membrane proteins were viewed with disgust by protein chemists, for they were generally insoluble in water, except in an indeterminate denatured condition in complexes with destructive detergents, such as sodium dodecyl sulfate, or fully unfolded in high concentrations of denaturants. Tanford and Reynolds found that the native states could be preserved in soluble complexes with benign detergents, which they carefully characterized. They devised a method of measuring the molecular weights of membrane proteins in this state by masking the detergent contribution to the buoyancy of the complex with D_2O. This made it possible to determine the sizes and subunit structure of these refractory proteins by sedimentation analysis.

The contemplation of membranes and their relation to the various states of amphiphiles, such as lipids, led to the culmination of Tanford's thinking about hydrophobicity. This he set out in a typically lucid and elegant book, encompassing the nature of detergent micelles, surface layers and membranes, "The Hydrophobic Effect: Formation of Micelles and Biological Membranes," and in an article in Science in 1978. With the new methods they had honed, Reynolds and Tanford made a number of inroads into membrane biology: With the neurophysiologist Arthur Karlin, they studied the acetylcholine receptor and, with Walther Stoeckenius, the structure of bacteriorhodopsin. They fractionated the proteins of the red cell membrane and determined their molecular weights, and, while on sabbatical leave in Germany, they immersed themselves deeply in the action of ion pumps.

Tanford's professional collaboration with Reynolds had long since blossomed into domestic harmony, he and his wife having divorced in 1968. In 1988, he and Jackie decided to retire. They settled in the small country town of Easingwold in Yorkshire and melted into its community. But they were far from idle, as they began a new joint career as historians of science. Tanford already had published a delightful popular book on membranes and surfaces, "Ben Franklin Stilled the Waves: An Informal History of Pouring Oil on Water with Reflections on the Ups and Downs of Scientific Life in General." Next, there emerged a typically original joint concept: "The Scientific Traveller: A Guide to the People, Places and Institutions of Europe" — a guidebook for the scientifically inclined tourist. It was so well received that the publisher demanded, and got, a second and equally captivating volume, "A Travel Guide to Scientific Sites of the British Isles." But the most important joint venture was still to come: "Nature's Robots: A History of Proteins" — a work of meticulous scholarship, delivered with style, wit and a fine narrative sweep.

Hilaire Belloc, historian and poet, wrote his own epitaph:

When I am gone, I hope it may be said
His sins were scarlet, but his books were read.

Tanford, alas, is gone, but his books and his papers are indeed still read.

Charles Tanford was a bracing and genial companion, and under the formidable exterior, a kind and generous man, ever willing to spend time explaining a tricky scientific point to a student or to anyone less intellectually agile. We will remember him with pleasure and gratitude. The following are thoughts and reflections from several of his friends and former colleagues.

When I was in graduate school, Charlie Tanford was one of my heroes. What I liked about Tanford's work was that he was interested in big-picture questions and found meaningful ways to get insights. As far as I know, he invented the idea of hydrophobicity scales and was the first, with his associate Yashuiko Nozaki, to determine such a scale for amino acids. He developed simple conceptual models of micellization and protein stability based on such ideas.

Tanford wrote with outstanding clarity and simplicity. He composed another "bible" in the field, called "The Hydrophobic Effect," in 1973, with very psychedelic 1970s lettering on the front cover. He once told me the story of how that book came about. In his early career, Tanford had been a protein chemist. Over time, his interests shifted to membrane proteins. He was simply looking for some rules for how to pick the right detergent for solubilizing membrane proteins so that he could then move forward and study them. He told me that, after 15 years, he never figured it out, but, even so, he wanted something to show for that effort, so he wrote that book.

Ken A. Dill
Professor of biophysics
University of California,
San Francisco

Charles Tanford was one of the great pioneers of protein biophysical chemistry. His data and ideas in the large number of areas he ploughed stand the test of time. His work on the effects of denaturants on protein denaturation is the basis of modern kinetic studies on the mechanism of folding. In his honor, I named the "beta value" for the position of the transition state for folding on the reaction coordinate as defined by solvent accessible surface area, "β_T."

Alan Fersht
Herchel Smith professor
of organic chemistry
University of Cambridge

Charles Tanford was one the great protein chemists of the 20th century. Equally comfortable with experimentation and theory, his contributions were numerous and fundamental, especially those on both protein denaturation and the hydrophobic effect. He was also an exceptional writer. His textbook, "Physical Chemistry of Macromolecules," was a staple for a generation of biophysics students (including myself), and his reviews in Advances in Protein Chemistry established a paradigm for understanding protein-folding thermodynamics. Upon retirement, he wrote several popular books, each with flair and each reflecting his distinctive view of the subject material. His work conditioned the way we all think about proteins.

George D. Rose
Krieger-Eisenhower
professor of biophysics
Johns Hopkins University

Tanford's contributions on the hydrophobic effect, amino acid solubilities and protein stability are well known. What is less known is that he was also a pioneer in structure-based thermodynamics calculations. In 1957 he published, with John G. Kirkwood, a continuum electrostatics model of proteins. At the time, this was probably the most important paper in the field since Linderstrøm-Lang's contributions 33 years earlier. The Tanford-Kirkwood model, as it is still known today, was a perfect marriage of Kirkwood's mathematical skills and Tanford's deep knowledge of ligand binding and multiple equilibria. With characteristic insight, Tanford, working with Robert Roxby, cast the model as an algorithm that could be solved with an iterative procedure. In 1972, they used it to calculate the proton titration curve of lysozyme starting from the coordinates of the crystal structure. He did not go back to work on this problem, but he sparred and watched closely and with curiosity over the shoulders of younger scientists working in Frank Gurd's lab to improve Tanford-Kirkwood calculations. Generations of scientists were stimulated by Tanford's work in protein electrostatics and continue to work on problems that Tanford first brought to the forefront.

Bertrand Garcia-Moreno
Professor and chair of the
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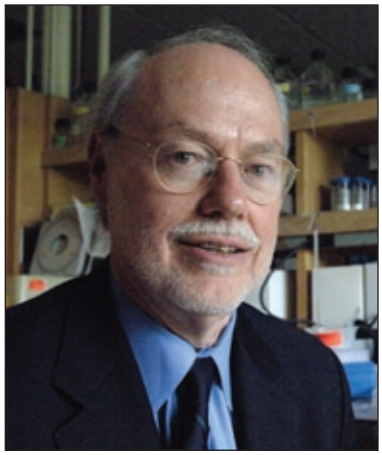
Walter Gratzer (walter.gratzer@gmail.com) is a professor of biophysical chemistry at King's College London.

Nobel Laureate Claims the 2010 Herbert Tabor Lectureship

BY ANGELA HOPP AND NICK ZAGORSKI



Phillip A. Sharp, a world leader of research in molecular biology and biochemistry and an institute professor at the Massachusetts Institute of Technology, has been named winner of the American Society for Biochemistry and Molecular Biology Herbert Tabor/Journal of Biological Chemistry Lectureship. Sharp will give his award lecture, titled "The Biology of Small RNAs," at 6 p.m. Saturday, April 24, at the 2010 annual meeting in Anaheim, Calif.

Sharp's research interests have centered on the molecular biology of gene expression relevant to cancer and the mechanisms of RNA splicing. His landmark achievement was the discovery of RNA splicing in 1977, for which he shared the 1993 Nobel Prize in Physiology or Medicine with Richard J. Roberts.

"Phil's work has been characterized by a remarkable creativity — he has literally broken open whole new fields — and also by an equally remarkable track record for training outstanding scientists," said ASBMB President Gregory A. Petsko. "I can personally testify to his willingness to help young colleagues and to the generosity with which he has given his time to numerous good causes. He is a shining example of what a senior scientist should be."

Currently, Sharp has turned his attention to understanding RNA interference, the process by which RNA molecules act as switches to turn genes on and off. This recently discovered phenomenon has revolutionized biology and could potentially generate a new class of therapeutics.

Sharp did his undergraduate studies at Union College in Barbourville, Ky., where he majored in chemistry and mathematics, then completed his Ph.D. in chemistry at the University of Illinois at Urbana-Champaign in 1969, studying under noted physical chemist Victor Bloomfield.

While at the University of Illinois, Sharp read the 1966 volume of the Cold Spring Harbor Symposium on Quantitative Biology, titled "The Genetic Code," and became interested in molecular biology and genetics. He subsequently obtained a postdoctoral fellowship at the California Institute of Technology, where he studied the structure of sex factor and drug resistance plasmids in bacteria. In 1971, Sharp began a second postdoc, studying gene expression at the Cold Spring Harbor Laboratory under the renowned James D. Watson.

In 1974, Sharp joined MIT's Center for Cancer Research, now known as the David H. Koch Institute for Integrative Cancer Research, and has remained on the MIT campus ever since. He has held numerous leadership positions along the way: He was director of the Center for Cancer Research from 1985 to 1991, head of the biology department from 1991 to 1999 and director of the McGovern Institute for Brain Research from 2000 to 2004.

Sharp, who has authored more than 350 scientific papers, has received numerous awards and honorary degrees and has served on advisory boards for the government, academic institutions, scientific societies and companies. His other awards include the Gairdner Foundation International Award, the General Motors Research Foundation Alfred P. Sloan Jr. Prize for Cancer Research, the Albert Lasker Basic Medical Research Award, the National Medal of Science and the inaugural Double Helix Medal from the Cold Spring Harbor Laboratory. Sharp is a member of the National Academy of Sciences, the Institute of Medicine, the American Academy of Arts and Sciences and the American Philosophical Society.

In addition, Sharp is a co-founder of Biogen (now known as Biogen Idec) and Alnylam Pharmaceuticals.

The Herbert Tabor/Journal of Biological Chemistry Lectureship was established by ASBMB to recognize the many contributions of Herbert Tabor to both the Journal of Biological Chemistry and to the society.

Angela Hopp (ahopp@asbmb.org) is managing editor for special projects at ASBMB. Nick Zagorski (nzagorski@asbmb.org) is a science writer at ASBMB.

Kinase Researcher Named Recipient of FASEB Award

BY ANGELA HOPP AND NICK ZAGORSKI

Susan S. Taylor, professor of chemistry and biochemistry, professor of pharmacology and a Howard Hughes Medical Institute investigator at the University of California, San Diego, has been named the recipient of the Federation of American Societies for Experimental Biology 2010 Excellence in Science Award. The award recognizes women whose outstanding career achievements in biological science have contributed significantly to furthering our understanding of a particular discipline by excellence in research.

