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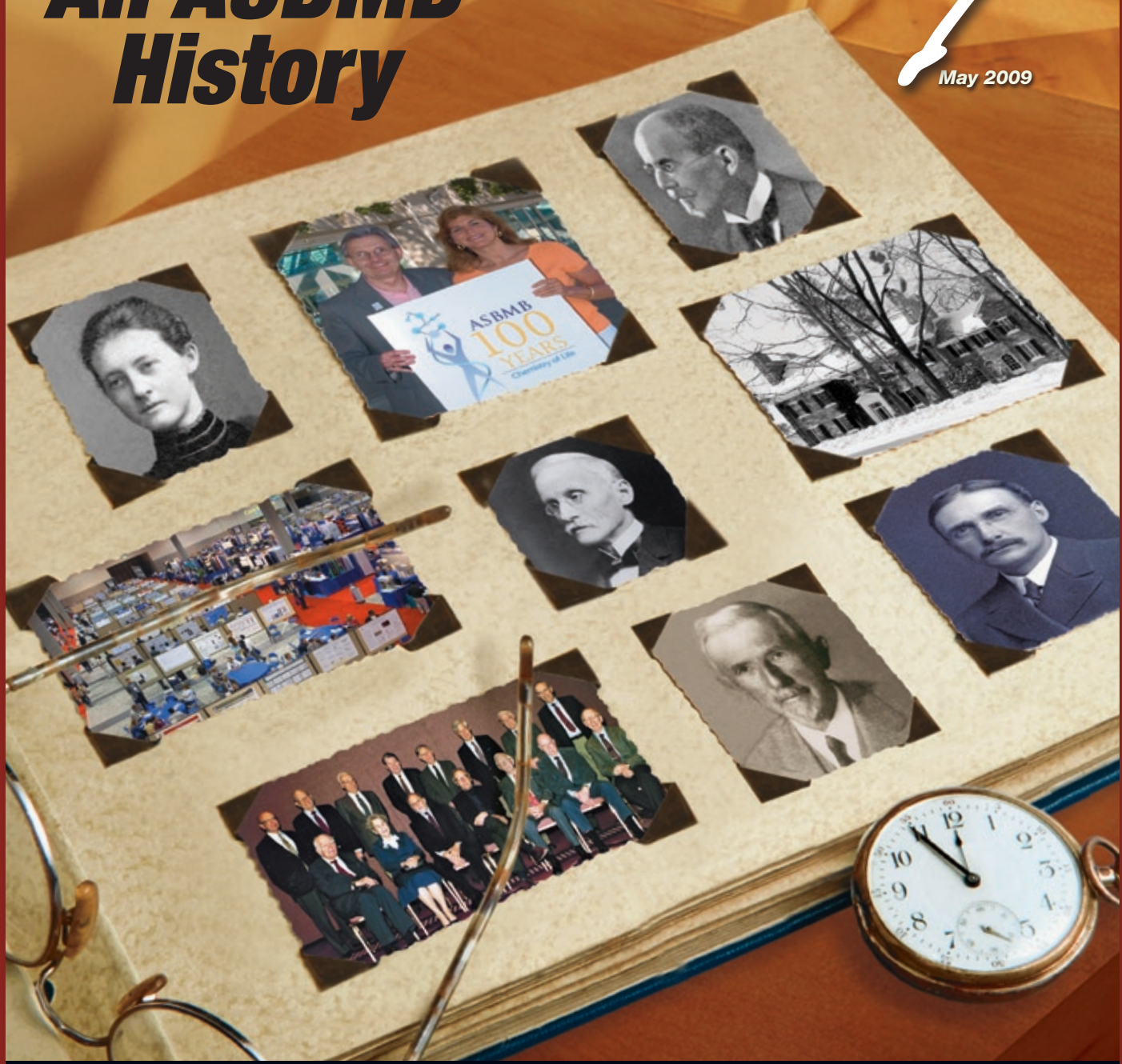
May 2009



American Society for Biochemistry and Molecular Biology

STUDENT CENTERED EDUCATION IN THE MOLECULAR & LIFE SCIENCES:

Essentials for Educating Biochemistry & Molecular Biology Undergraduates

August 5-8, 2009
Colorado College, Colorado Springs, Colorado

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A Call to Action – Opening Plenary
Liberal Learning in Life Sciences
Teaching Biochemistry and Molecular Biology
Incorporating Math into Biochemistry and Molecular Biology
Faculty Mentoring
Communicating Science
Thinking Creatively As a Teacher-Scholar

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Undergraduate Research – How to Establish Effective
Undergraduate Research at a PUI institution
Service Learning and Outreach
Molecular Visualization
Biochemistry and Molecular Biology and Liberal Education
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Best Practices in BMB Teaching
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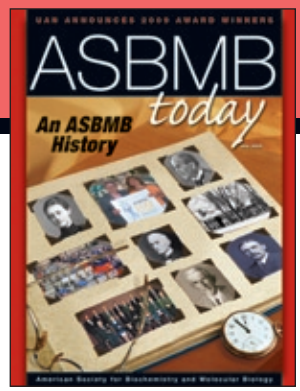

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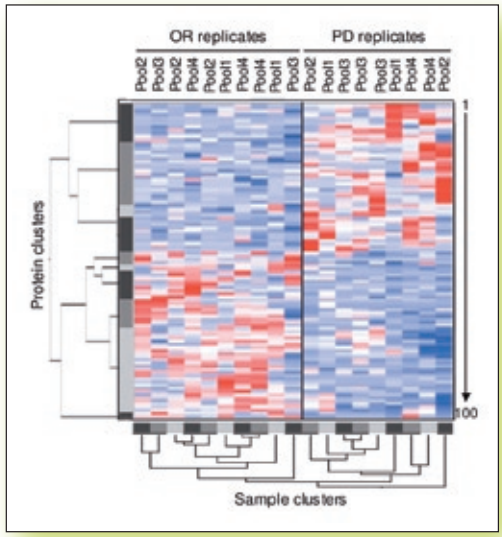

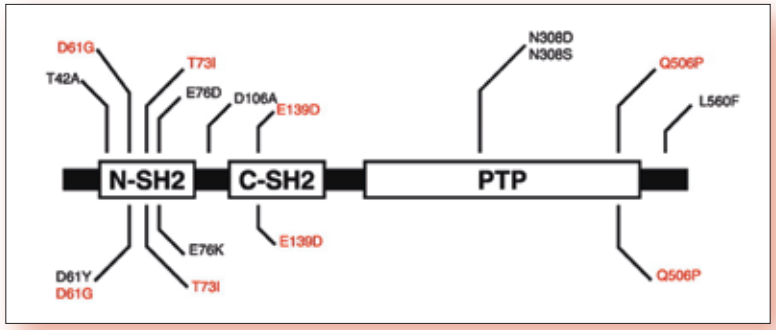

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podcast summary

Tune into this month's podcasts and hear interviews with the authors of the *JBC* thematic minireview series "Metals in Biology" and "The Biochemical Basis for Triplet Repeat Neurodegenerative Diseases."

You can listen to the podcasts at www.asbmb.org/Interactive.aspx

ASBMB today

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2008 APEX® AWARDS FOR PUBLICATION EXCELLENCE

letter to the editor

Facts and Fictions

Dear ASBMB,

Rewriting history is an unsavory process that creates confusing paradoxical views between those who believe and those who remember. Your ASBMB interview with Daniel Steinberg illustrated some of the allusions and illusions (and the "drift" in truth) that underlie "The Cholesterol Wars." Of course, you merely report what Steinberg answered, and the task of verifying a story remains for some other venue. If you had the time to do so, you might have seen how the facts were misrepresented in your article. Steinberg claimed that Norum's questionnaire asked: "Do you think that the evidence supports cholesterol as a major contributor to atherosclerosis and heart attacks?" and he also claimed that the "experts" said "yes" to that question. They did not. This is how misunderstandings begin.

The scientists in 1978 clearly saw an ASSOCIATION of food calories with elevated blood cholesterol. They did not elevate the association to a PROOF OF CAUSE—as Steinberg implies. We still have concerns about the flow of information today.

One vital principle is that majority votes do not constitute a logical scientific proof.

Sincerely yours,
William E. M. Lands

RESPONSE

Dear Dr. Lands,

Thank you for your input on this topic. First, we would like to state that our ASBMB Roundtable series is designed to be informative yet informal and that the views expressed by the speakers are their own thoughts and perceptions on matters of interest. In regard to the specifics of the question, I have carefully looked over Norum's questionnaire (Norum, K. R. (1978) *Nutr. Metab.* **22**, 1–7), and yes, the particular question highlighted in your letter was phrased differently than as Dr. Steinberg stated. The question reads: "Do you think there is a connection between plasma cholesterol levels and the development of coronary heart disease?"

However, it may not be entirely accurate to label Dr. Steinberg's comments as a misrepresentation of the truth; rather, it is just his interpretation of an open-ended question. For although Norum's questions do not specifically address a "proof of cause," they do not discount it either, and as one of the 200+ scientists who took part in the survey, Dr. Steinberg is simply relating his belief in what the question means. It is possible that many of the other survey participants believed the connection was causal as well; we cannot be sure. However, it is interesting to note that Norum himself pointed out that, because a few of the survey participants hesitated to call any dietary connections "causal," the answers to the key question, "Do you think that our knowledge about diet and coronary heart disease is sufficient to recommend a moderate change in the diet for the population in an affluent society?" were of great interest. And in this area, 92 percent said "Yes," suggesting a belief that diet and cholesterol play a contributory role, as Steinberg said.

Nick Zagorski
ASBMB Science Writer

Too Big to Succeed?*

BY GREG PETSKO

We hear the phrase "too big to fail" a lot these days. It means that a company is so vital to the national economy that its demise would be catastrophic, so the government will go to extraordinary lengths to keep it afloat. General Motors Corporation, the sinking U.S. car maker, is said to be too big to fail. Lehman Brothers, the investment bank whose collapse precipitated financial crises around the world, was too big to fail—although George W. Bush's Secretary of the Treasury, Henry Paulson, didn't realize that in time. And, as the world credit market tries to become unstuck before a global depression sets in, we hear the same thing about two U.S. bank holding companies, Bank of America and Citibank.

But what exactly does it take to make a company too big to fail? In the case of General Motors, it is the huge number of jobs that would be lost if it went under, but that consideration doesn't apply to a financial services firm, at least not directly. In the case of banks, it's the magnitude of the monetary loss that matters. Bank of America has assets of approximately $2.7 trillion and Citibank has assets of around $2.3 trillion. The Gross Domestic Product (GDP) of the United States is $14 trillion, so each of these banks has assets in excess of 14 percent of the yearly output of the largest economy on Earth. That's too big to fail.

But I would argue that, if you can be too big to fail, you also can be too big to succeed. Your very size can be your undoing, as it may have been for the huge, lumbering dinosaurs who weren't flexible enough to survive the global catastrophe that our small, furry, mammalian ancestors were able to weather.

Consider the two giant banks. Over $2 trillion in assets sounds great, right? Well, maybe, but there's also the small matter of their liabilities. Both banking companies hold enormous quantities of so-called "toxic securities," which is a polite way of saying mortgage-backed debts. As many of the mortgages are effectively worthless, these companies may have huge liabilities. It's estimated that there might be as much as $11 trillion of such debt in the U.S. economy, because many large banks essentially bet the farm on the incredibly naive idea that house prices would rise forever. The fact that they had always gone through cycles of rising and falling for, oh, the previous 5,000 years or so, seems to have been lost on the self-styled geniuses who created the mess we're in.

The real problem, though, is that nobody knows if that $11 trillion figure is right because nobody knows what the toxic securities are really worth. They may be worth anything from close to their nominal value to zero, and that's a heck of an error bar. So let's look at Citibank. Yes, it has $2.3 trillion in assets, but it also has big liabilities. How big? It's unknown. There might be, say, $1 trillion in liabilities, in which case Citibank is in great shape. But there could well be $3 trillion in liabilities, in which case this enormous bank is actually broke. And no one, not the chief executive of Citibank nor the head of the U.S. Treasury nor a gypsy reading tea leaves, can say which is the case. The banks had grown so large and had created such an elaborate web of interdependent, chopped-up, over-leveraged securities that their own financial people had no real idea of how much debt they were taking on.