"I am honored that Dr. Susan Taylor has been selected to receive the 2010 Excellence in Science Award during my term as FASEB president," said Mark O. Lively. "Dr. Taylor is an outstanding biochemist and structural biologist whose laboratory has made fundamental contributions to the understanding of cellular regulation by protein phosphorylation. Just as the cAMP-dependent protein kinase that she studies is the prototype of this critically important family of enzymes, Dr. Taylor is an exemplar for the truly meritorious women scientists whose career achievements are celebrated by the Excellence in Science Award."

Taylor, one of more than 50 women nominated for the prestigious award, will receive an unrestricted research grant of $10,000 sponsored by Eli Lilly and Co. She will also give a talk titled "Dynamics of PKA Signaling" at 2:15 p.m. Tuesday, April 27, at the 2010 annual meeting in Anaheim, Calif.

Taylor, who received her Bachelor of Arts in chemistry from the University of Wisconsin and her doctorate in physiological chemistry from the Johns Hopkins University, is regarded by many as the world's foremost expert on cAMP-dependent protein kinase (PKA), the archetype for all the protein kinases and one of the most important regulatory molecules in a cell.

Taylor was first introduced to PKA by a colleague at UCSD, shortly after she started her own lab in 1972 after postdoctoral studies at the Medical Research Council Laboratory of Molecular Biology in Cambridge, England (1969-1970) and UCSD (1971-1972). Taylor's extraordinary work has led to identification of functional residues important for catalysis and subunit interaction and has provided critical insight related to cAMP binding.

In 1991, Taylor and her colleagues at UCSD determined the three-dimensional structure of the catalytic subunit of protein kinase A — the first crystal structure solved for any protein kinase. Even today, the structure continues to serve as a prototype for the entire protein kinase family. In subsequent years, Taylor has solved the structures of the protein's regulatory subunits, as well as the structure of the entire multisubunit PKA complex, which provides insights into cAMP activation and PKA cooperativity.

"[Susan Taylor's] structure of protein kinase A changed the way we think about kinases," said Jack Dixon, a professor at the University of California, San Diego, and vice president and chief scientific officer of the Howard Hughes Medical Institute. "These enzymes have become important drug targets for cancer and other diseases, and Susan's thoughtful insights into their structure and function have led the field for many years."

More recently, Taylor has been addressing other PKA-related topics such as identifying its subcellular location, in collaboration with Roger Y. Tsien, and examining how the scaffold proteins DAKAP-1 and -2 bring together PKA and its substrates.

Taylor has received numerous awards for her studies, including the American Society for Biochemistry and Molecular Biology's William C. Rose Award, the Wyeth Research Chemistry Award, the American Chemical Society's Garvin-Olin Medal and the Institute of Electrical and Electronics Engineers' Forefronts of Large Scale Computation Award. She was elected to the American Academy of Art and Sciences in 1992 and to both the Institute of Medicine and the National Academy of Sciences in 1997. Taylor also served as ASBMB president in 1995.

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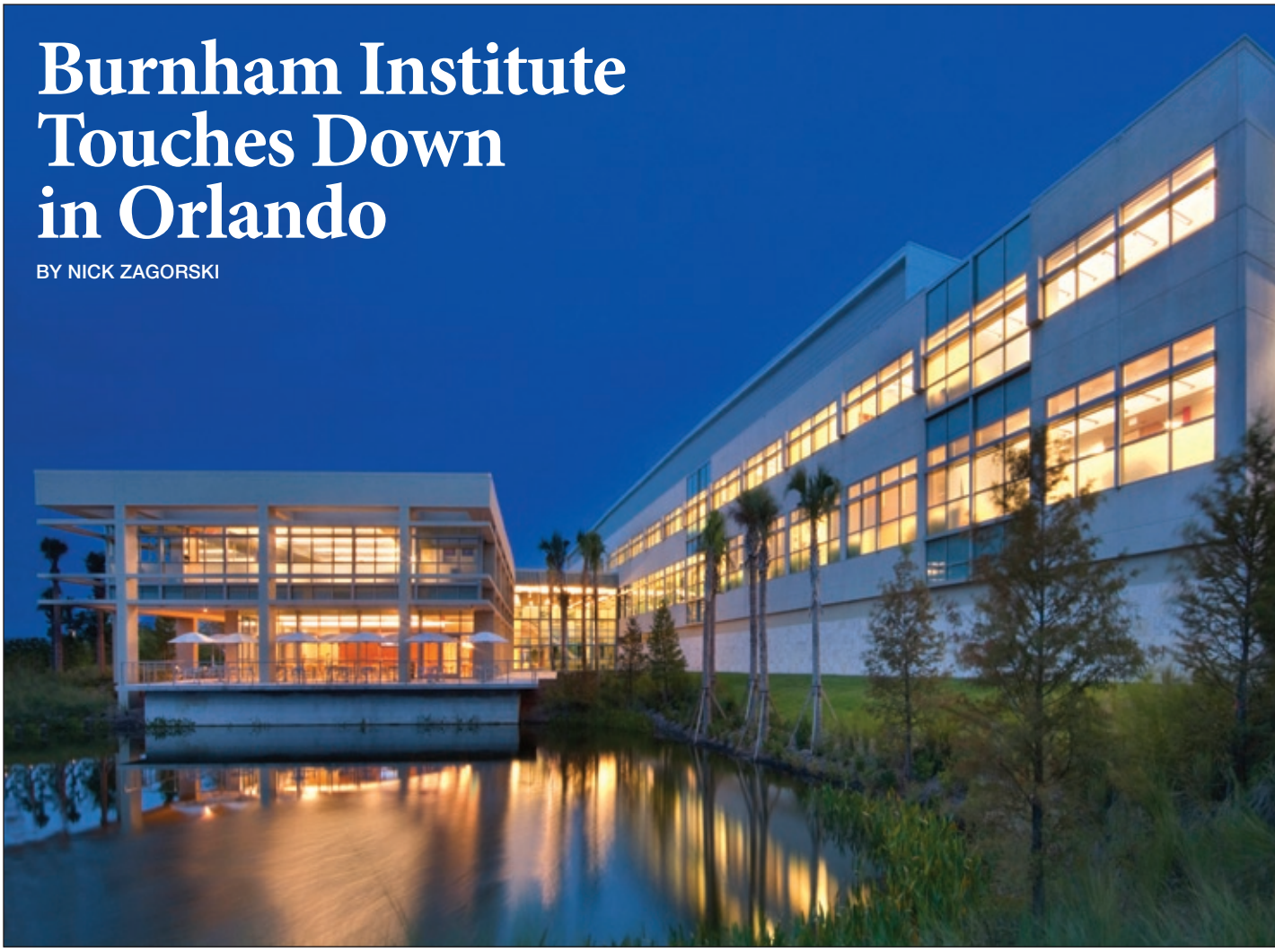
Burnham Institute Touches Down in Orlando

BY NICK ZAGORSKI



In 1963, Walter Elias Disney flew over an uninhabited stretch of swampland near Orlando, Fla., and saw a vision of the future: a completely new type of theme park that would dwarf even his revolutionary Disneyland in Anaheim, Calif. Occupying more than 20,000 acres, this new amusement park in the center of the Sunshine State would be large enough to contain all the necessities of a family vacation — attractions, dining, shopping, leisure — and also grow and change over the years.

Although Disney did not live to see the opening of his "Florida Project," his dream definitely has been realized, for those once-empty parcels of land now contain one of the most-visited destinations in the world — a grand resort that helped transform the theme park and tourism industries.

Thirty-six years later, another successful California enterprise has come to Orlando, as this past October La Jolla's Burnham Institute for Medical Research has opened up a brand new $85 million research facility. Burnham's new building may not be quite as eye-catching as Spaceship Earth at Epcot, and it probably won't bring in quite as many tourists as its illustrious neighbor; however, the expansion of this private biomedical research institute into Orlando, along with the other planned research and medical facilities that eventually will make up a biotechnology park, has just as much potential to be extraordinarily transformative to the state of Florida as Walt Disney World.

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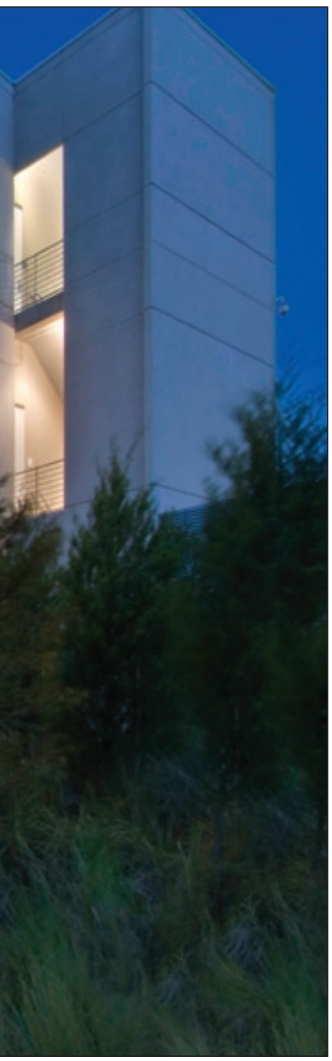
Traditionally, Florida's economy has been supported by three primary industries: tourism, agriculture and construction. All of those, though, are sensitive to factors beyond the state's control, such as unpredictable weather and global economic factors. And, much like any three-legged



A side view of the Burnham Institute at Lake Nona building, which officially opened with a dedication ceremony on Oct. 8; the front portion of the building (left) houses the administrative wing, while the labs and technology centers are in the back (right).

object, kicking out even one leg destabilizes the whole thing.

Back in 2003, then-Florida Gov. Jeb Bush began looking for a fourth leg to provide more long-term economic growth and stability and saw an opportunity in biotechnology.

Somewhat surprisingly, despite having the fourth-largest state population, four major metropolitan areas and several large universities and hospitals, Florida never has been a major player in biotech. Burnham associate professor Masanobu Komatsu, who completed his undergraduate, graduate and first postdoctoral work at the University of Miami, saw that firsthand. "I really liked the area. It's where I met my wife, and I didn't want to leave, but at that time Florida didn't offer much of a career future in cancer research."

Bush hoped to change such perceptions, and he drew inspiration from another sunny, tourist-driven location: San Diego, which gradually had built up a vibrant biotechnology industry, basically starting from scratch. It most certainly would be a risky proposal, but it would be one with high reward potential. A successful biotech cluster would create thousands of jobs, generate tremendous revenue and increase Florida's intellectual capital. So, the state began wooing the best in biotech to its sunny shores.

And, although the Burnham Institute for Medical Research was not the first to set foot in Florida — that honor actually would go to its neighbor in La Jolla, the Scripps Research Institute — its arrival is part of Florida's most ambitious recruiting effort to date. While other biotechnology hubs like San Diego and Boston took decades to fully develop, Orlando hopes to jump-start the biotech boom by quickly attracting multiple established institutes, as opposed to untested startups, to a ready-to-develop 600-acre site in southeastern Orlando near Lake Nona known as "Medical City."

And the cornerstone of this city would be the Burnham Institute for Medical Research.

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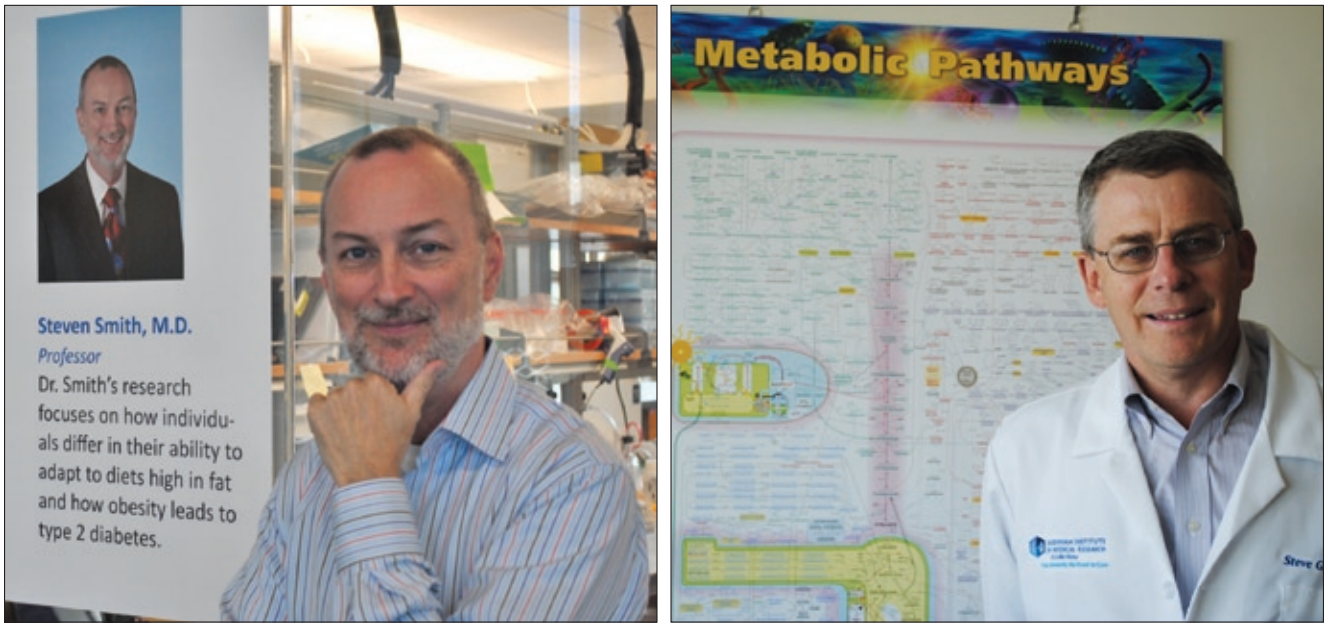
From its origins as a research center aimed at understanding the development of cancer, Burnham has built up a scientific mission of tackling disease via fundamental discovery and innovative technology, whether through its continued work as a National Cancer Institute-designated cancer center, or other areas, such as infectious and inflammatory disease, neuroscience and stem-cell research.

That disease-driven mission will continue to be represented in Orlando, although, like any sibling, this site also will find its own identity by pursuing an avenue of research that is complementary to research at the La Jolla institute: understanding metabolism and how it relates to obesity, diabetes and cardiovascular disease. "This new center is thematically distinct, which gives us a reason to be," explains Burnham at Lake Nona scientific director Daniel P. Kelly, "but our studies also extensively cross-cut with Burnham's other themes, which lets the two campuses stay connected."

The Lake Nona institute will be headlined by the Diabetes and Obesity Research Center, which is composed of two distinct programs: the metabolic signaling and disease program and the cardiovascular pathobiology program. In turn, the research carried out by those two programs will be supported by several advanced technology platforms, such as high-throughput small-molecule screening, genomics, metabolomics, medicinal chemistry and pharmacology. Some of the technologies, like medicinal chemistry, are extensions of platforms that Burnham has in La Jolla, while others, like genomics, were developed to complement Lake Nona's research areas. Two platforms, though, were developed specifically to give this new center a unique feel.

The first technology is a very extensive small-animal phenotyping core that will allow researchers to evaluate insulin resistance, body fat mass and composition, heart function and energy expenditure of mouse models. The second is a metabolomics platform, set up in collaboration with Duke University's Sarah W. Stedman Nutrition and Metabolism Center, which will conduct mass-spectrometry-based metabolite profiling.

"Both of these sophisticated technology resources can put into overdrive our opportunity to do translational



Burnham Institute researchers Steven R. Smith (left), director of the Florida Hospital-Burnham Institute Translational Research Institute, and Stephen Gardell, director of Burnham's translational research resources, both will be instrumental in fulfilling the institute's aims of pushing its fundamental discoveries toward clinical and industrial utility.

research that could not be done at traditional academic institutes," says Kelly, who was at Washington University School of Medicine in St. Louis prior to taking the scientific director role in early 2008.

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"An Out-of-the-Box Proposal." That curiously titled e-mail header, from Kelly, was Philip A. Wood's first introduction to Burnham's Orlando facility. "I had known Dan for about 20 years," says Wood, who was a professor at the University of Alabama at Birmingham when that message hit his inbox last year. "We had published some papers together and gave talks on the same stages, so I decided to give it a look. After all, an out-of-the-box proposal was exactly what I needed at that point in my career."

After a visit to Orlando that he describes as completely first class, Wood was hooked. "Everything was just so well done and efficient; all the resources I wanted for my studies into fatty acid oxidation and how the body handles increased fat loads — metabolic physiology, genomics and metabolomics — were under one roof, and I realized I could do my research here with minimum aggravation. Add in the fact that I don't really like snow, and coming here was a no-brainer."

From Kelly's point of view, bringing Wood on board was also an easy decision. As a trained veterinarian with more than 30 years of experience, Wood knew the medicine and genetics of seven different species, which allowed him to think in comparative terms. That kind of broad expertise was perfect for Kelly's vision of assembling a diverse research team that could take advantage of the technology platforms.

"I was very keen on developing an environment without barriers," says Kelly. "Looking at it from a discovery sense, we need to consider metabolism from many different disciplines."

That meant bringing in scientists with Ph.D.s, M.D.s and even D.V.M.s, as well as mixing strong academics like Timothy Osborne, who was a professor of biochemistry and molecular biology at the University of California, Irvine, before coming over as metabolic signaling and disease program director, with industry types like Stephen Gardell, who had spent 20 years working in drug discovery at major pharmaceutical companies.

The pace of hiring has been extremely rapid, with 14 of an anticipated 30 lead scientist positions already filled since Burnham first agreed to expand to Orlando back in August 2006. Kelly attributes that pace partially to luck, partially to Burnham's existing reputation and partially to his nature. "I don't want a sparsely populated building, you know, because the technology cores need collaborators to get up and running," he says. "So I've been hard on the recruitment trail."

The location certainly helps as well: "I grew up in Wisconsin and was always a Midwest guy, so Florida was always the least likely area I thought I would live in," Kelly says. But he adds that for others, such as empty-nesters or people with children, Florida has a sort of magnetic appeal.

Osborne is a prime example. Tenured and quite content at Irvine, he initially came to visit with his wife out of curiosity and professional courtesy, but he was quickly won over. "Everyone we met, none of whom knew us from Adam, was amazingly friendly and treated us so well, and the facilities were amazing," he says. "To put it simply, we were just floored."

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While Burnham received a generous start-up package from state, local, and private groups, Kelly acknowledges that, in the long term, Burnham at Lake Nona cannot be sustainable purely on the National Institutes of Health funding received by its scientists.

For its continued success, and the success of Florida biotech, it'll need philanthropy and business interests, and therefore productive partnerships with universities, hospitals and companies. Fortunately, buoyed by Burnham's early commitment, Medical City will provide many partnership opportunities; already, the University of Central Florida is nearing completion of its brand new medical school just down the road from Burnham, while Nemours Children's Hospital, the M.D. Anderson Cancer Center Orlando and the University of Florida also have agreed to build facilities there.

But while the presence of a life science cluster at Lake Nona will be extremely beneficial, Burnham also has undertaken a forward-looking model to ensure its research effort is maximized.

That's where Gardell comes in. In his specialized role as director of translational research resources, he oversees Burnham's two flagship high-technology platforms — metabolomics and cardiometabolic phenotyping — and assists researchers in shepherding their projects toward clinical utility, which in turn, he believes, will further Burnham's mission. "Translational research is a circular process," he says. "It involves bench-to-bedside — and bedside-to-bench research pursuits. Discoveries made in the clinics must feed back to guide basic research. This is a critical component of overall success."

Speaking of bedsides, Gardell will work closely with Steven R. Smith, a trained endocrinologist who was hired by Burnham in a joint appointment with Florida Hospital. When he's not in lab studying genetic and epigenetic changes that may alter muscle metabolism, Smith heads the Florida Hospital-Burnham Institute Translational Research Institute. The TRI, which will also soon have its own state-of-the-art building, employs clinical scientists conducting patient-oriented research who will work closely with Burnham to apply their work back to basic research. Smith envisions that, just like him, some other TRI researchers will have joint labs at Burnham, thus making the collaboration even more intertwined.

Such collaboration will be essential because, in choosing diabetes and obesity as its research focus, Burnham at Lake Nona has taken up quite a challenge. As Smith discusses his clinical work, he points to a graph of obesity trends, and the hockey-stick like rise seen over the past decade. Diabetes rates have not yet advanced that high, but Smith notes somberly, "Diabetes usually follows obesity by about 10 years."

And diabetes is no simple beast: "You can find as many theories about the mechanisms underlying insulin resistance as you have labs working on it," Wood says, adding, "Just look at cholesterol problems by comparison, where statin drugs are highly effective. We have no statin equivalent in diabetes; after all these years, the best treatment is still diet and exercise."

If anyone's up to the challenge of changing that, it may be the Burnham. "We've got a great institute that's focused on a core set of principles, where everyone loves to get together and talk about ideas," Smith says. "I'm optimistic we'll get some good things done."

Familiar Neighbors

While both Burnham and Scripps are focused inward, and are making sure their new centers can be the best they can be, neither is blind to the fact that the other also has set up shop in Florida. So, will this development add a new layer to a spirited biomedical rivalry? The directors of the institutes share their thoughts:

Burnham at Lake Nona scientific director Daniel P. Kelly:

Well, I think in many ways Scripps and Burnham are both beginning to establish their own ecosystems here in Florida. Both institutes have pushed for a strong translational element. Scripps has focused on a fundamental drug-discovery theme. While Burnham has drug-discovery platforms, it is moving toward a translational medicine theme by partnering with regional health systems. This could set the stage for highly productive collaborative interactions between the institutes.

Scripps Florida operations director Harry Orf:

Will Scripps researchers be competing for grants and awards with people at Burnham, Torrey Pines and even nearby Max Planck? Sure. At the same time, though, having these other institutes here opens up tremendous opportunities; imagine how strong a joint Scripps-Max Planck grant application would be. And, in the big picture, having more Florida centers is a good thing; as they say, a rising tide raises all boats.

Jupiter Rising

Scripps Leads Biotech Effort in South Florida

Amongst the numerous scientists, politicos and other guests present at the Burnham's Institute's opening ceremonies in Orlando, there was someone quite familiar with a gala such as this. In fact, just a few months before, Harry Orf was presiding over a similar dedication just down the expressway in the town of Jupiter, when the Scripps Research Institute cut the ribbon on its own brand new three-building, 350,000-square-foot Florida campus.

That ceremony in February was the culmination of a marriage of opportunity that started in 2003. Richard A. Lerner, CEO of Scripps, was looking to expand the institute's footprint, preferably on the East Coast, while then-Gov. Jeb Bush was searching for a scientific powerhouse to take the lead in Florida's ambitious and unpredictable biotechnology development plan.

The pair met, and, although Lerner initially had thought about established locales like North Carolina's Research Triangle Park, the idea of being a biotech trailblazer fit well with Scripps' pioneering nature, and Lerner agreed to take the plunge.

Being the first would require strong leadership, and, in looking at his credentials, one can see why Scripps tapped Orf as operations director for its new campus. He spent more than 30 years at Harvard University and had witnessed the birth and growth of biotech in Boston; in fact, he even helped nudge it along, as he was part of a consulting company that had helped develop more than 65 startup biotech companies. Orf also brought tremendous administrative, recruiting and laboratory design experience to the fold, having served as director of the molecular biology laboratories at Massachusetts General Hospital for 20 years.

However, at the time, in 2003, Orf was serving in a different capacity: as a nuclear medicine officer in the Army Reserve who had just been called up — on two days notice — to Iraq.

"And wouldn't you know it, I started getting job offers," he says. First, a recruiter for the Howard Hughes Medical Institute inquired whether he would be interested in being a part of its Janelia Farm project, but they needed him to start by January 2004 at the latest, and, as he notes, "I couldn't just call up the Army and tell them, 'Hey, I have to go now.' So, I had to pass on the opportunity."

A few weeks later, he received an e-mail from the same recruiter telling him about the Scripps Florida project, and by then he had received notice that he would be back stateside in February, so he decided to find out more. "And God bless the U.S. government, because the defense operators arranged a call from Iraq to the San Diego Naval Yard and got me connected with Dr. Lerner. We spoke at length, and, since I was planning on taking my wife and son to Disney World when I got back, he told me, 'While you're down there, drive over to Palm Beach, and we'll talk some more.'"

"It was kind of funny," Orf continues. "Before that meeting, I thought about Florida more as a place to retire than a place to start a new career, but, after hearing about how Scripps' enterprise could lead this major scientific vision that Florida had, I readily signed on."

Of course, then came the challenge of getting others to sign too, which could be tricky, especially in the early days when Scripps Florida was more promise than substance.

Patrick R. Griffin, chairman of the molecular therapeutics department and one of three faculty members who arrived in Florida before Orf, recalls those early times. During his recruitment visit, the facilities tour consisted of driving by an orchard that had a big fence with a sign that said "Do Not Enter," and he was told that his initial research space would be half a bench in a laboratory at Florida Atlantic University's Boca Raton campus.

"I basically had to take it on faith that everything — the buildings, funding, recruiting — would work out," he says. Still, Griffin, then running a small biotech company called ExSAR Corp., was looking for something different, and Scripps' pre-existing reputation eventually swayed him.

Scripps Florida's central building, which houses administrative offices, a cafeteria and an amphitheater in addition to labs and classrooms, is crowned by a symbolic interpretation of the DNA double helix.

And while there were a few other bumps in the road, like an environmental lawsuit over the initial proposed site that delayed building construction, the recruiting progress has been strong, and Scripps has more than 30 out of 60 investigator positions filled and more than 350 staff overall. As Orf says jokingly, "It feels like we bring in someone new every week."

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Much like the relationship between the two Burnham centers, Scripps Florida will share the same mission as its parental institute but also stake out its own identity. Of the six research departments at Scripps Florida — cancer biology, chemistry, infectology, metabolism and aging, molecular therapeutics and neuroscience — all but chemistry were established specifically for the Florida center, and the departmental chair and a majority of researchers for those five departments resides in Florida. Most departments, however, do have faculty members on each coast and, as a result, several major grants at Scripps are true bicoastal collaborations.

Despite such similarities, though, Orf stresses that Scripps Florida is not a clone. "While we still pursue basic biomedical research, the funding we received from the state allowed us to try something new, so we established cutting-edge technology cores, which we used to create a therapeutic discovery platform here at Florida," he says.

Those cores consist of advanced technology components, featuring emerging tools like genomics, proteomics, cell-based screening, flow cytometry and a drug discovery platform with several screening and pharmacology technologies, including a Kalypsys robotic system that can screen more than 1 million compounds in 24 hours.

Harry Orf, Scripps Florida's operations director, surveys the scene outside his office. Despite some initial delays, the Scripps campus in Jupiter is now operational.

Together, they comprise Scripps' Translational Research Institute — sort of a center within a center — that works with the basic research arm to develop new lead compounds to fight disease. "This translational component lets our researchers take their projects further than they could most anywhere else," says Griffin, who has joint duty as head of the TRI.

Interestingly, of the various technology platforms Scripps had intended to develop as part of the TRI, the one that it eventually lagged on — bioimaging — proved to be a blessing. As the anchor for biotech development in South Florida, Scripps was expected to help bring in other scientific entities to the area, and soon Lerner found out that an institute well known for imaging — the Max Planck Institute — was interested in building a new facility.

As a recruiting effort, Lerner convinced Max Planck President Peter Gruss and his scientific directors to visit Jupiter for a two-day symposium. "At first, they were convinced that any American expansion had to be in Boston, San Diego or someplace like that. But, by dinner the first night, Gruss said his directors had done a complete 180 and told him Max Planck *had* to build their new center here.

"That was a big win for us," Orf adds. "Not only does it give us a perfect institution to complement our research and technology strengths, but it legitimizes this area as a science hub."

Since that announcement, two other institutes, the Torrey Pines Institute for Molecular Studies — another one of Scripps' San Diego neighbors — and Oregon Health and Science University's Vaccine and Gene Therapy Institute, have developed sites in nearby Port St. Lucie, and some clinical organizations also have expressed interest in helping Scripps Florida move its discoveries into community clinics.

Scripps also has been hard at work on another mandate: to collaborate with state academics. As Orf notes, science education is a significant element of Scripps. "People tend to overlook this, because we don't have undergraduates, but I always like to point out that we are Scripps dot edu. The institute definitely has an entrepreneurial bent, but we are foremost a research and academic institution."

So, in addition to its own education efforts — like at the La Jolla campus, Scripps Florida offers graduate degrees in chemistry and biology — Scripps Florida has peer-to-peer collaborations and cooperation agreements (basically an agreement that whenever scientists from separate institutions talk to each other, lawyers don't have to get in the way) with each major research university in Florida as well as internships and summer programs with local colleges and high schools.

"There is an amazing sense of community and collaborative spirit among the researchers here," says Roy Smith, chairman of the metabolism and aging department, who admits he was initially skeptical before coming to Scripps because of the lack of scientific culture in the area, though he absolutely has no regrets now. "Everyone knows that we're building something brand new and unique here, for ourselves and the state, and everyone is determined to make it work."

Nick Zagorski (nzagorski@asbmb.org) is a science writer at ASBMB.

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Norbert Perrimon
Harvard University
Phosphorylation Networks and Orthogonal RNAi Screens

Nikolaus Rajewsky
Max Delbrück Center for Molecular Medicine
Proteome Targets of microRNAs and RNA Binding Proteins

Conference Sessions and Invited Speakers

Talks selected from submitted abstracts will be included in each session.

Biomarkers
Sabine Bahn, *University of Cambridge Biotechnology Institute*
Steven A. Carr, *Broad Institute*

Computational MS and Bioinformatics
Keith Baggerly, *M. D. Anderson Cancer Center*
Pavel Pevzner, *University of California, San Diego*
Vicki H. Wysocki, *University of Arizona*

Glycoproteomics
Susan J. Fisher, *University of California, San Francisco*

Oxidative Stress
D. Allan Butterfield, *University of Kentucky*

Post-Translational Modifications
Yingming Zhao, *University of Chicago*

Profiling Human Diseases
Peipei Ping, *University of California, Los Angeles*

Profiling the Metabolome
Oliver Fiehn, *University of California, Davis*
Robert C. Murphy, *University of Colorado, Denver*
Gary Siuzdak, *The Scripps Research Institute*

Protein Interactions
Jack Greenblatt, *University of Toronto*
Cammie Lesser, *Harvard University*
Deborah Morrison, *NCI - Frederick*

Proteomics and Chemical Biology
Matthew Bogyo, *Stanford University*
Laura L. Kiessling, *University of Wisconsin,*

Proteomics and Clinical Diagnostics
Leigh Anderson, *Plasma Proteome Institute*
Ronald Hendrickson, *Merck Research Laboratories*
Andrew Hoofnagle, *University of Washington*

Proteomics Technology
Joshua LaBaer, *Arizona State University*
David Muddiman, *North Carolina State University*

Top Down Mass Spectrometry
Neil L. Kelleher, *University of Illinois*

Important Deadlines

December 7, 2009
- Abstract submission
- Student travel application

February 15, 2010
- Advance conference registration
- Hotel reservation at the conference rate

OTHER HIGHLIGHTS

- **Short Courses, March 7** (Course descriptions and registration at ushupo.org)
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Bringing Active Learning to the Biochemistry Classroom One Step at a Time

BY JENNIFER LOERTSCHER

In one of his recent President's Messages ("A Teachable Moment," October 2009), Gregory A. Petsko reflected on the potential of the American Society for Biochemistry and Molecular Biology to lead the way in revitalizing biochemistry and molecular biology education. In response to findings and directives from the Teagle working group (1), Petsko suggested that the time is right for our community to broaden educational goals within the BMB major. This is also a current priority for the National Science Foundation and the National Academy of Sciences (2). In addition to increasing student engagement in the classroom, teaching strategies that promote active learning help students improve skills such as writing, speaking, critical thinking, problem solving and teamwork. Although our colleagues in the humanities and social sciences bear some responsibility for helping our students to learn these skills, ultimately, if we expect future biochemists and molecular biologists to have these competencies, we need to step up our teaching efforts in those areas.

College and university science teachers long have considered the laboratory the most appropriate arena in which to help students develop the thinking, communication and social skills necessary to succeed in scientific and medical professions. Focusing on scientific skills during lab is effective, but, as we try to elevate performance so that students can compete on a global level, teaching skills in the classroom is essential. Fortunately, a number of resources already exist for those who are interested in doing this.

POGIL

Process-oriented guided inquiry learning (POGIL) is one approach that aims to help students build an understanding of scientific concepts while simultaneously developing skills such as oral and written communication, problem solving, critical thinking and teamwork (3). A typical biochemistry POGIL activity includes three parts: a pre-class assignment, an in-class activity, and a post-class homework assignment (4, 5). The preclass assignment helps to prepare students for the activity so that they are ready to fully participate during class time. The purpose of the in-class activity is to help students learn concepts and skills. Those activities consist of a series of questions related to one topic, and they become progressively more challenging throughout the class period. In practice, the process by which students work through activities under faculty guidance resembles Socratic questioning. The questions in the activities lead students through a logical thought process that asks them to analyze information and question their own assumptions (6). Students continue to develop knowledge and skills in the homework assignment. Although other active pedagogies such as problem-based learning (PBL) and case-based learning are effective and well established in BMB education, POGIL has some characteristics, described below, that could make it more amenable to implementation in a variety of classroom settings.

In 2007, my colleague Vicky Minderhout and I received funding from NSF to improve, assess and disseminate POGIL materials for biochemistry. An ongoing aspect of our project is assessment of prerequisite chemistry and biology knowledge that students bring to biochemistry courses and evaluation of learning that takes place in biochemistry classrooms using POGIL materials. Even more important, given the recent call to action by Petsko and others, is the part of our project aimed at broad and effective dissemination of POGIL materials for the biochemistry classroom. To accomplish this, we have communicated with a variety of colleagues, including those who teach in biology, biochemistry or chemistry departments, those who teach large classes and those who have experience with other active learning approaches. As a result of these interactions, we have a greater understanding of the barriers that prevent faculty members from making changes in their classrooms and have begun to identify strategies to overcome those barriers. Some of these ideas are described next.

Overcoming POGIL-usage Barriers

Modular activities can be introduced gradually and mixed with existing course structures: Those of us in the active learning community sometimes have failed to communicate the versatility of active learning approaches. As a result, many instructors who are new to POGIL are under the impression that the only effective way to implement it is to convert an entire course from lecture to POGIL. In our experience, very few people have the time and support to make sweeping changes in their classrooms and more often than not, major changes are not necessary. There is a growing consensus that the effect of many people making incremental changes in their classrooms is greater than a small number of people making radical changes. Therefore, in preparing POGIL biochemistry materials for dissemination, we were careful to create free-standing modules that could be interspersed in an otherwise lecture-based course. Many core collaborators and faculty beta testers have used our POGIL activities in combination with a number of other approaches, including lectures, PBL, cases or literature-related projects.

Workshops have helped faculty members recognize and develop their natural inclinations and abilities in the classroom: Workshops have been instrumental in helping faculty members move from theory to action with regard to active learning. Workshops are powerful because they bring together diverse people with common interests and give them a forum in which to explore and wrestle with new ways of thinking about teaching and learning. It is striking how often faculty members at workshops realize that their personal teaching philosophy has much in common with POGIL and that they already have much of what it takes to implement POGIL.

Establishing faculty networks is essential for increasing and sustaining classroom innovations: Feedback from participants in our project has convinced us that obtaining materials or attending one workshop is not enough to foster real and lasting changes in teaching. Connections with like-minded faculty members at one's home institution or elsewhere are necessary to ensure implementation of new approaches and their future growth and adaptation. Therefore, societies like ASBMB have the potential to make or break teaching innovations, given the leadership roles professional societies can play in shaping the direction of a field. ASBMB can help connect and support networks of faculty members researching teaching innovations by maintaining databases of instructors using specific pedagogical methods, by prominently featuring education symposia and poster sessions at national meetings, and by actively promoting institutional changes that lead to innovative education research and practices that are now more highly valued at colleges and universities.

Two years into our efforts to disseminate POGIL materials for biochemistry, a diverse community of biochemists using POGIL materials in their classrooms has become well established. However, we still need your help — the greatest changes in BMB education will happen when we all do what we can to improve learning, one step at a time. ΧΩΛ

Jennifer Loertscher (loertscher@seattleu.edu) is an assistant professor of chemistry at Seattle University.

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For more information

- For more on POGIL materials, locations of upcoming workshops and contact information for people using POGIL in your area, e-mail Jennifer Loertscher at loertscher@seattleu.edu.
- For two POGIL activities you can use in your classroom, go to www.pcrest2.com/biochemistry/flyer.htm.

Effective Laboratory Management

BY FABIAN V. FILIPP

You've finished your postdoctoral fellowships, your official training period is over and you've been hired to head your own laboratory. You are finally the boss! But with this new role comes responsibilities, many of which you may have never done before, and you're not alone — ScienceCareers.org surveyed principal investigators, postdocs and graduate students and found that 86.6 percent never received formal management training.

Becoming a Ph.D. is mostly about managing your own time. When you are a lab leader, your role is to manage other peoples' time. Vish Krishnan of the Rady School of Management at the University of California, San Diego, explains, "The day-to-day operation of your laboratory will require both a strong leader and an effective manager. Managers are good at doing things right; leaders do the right things."

Krishnan adds, "The members of your research team, especially postdocs, are highly educated people. The fundamental challenge is to make them want to do what you want to do. Lab leaders who get good research results show planning, structure and synchronization."

When you were hired by your institution, you were selected for your scientific excellence and your plans to contribute to an important niche. Now, you have to communicate these goals to your team. "Everybody has to be aware what the laboratory is going after," Krishnan explains. "A laboratory head is good at setting the direction, as well as defining, decomposing and communicating the work clearly." A productive and stimulating research environment provides the right overlap between individuals. The challenge for you is to divide up the pieces and be able to put them back together.

Take Management Training Courses

To avoid mistakes as young lab leader, Krishnan recommends attending management courses, such as the San Diego laboratory management symposia organized by the San Diego Postdoc Training Consortium. Already in its third year, the workshops provide postdocs and junior faculty a practical guide for managing their research programs while balancing the demands of a new tenure-track position.

The Rady School of Management also has developed a short executive certificate for scientists at the postdoctoral stage. "We talk about ways to align truth-driven scientific matter and economical goals," Krishnan explains. "Those two forces seem to be at odds. However, many times the reason for high research costs is that people chase something that is not true and keep doing experiments. If you adjust a process at the right end, you will get results faster and cheaper."

Manage Your Time and Delegate

Time is very important in both the science and business worlds. Do you schedule your day efficiently? People who are most productive in the morning will do most of their intellectual work before lunch and spend the later part of the day in meetings. People who focus better in the afternoon will do the opposite.

As you move up, you'll learn to leverage the resources you have. It is impossible to do everything yourself. Delegate and free up your time. To reduce your workload, you have to train your research and administrative staff to take over some of the work. Krishnan explains, "A common mistake is to keep doing what you had been doing before and take on more responsibility. The result is you get overloaded, and projects start waiting for your attention."

Krishnan also stresses managing your capacity.

"Understand what capacity you have available and find the demands on that capacity. The general rule in operations management is not to push your capacity beyond 90 percent, if you want to have an efficient and responsive system. You should have 10 percent slack time built into the plan for creativity and in case an unknown factor requires additional attention. This is easier said than done, because the business world operates on everybody being busy and scheduled for 100 percent of their time. If you want to have relaxed productivity in science, you must learn to delegate. Do less and get more!"

Building a hierarchy helps manage your workload: Project leaders report to the lab head, and senior scientists train junior scientists. "A rule of thumb is that the number of people reporting to you should not be more than seven," says Krishnan. "Watch out and minimize the bureaucracy that this may create. Weekly prescheduled team meetings save time. You can have regular meetings as early as 7:30 a.m. If everybody knows Thursday morning is discussion time, everybody will prepare their results by Wednesday. You create a natural rhythm, and you will see that synchronization and structure is helpful in getting results."

Every meeting and commitment has to be questioned: Do I really need to do this? Does the cost-benefit ratio justify the time investment? The laboratory leader also needs some time in the middle of the day for horizontal project management. Even in big groups, at least an hour a day without meetings is essential. How can you keep several projects moving in parallel and jump from one to another without slowing the process? It could happen that a person who is not well trained gets overwhelmed, and the process slows for all participating parties. As you move up in the scientific hierarchy, you must manage projects vertically from start to finish.

Keeping track of all the projects that you are involved with can be challenging. New laboratory-management software, including Web-based tools, can facilitate documentation, data sharing, planning, controlling and synchronization. "It is not very complicated to set up," says Krishnan. "You can even use a spreadsheet or an electronic calendar to create a pretty good management system. If it becomes a bigger team, you may have to turn to commercial, off-the-shelf software. It is important to facilitate the process and not spend more time organizing the organization tools."

"Becoming an effective leader is a continuous process of evaluation, trimming and progress," Krishnan concludes. "In my experience, trimming is something we usually don't do; we keep adding! In my own research, I try to do more trimming and focus on a few high-impact projects. Prioritization is a key ability to develop over the years. A successful leader in research science understands which projects are the most important for the laboratory and which ones are not worth their time."

Fabian V. Filipp (filipp@burnham.org) is a Burnham Fishman postdoctoral fellow at the Burnham Institute for Medical Research.

Looking for more information on laboratory management? Here are some resources:

- The ASBMB collection of materials on preparing future faculty: **http://bit.ly/4o4zYy**
- The HHMI collection of management materials: **www.hhmi.org/resources/labmanagement**
- The 2009 San Diego lab-management symposium: **http://bit.ly/6iDKj**
- The National Institute of General Medical Sciences workshop for postdocs transitioning to independent positions: **https://workshop.nigms.nih.gov**

ASBMB MAC Reaches Out to Diverse Undergrads

BY SONIA C. FLORES

We just finished Hispanic history month, and, in this spirit, the newly energized American Society for Biochemistry and Molecular Biology Minority Affairs Committee is meeting the challenges of the 21st century head-on. Although underrepresented minorities and disadvantaged students comprise at least 30 percent of the U.S. population, the percentage of graduate degrees awarded to these underserved populations is less than one-third of that number. This is even worse when you look at the number of senior faculty with diverse backgrounds. Thus, there is a dearth of qualified diverse mentors who understand the hurdles faced by underrepresented students. Exposing students to hands-on research and giving them access to senior investigators can increase their interest in pursuing a research career, and, the earlier the intervention, the more of a chance we have to capture their attention.

Graduate Experiences for Multicultural Students participants took part in an intense eight-week research experience at the University of Colorado Anschutz Medical Campus.

ASBMB is playing a proactive role in addressing these disparities. We recognize that the best way to do this is by starting early; therefore, we have partnered with organizations that cater to students from diverse backgrounds, such as the Society for the Advancement of Chicanos and Native Americans in Science and the Annual Biomedical Research Conference for Minority Students.

The SACNAS Meeting

ASBMB donated money and sponsored an information booth at the SACNAS meeting in Dallas in October. The undergraduate and graduate students who stopped by the booth learned about our society and were, in many instances, surprised to find out that we publish the Journal of Biological Chemistry. Our basic missions of support for science education at all levels and promoting the diversity of individuals entering the scientific work force were in full display at the meeting. As part of our commitment, undergraduate students were offered free memberships that provide online access to all three of our journals and a print subscription to ASBMB Today. In addition, we invited all undergraduate ASBMB members to participate in our upcoming annual meeting and 14th annual undergraduate student poster competition in April in Anaheim, Calif.

This past spring, SACNAS sponsored a leadership institute in Washington at the headquarters of the American Association for the Advancement of Science. The objective was to develop the next generation of leaders who will become role models for the upcoming generations. The alumni from that institute reunited on the first day of the SACNAS meeting and participated in breakout sessions that addressed such issues as navigating the promotions process, negotiating a recruitment package and taking chances on careers. Those leaders also were highlighted throughout the meeting and had a large presence at the closing ceremonies.

Graduate Experiences for Multicultural Students

I was one of the institute's alumni and, as a new MAC member, hope to use my experiences from the institute to help develop pipeline programs and partnerships that address disparities in representation. Currently, I direct a short-term training program for diverse and underrepresented students at the University of Colorado Denver School of Medicine, funded by the National Heart, Lung and Blood Institute. This program, called "Graduate Experiences for Multicultural Students," pairs students from diverse and disadvantaged backgrounds from around the U.S. with research mentors. The program has been in

existence in various iterations for approximately 20 years, sponsored by both the National Institutes of Health and John Freed, dean of the graduate school at the University of Colorado Denver.

The program focuses on promoting diversity in undergraduate student populations and supporting and stimulating career development for those who study cardiovascular and pulmonary disorders. Students typically arrive at the beginning of the summer and spend eight to nine weeks engaged in an intensive research experience in the laboratories of several medical school mentors. During this time, they also participate in brown bag seminars covering topics such as ethics in science and medicine, how to put together an effective oral or written presentation and graduate school admission. At the end of the summer, students present their work orally and as written scientific manuscripts. Faculty judges then choose the best presentations. The program also defrays the costs of travel to a national scientific meeting. GEMS students have presented at SACNAS, ABRCMS and the Conference on Retroviruses and Opportunistic Infections, as well as annual meetings for the Society for Free Radical Biology and Medicine, the American Thoracic Society, the Endocrine Society and the Federation of American Societies for Experimental Biology.

In 2006, 13 students were admitted to the program: 10 were funded by the NIH grant, one was funded by the graduate school, one was funded by an institutional Research Initiative for Scientific Enhancement program and one was funded with a FASEB grant. Nine of those students attended either the ABRCMS or SACNAS meeting (or both), one presented his work orally at CROI, one presented at the SFRBM meeting that year and one received an award for her work at ABRCMS. The student who presented at CROI originally had medical school as his sole career choice, but, after participation in GEMS, he decided that he loved research so much that he is now a graduate student in biochemistry and cell biology at Rice University. In 2008, 13 students participated in GEMS: five are in graduate school and credit GEMS with opening their eyes to research as a viable career. All of the GEMS student participants were from underrepresented groups including Hispanic/Latinos, African-Americans, Native Pacific-Islanders, Native Americans, the hearing-impaired, first-generation college attendees, low-income families and students from rural areas.

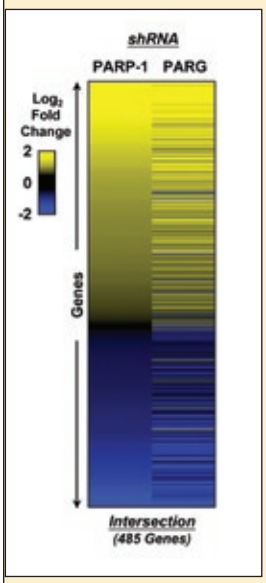
It is my hope that ASBMB eventually will participate in the GEMS program, sponsoring students interested in biochemistry and molecular biology. This would allow ASBMB to use the GEMS infrastructure without having to create a program de novo. GEMS would benefit, too, by having additional research areas for students to explore. You can find out more about GEMS and other summer research opportunities by visiting the ASBMB Web site.

Sonia C. Flores (sonia.flores@ucdenver.edu) is a member of the ASBMB Minority Affairs Committee and a professor of medicine at the University of Colorado Health Sciences Center.

For more information

- Learn about the Graduate Experiences for Multicultural Students program at http://bit.ly/4ilvaQ.
- Find student research opportunities at www.asbmb.org/Page.aspx?id=3494.

PARP and PARG Cooperation



Heat map showing the similar expression profiles of the 485 commonly regulated PARP-1 and PARG genes.

Poly(ADP-ribose) polymerase 1 (PARP-1) and poly(ADP-ribose) glycohydrolase (PARG) regulate transcriptional activity by modifying target nuclear proteins with the addition and removal of ADP-ribose polymers, respectively. While the role of PARP-1 has been established, the exact function of PARG in the nucleus is less clear, although it's assumed that PARP-1 and PARG have opposing functions in gene regulation. In this article, however, the authors show that this is not the case. Combining short hairpin RNA (shRNA) knockdown with microarray analysis in MCF-7 cells, they determined that these two enzymes often act in a similar, rather than antagonistic, manner. PARP-1 and PARG generally localized to similar target promoters, most notably in genes for stress response and metabolism, and, in about half of the genes tested, PARP-1 binding was dependent on PARG. In addition, studies using shRNA-resistant catalytic mutants revealed that enzymatic activity was not required in some target genes. So, rather than being opposing forces, PARP-1 and PARG may act cooperatively to maintain the proper levels of ADP ribosylation on target genes.

Global Analysis of Transcriptional Regulation by Poly(ADP-ribose) Polymerase-1 and Poly(ADP-ribose) Glycohydrolase in MCF-7 Human Breast Cancer Cells

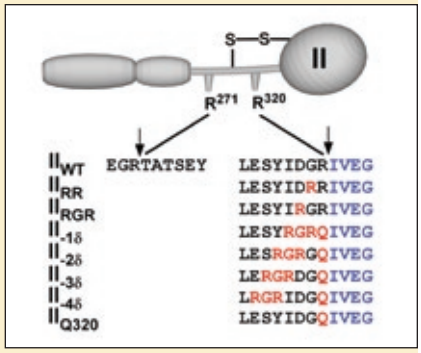
Kristine M. Frizzell, Matthew J. Gamble, Jhoanna G. Berrocal, Tong Zhang, Raga Krishnakumar, Yana Cen, Anthony A. Sauve and W. Lee Kraus

J. Biol. Chem., published online Oct. 7, 2009

jbc

Prothrombin Docking Maneuvers

The conversion of prothrombin to thrombin is crucial for proper clot formation during wound repair. This conversion is handled by the membrane-bound prothrombinase complex, which contains a protease that sequentially cleaves prothrombin at Arg^{320}, followed by Arg^{271}. This defined chain of events is believed to occur through exosite-dependent binding of prothrombin to prothrombinase, arranging the substrate to precisely present Arg^{320} in the protease active site. The recent discovery of a reduced-activity prothrombin with a G319R mutation questions the necessity of precise geometry. In this study, the researchers systematically assessed the importance of substrate positioning. They used a series of cleavage site variants that incrementally shifted the Arg^{320} site toward the Arg^{271} site. Functionally, they observed that prothrombinase was quite tolerant of N-terminal shifts of the cleavage site by one or two residues, although larger shifts led to an abrupt loss in activity. In contrast, prothrombin docking was strongly dependent on the position and sequence of the scissile bond segment, and even minor perturbations resulted in strong thermodynamic increases.



A list of the prothrombin variants used to demonstrate the importance of geometric positioning in prothrombinase activity.

Regulated Cleavage of Prothrombin by Prothrombinase. Repositioning a Cleavage Site Reveals the Unique Kinetic Behavior of the Action of Prothrombinase on Its Compound Substrate

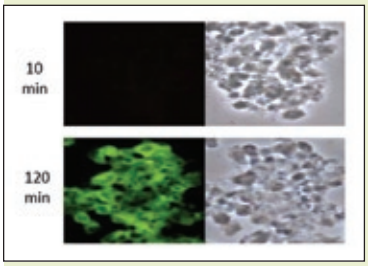
Harlan N. Bradford, Joseph A. Micucci and Sriram Krishnaswamy

J. Biol. Chem., published online Oct. 26, 2009

jbc

A Cell-based Glycosylation Assay

Glucosylceramide synthase (GCS) catalyzes the first step of glycosphingolipid synthesis by adding glucose residues to ceramide (Cer) to produce glucosylceramide (GlcCer). As GlcCer is a core component of more than 300 different glycolipids, which have diverse roles in physiology and disease, GCS may be a potential biomarker and drug target. However, current enzyme assays typically involve in vitro reactions using prepared enzyme samples, which may not directly correlate with enzyme activity in a cell. In this study, the researchers introduced an approach to determine direct GCS cellular activity using fluorescent NBD C6-ceramide. They were able to separate C6-glucosylceramide from C6-ceramide in cellular extracts using thin-layer chromatography and then quantified the levels by spectrophotometer. This cell-based method is highly sensitive, being able to quantitate values from as little as 1 mg of tissue (~50,000 cells), and the researchers successfully evaluated GCS enzyme activity in multiple cell and tumor samples. The results suggest that this cell-based fluorescent approach would be a simple, reliable and direct means to evaluate GCS in cells and tissues for applications such as predicting drug resistance for cancer.



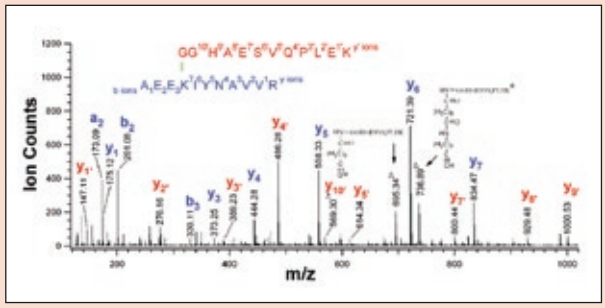
Fluorescent (left panel) and visible light (right) imaging of NCI/ADR-RE tumor cells incubated with NBD C6-Cer, revealing the accumulation of sphingolipid in the cells.

Direct Quantitative Determination of Ceramide Glycosylation in Vivo: A New Approach to Evaluate Cellular Enzyme Activity of Glucosylceramide Synthase

Vineet Gupta, Gauri A. Patwardhan, Qian-Jin Zhang, Myles C. Cabot, S. Michal Jazwinski and Yong-Yu Liu

J. Lipid Res., published online Oct. 13, 2009

Cross-linking Analysis Made Easy



Structure and low-energy CID spectrum of the cross-linked species with an *m/z* value of 670.85^{4+} from a digest of an ecotin dimer; the cross-linker bridge is shown in green.

Chemical cross-linking is a well-established method of studying protein-protein interactions, and, when combined with mass spectrometric analysis of the cross-linked proteins, it can be a powerful approach to probe the topologies and interacting surfaces of protein assemblies. However, comprehensive analysis of cross-linked peptides and protein assemblies is challenging, as most cross-linking reagents react with multiple residues and the solvent, which can inactivate the reactive groups and lead to "dead-end" links. The high complexity of cross-linked samples requires tandem mass spectrometric fragmentation data for confident identification, as available bioinformatic tools for automatic analysis of cross-linked spectra are far from robust. The researchers behind this study, however, demonstrate a new bioinformatic approach that may change that. Using multiple program modules within the Protein Prospector software package, they developed a strategy that greatly facilitates the discovery of cross-linked peptides in chemical cross-linking studies, allowing for results from a single data set.

Finding Chimeras: A Bioinformatic Strategy for Identification of Cross-linked Peptides

Feixia Chu, Peter R. Baker, Alma L. Burlingame and Robert J. Chalkley

Mol. Cell. Proteomics, published online Oct. 6, 2009

Jump, Don't Fall, into Your Career Transition

BY JEANNE MCADARA-BERKOWITZ

From the moment my parents gave me my first microscope, I never imagined I'd grow up to become anything other than a scientist. I designed my entire scholastic trajectory with that goal in mind, and I never questioned my plan until I was well into my Ph.D. candidacy. Despite a growing discontent with bench science, I managed to complete my thesis work and even did a postdoctoral fellowship. But even wonderful mentors, great co-workers and interesting projects couldn't keep my heart in the laboratory. I eventually made the decision — one that was absolutely devastating at the time — to begin looking for a new career.

Today, I am a professional science and medical writer and communications strategist, and I couldn't be happier. I work on a variety of communications projects, from media relations, marketing and Web sites, to deeply technical projects like helping researchers turn clinical studies into journal manuscripts. It's interesting, varied and fast-paced work that is intellectually challenging, both scientifically and from a business standpoint.

Making the decision to leave the lab bench might have been the hardest part of my career transition, but the next hardest part was figuring out what to do and how to get there.

Almost Everyone "Falls Into" His or Her Career

The path that led me from unhappy lab researcher to successful consultant may seem like random coincidences and luck. But, over the years, I've found the common theme among most of the "alternative career" crowd is that everyone's career history is a seemingly random amalgamation of network connections, referrals and opportunities that came together in the end. We all created environments that fostered connections and remained vigilant, so we recognized opportunities when they presented themselves.

For example, in the midst of my postdoc, when the angst of not knowing what to do with my life was at its peak, a friend who was a technician in my graduate school lab got a freelance gig writing for a magazine aimed at lab scientists. He put in a word with the editor, who then gave me a trial assignment. I was terrified. What did I know about writing an article? I probably worked harder on that 500-word product review than I have on anything since. But, that first assignment led to more writing work, and it also gave me a pretty good idea that, whatever I decided to do, I wanted writing to be a part of it.

The lesson here is not "find a friend who works for a magazine, and see if you can get a freelance assignment." The lesson is: Share your hopes and plans for a career change with anyone you trust, even if you're not sure what you want to do. He or she might know someone, or know someone who knows someone, so keep your ears open and jump at any opportunity that comes your way no matter how scared you might be of failing. Ask people to tell you their stories, and volunteer to help them with their work. Give it everything you've got. If you can't summon your "everything," look elsewhere, because that's a clue that this is not what you're suited for. And use any small successes to propel you forward.

Jeanne McAdara-Berkowitz received her Ph.D. in macromolecular and cellular structure and chemistry from the Scripps Research Institute in La Jolla, Calif. She did a postdoctoral fellowship at the University of California, Los Angeles, Jonsson Comprehensive Cancer Center and then joined Fischer-Health Strategic Communications. After three years at the agency, Jeanne founded Biolexica, a communications consultancy specializing in the health sciences.

Don't Wait for Opportunities — Create Them

My experience with the magazine inspired me to go into communications. I signed up for university

extension courses in journalism and public relations and worked up the nerve to introduce myself to the instructors. I sought out mentors, cold calling people in the communications department at the university where I worked and asking them to lunch to learn about what they did. I asked if there was work I could help with on a volunteer basis, and I met with their friends when they offered introductions. I studied everything I could about communications in science and researched potential employers who might need a Ph.D. scientist who liked to write. I tracked down phone numbers and called the executives of companies and took them to lunch. I handed them writing samples from my magazine gig. I kept learning about my prospective new field, and eventually I landed a job at a public relations agency specializing in health care communications.

Again, the takeaway message is that we have to create our own opportunities — I did not get that job from a posted ad or even through a personal referral. My first off-the-bench job was a direct result of my own research efforts and relationships I'd created from scratch. By seeking out connections, asking them questions and building relationships, I was able to figure what I wanted to do. And eventually, I gained the confidence I needed to contact people who might need me and convince them that they did need me.

Make Every Step in Your Transition a Learning Experience

My first job wasn't perfect — the agency's client roster was heavily weighted toward medical-device companies and hospitals, and, although they'd been hoping to move more into biotechnology and pharmaceutical work, they didn't have the senior-level strategic expertise to attract those kinds of clients. But, during my three years there, I learned about the business of communications — about working on multiple projects under deadlines, tracking and billing for time, managing clients and accounts, and the fundamental strategic principles of marketing communications that apply to any industry. Most importantly, I learned that I loved both the actual mechanics of science writing and the strategy that tells us what to write and why. The key was that I approached my work with passion — and always with my eye on the most successful people. I learned the business by watching them, even while I was learning the basics.

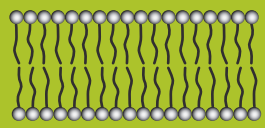
After I'd been at the agency for a few years, my husband and I were ready to start our family, and my long commute and demanding work schedule didn't seem compatible with my vision of parenthood. I negotiated a small but steady freelancing agreement with my employer, and, with that bread-and-butter arrangement in place, I turned to my professional network. Over the years, the colleagues and clients I'd met and friends I'd made had moved on to new jobs themselves, and they have become a self-perpetuating source of referrals.

"...everyone's career history is a seemingly random amalgamation of network connections, referrals and opportunities..."

Push the Finish Line Ever Farther

Working for myself, I've been able to mold my client and project roster toward my favorite kind of work — long-term relationships with a strategic component and lots of deep-level scientific writing. I've also been able to let my workload ebb and flow as my family has grown and changed. But, I've made a point never to become complacent about my career. With each new prospect, I look for personal and professional growth opportunities. I routinely take on projects that require me to stretch intellectually — and I do the requisite studying to make sure I'm providing the best service I can for my clients. I continue to network and meet new people and join and become involved in professional organizations so I can learn from others.

In the end, I found what I wanted to do, and I get to do it every day. But it didn't just happen to me — I made it happen. So, to any aspiring career-changers out there who might be discouraged, wondering how on Earth a crazy set of coincidences will ever happen to them, I say "close your eyes and jump." Go out and create the coincidences that will form your path to a fulfilling career. It takes work, and guts, but you can do it. XXX



Stress, Fat and Lipid Wikis

BY SUZANNE JACKOWSKI

As the holiday season approaches, many scientists are preparing to adjust their habits to cope with the occasional stress arising from the conflict between the demands of the lab and family. Stress is also sensed at the cellular level, and there is growing evidence that an imbalance in lipid homeostasis triggers compensatory alterations in metabolism to relieve stress and rebalance the system.

The endoplasmic reticulum is a principal site for membrane biogenesis and a major distribution hub for lipid trafficking to and from the cell. It is not surprising, then, that the endoplasmic reticulum (ER) is the focus of the cellular response to stress arising from lipid overload or lipid depletion. The ER stress response has been defined by delineating the biochemical signals and associated adaptations triggered by misfolded ER lumenal proteins or defects in protein glycosylation. Those stressors, acting through their downstream transcriptional effectors, also elicit significant changes in lipid metabolism, linking ER lipid homeostasis and protein quality control.

The transcriptional changes activated by ER stress target the biosynthetic pathways for cholesterol, fatty acid, phospholipid and/or triglyceride biosynthesis and can result in significant alterations in lipid composition, depending on the cell lineage and nature of the stress. Fatty acids, whether derived from the diet or synthesized de novo, are destined for either destruction by oxidation or incorporation into membrane structural lipids. If the fatty acid supply exceeds the capacity of these two processes, the excess fatty acids are converted to cholesterol esters and triglycerides and packaged into lipid droplets. Lipid droplet accumulation serves as an outlet to relieve the stress of fatty acid overload on ER membrane lipid biogenesis.

LipidomicsWiki (www.lipidomicnet.org) provides a common lipid knowledge base that is a freely available resource for all biomedical scientists.

LipidomicNet

In September, the 50th International Conference on the Bioscience of Lipids was held in Regensburg, Germany. The five-day meeting focused on the biological and regulatory functions of lipid molecular species, but each session had presentations that touched on factors that govern lipid homeostasis and lipid droplet formation.

The presentations reflected the early development of LipidomicNet, the European Union Framework VII project focused on the structure of lipid droplets and their function in human health and disease that kicked off just last year. Lipid droplet formation is a hallmark of "energy-overload" metabolic diseases that are a major heath concern. One goal of LipidomicNet is to integrate lipid structure profiles with proteome and transcriptome analysis to reveal the interrelationship between gene expression and lipid droplet formation.

The project also manages the LipidomicNetWiki (www.lipidomicnet.org), in close collaboration with LIPID Metabolites and Pathways Strategy (LIPID MAPS) and Lipid Bank-Japan. One hope is that those investigators who "bump" into lipid metabolism in their work will take advantage of the LipidomicsWiki to help sort out the cellular responses to metabolic stress.

All members of the Lipidomics Expertise Platform are allowed to edit and add content to LipidomicNet-Wiki, so I encourage you to register with the LEP (http://bit.ly/2Y2nOo) and start contributing.

As for preventing holiday stress, I recommend watching out for lipid overload! XXXX

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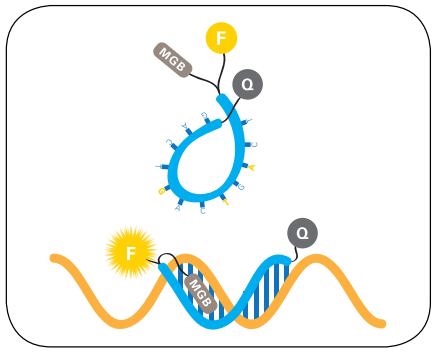

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scientific meeting calendar

DECEMBER 2009

49th Annual Meeting of the American Society for Cell Biology
DECEMBER 5–9, 2009
SAN DIEGO, CA
www.ascb.org/meetings

JANUARY 2010

Keystone Symposium—Structural Genomics: Expanding the Horizons of Structural Biology
JANUARY 8–13, 2010
BRECKENRIDGE, CO
keystonesymposia.org

Keystone Symposium—Triglycerides and Triglyceride-rich Particles in Health and Disease
JANUARY 9–14, 2010
BIG SKY, MT
keystonesymposia.org

Keystone Symposium—Molecular Basis for Biological Membrane Organization and Dynamics
JANUARY 10–15, 2010
SNOWBIRD, UT
keystonesymposia.org

Keystone Symposium—Adipose Tissue Biology
JANUARY 24–29, 2010
KEYSTONE, CO
www.keystonesymposia.org

5th Human and Medical Genetics Meeting
JANUARY 28–30, 2010
STRASBOURG, FRANCE
www.assises-genetique.org/fr

FEBRUARY 2010

15th Annual Proteomics Symposium
FEBRUARY 4–7, 2010
LORNE, AUSTRALIA
www.australasianproteomics.org

Gordon Research Conference—Glycolipid and Sphingolipid Biology
FEBRUARY 7–12, 2010
VENTURA, CA
www.grc.org

Keystone Symposium—Advances in Molecular Mechanisms of Atherosclerosis
FEBRUARY 12–17, 2010
BANFF, CANADA
keystonesymposia.org

AAAS Annual Meeting
FEBRUARY 18–22, 2010
SAN DIEGO, CA
www.aaas.org/meetings

Biophysical Society 53rd Annual Meeting
FEBRUARY 28–MARCH 4, 2009
BOSTON, MA
www.biophysics.org/2009meeting

MARCH 2010

Deuel Conference 2010
MARCH 2–5, 2010
DANA POINT, CA
deuelconference.org

3rd Singapore Lipid Symposium
MARCH 3–5, 2010
NATIONAL UNIVERSITY OF SINGAPORE, SINGAPORE
www.lipidprofiles.com/index.php?id=82

Keystone Symposium—Biomolecular Interaction Networks: Function and Disease
MARCH 7–12, 2010
QUEBEC CITY, CANADA
www.keystonesymposia.org

APRIL 2010

Keystone Symposium—Diabetes
APRIL 12–17, 2010
WHISTLER, CANADA

4th ESF Functional Genomics Conference
APRIL 14–17, 2010
DRESDEN, GERMANY
www.esffg2010.org

ASBMB Annual Meeting
APRIL 24–28, 2010
ANAHEIM, CA
www.asbmb.org/meetings.aspx

MAY 2010

Euro Fed Lipid International Symposium on Microbial Lipids
MAY 13–15, 2010
VIENNA, AUSTRIA
www.eurofedlipid.org

2010 American Thoracic Society International Conference
MAY 14–19, 2010
NEW ORLEANS, LA
www.thoracic.org

101st AOCS Annual Meeting and Expo
MAY 16–19, 2010
PHOENIX, ARIZONA
www.aocs.org

6th International Atherosclerosis Society Workshop on High Density Lipoproteins
MAY 17–21, 2010
WHISTLER, CANADA
www.athero.org

JUNE 2010

3rd European Workshop on Lipid Mediators
JUNE 3–4, 2010
PARIS, FRANCE
www.workshop-lipid.eu

8th International Conference on Hyaluronan of the International Society for Hyaluronan Sciences
JUNE 6–11, 2010
KYOTO, JAPAN
www.ISHAS.org

Keystone Symposium—Bioactive Lipids: Biochemistry and Diseases
JUNE 6–11, 2010
KYOTO, JAPAN
www.keystonesymposia.org

78th European Atherosclerosis Society Congress
JUNE 20–23, 2010
HAMBURG, GERMANY
www.kenes.com/eas

Gordon Research Conference—Lipoprotein Metabolism
JUNE 20–25, 2010
WATERVILLE VALLEY, NEW HAMPSHIRE
www.grc.org/programs.aspx?year=2010&program=lipopro

11th International Symposium on the Genetics of Industrial Microorganisms
JUNE 28–JULY 1, 2010
MELBOURNE, AUSTRALIA
www.gim2010.org

SEB Annual Main Meeting
JUNE 30–JULY 3, 2010
PRAGUE, CZECH REPUBLIC
www.sebiology.org/meetings

JULY 2010

Scandinavian Pediatric Obesity Conference (SPOC) 2010
JULY 9–10, 2010
STOCKHOLM, SWEDEN
www.childhoodobesity.info/spoc2010

19th International Symposium on Plant Lipids
JULY 12–16, 2010
CAIRNS, AUSTRALIA
http://ispl2010.org

AUGUST 2010

24th Annual Symposium of the Protein Society Looking at Proteins: Expanding Perspectives and New Technologies
AUGUST 1–5, 2010
SAN DIEGO, CA
www.proteinsociety.org

9th International Mycological Congress (IMC9): The Biology of Fungi
AUGUST 1–6, 2010
EDINBURGH, UNITED KINGDOM
www.imc9.info

14th International Congress of Immunology
AUGUST 22–27, 2010
KOBE, JAPAN
www.ici2010.org

SEPTEMBER 2010

British Mass Spectrometry Society Meeting
SEPTEMBER 5–8, 2010
CARDIFF, WALES
www.bmss.org.uk

HUPO 9th Annual World Congress
SEPTEMBER 19–24, 2010
SYDNEY, AUSTRALIA
www.hupo.org

OzBio2010
SEPTEMBER 26–OCTOBER 1, 2010
MELBOURNE, AUSTRALIA
www.asbmb.org.au/ozbio2010

Transcriptional Regulation by Chromatin and RNA Polymerase II
SEPTEMBER 30–OCTOBER 4, 2010
TAHOE CITY, CA
www.asbmb.org/meetings.aspx

OCTOBER 2010

Biochemistry and Cell Biology of ESCRTs in Health and Disease
OCTOBER 14–17, 2010
SNOWBIRD, UT
www.asbmb.org/meetings.aspx

Post Translational Modifications: Detection and Physiological Evaluation
OCTOBER 21–24, 2010
TAHOE CITY, CA
www.asbmb.org/meetings.aspx

Biochemistry of Membrane Traffic: Secretory and Endocytic Pathways
OCTOBER 28–31, 2010
TAHOE CITY, CA
www.asbmb.org/meetings.aspx

Asian-Pacific Society of Atherosclerosis and Vascular Diseases (APSAVD) 2010 Congress
OCTOBER 27–29, 2010
CAIRNS, AUSTRALIA
apsavd.org

NOVEMBER 2010

8th Euro Fed Lipid Congress
NOVEMBER 21–24, 2010
MUNICH, GERMANY
www.eurofedlipid.org

APRIL 2011

ASBMB Annual Meeting
APRIL 9–13, 2011
WASHINGTON, D.C.
www.asbmb.org/meetings.aspx