In other words, I think Bank of America and Citibank (as well as Lehman Brothers and most of the other companies at the heart of the global financial crisis) have become too big to succeed because they are too big to be managed. No one individual—or group of individuals—can assimilate the amount of information needed to keep tabs on what goes on at a company that size, so even if they themselves are not crooked or incompetent, they are fated to be hostages to crooked or incompetent people who work, undetected, at some lower level of the Byzantine corporate structure. Yet, until recently, these companies were touted as the epitome of excellence, precisely because, through mergers and acquisitions, they had grown so enormous.

Why do we mistake growth for success? When did sheer size become equivalent to excellence? Because a monomaniacal insistence on being the biggest so often derives entirely from the person at the top, it seems fair to ask if there isn't some psychological explanation. *Washington Post* columnist Sally Jenkins had a marvelous article in the February 19, 2009 issue, titled "Arm-

chair Field Generals, Getting Sacked on Wall Street," in which she notes that the hypercompetitive CEOs of large corporations were usually good sportsmen but never quite good enough to become great. "Maybe the real lesson," she writes, "is to beware of the wannabe. Some of these people seem to fall into the dangerous category of 'pretty good' athletes… Experience plus some armchair Freudian analysis tells us there are a fair number of overcompensated jerks out there who almost made it in sports… There's the sneaking suspicion that more than one shareholder is suffering from these guys' sublimated failures to reach the top in the more primal competitions of their youth… The most important quality of leadership," she goes on to state, "is not competitiveness, but judgment."

And as corporate boards, which appoint CEOs, are usually stocked with present or past CEOs of other corporations, it shouldn't surprise us when these win-at-all-cost shortsighters pick people like themselves to head the companies they oversee. And so the culture of "whoever has the most when he dies, wins" goes merrily on.

But where did that culture come from, and why did it get so out of control? I think the answer might be pretty simple, and if I'm right, it explains why I also think the current debate about excessive CEO compensation misses the point. You will recall that, as part of the financial bailout, the government proposed to limit the bonuses and other payouts to the CEOs of the corporations receiving federal funds, which provoked an immediate outcry on the part of their boards, the claim being that, without enormous compensation, companies would not be able to hire or retain the best people. Don't worry about this side issue, they said, fix the real problems.

Well, never mind that "the best people" have just lost hundreds of billions of dollars and nearly wrecked the economy of the world. (I could do that and would happily accept a lot less in pay and bonuses than they keep demanding.) And never mind that I am unaware of a single study that shows a correlation between the salary and bonuses paid to executives and their talent (in fact, in many professions, like ours, money usually isn't the motivating factor in a career at all). The uproar in the United States over bonuses just paid to some of the very employees of the insurance giant AIG, who caused the mess that the company is now in, suggests that the public has realized something that the Bush Administration never did and that the Obama Administration may not have figured out yet: CEO compensation is not a side issue; CEO compensation is the problem. If you offer outrageous salaries to people who run your companies and give them even more outrageous bonuses if they increase share prices and revenues—not profit, revenues—then it stands to reason that you will probably attract greedy, aggressive people who are only interested in short-term results. That's what created the Wall Street culture that has gotten us into this fix.

And the reason you're reading this in *ASBMB Today*, instead of in *The Economist*, is that I fear this culture may now be spreading, like some virulent flu strain, to the pharmaceutical industry. Look at what has happened in the past 15 years. A wave of mergers is threatening to reduce the number of so-called "big pharma" companies to a handful, and the results haven't always been pretty. Pfizer almost choked to death from swallowing Pharmacia/Upjohn a few years ago and now is planning to acquire Wyeth. Merck has announced plans to merge with Schering-Plough. And analysts (more about them later) are busily proposing other fusions.

> **"There are no data indicating that increasing the size of a pharmaceutical company leads to increased ability to make pharmaceuticals."**

I'm not sure this trend makes much sense from the point of view of the primary purpose of these companies, which is to discover new drugs (although in the short term it may help fill one of the companies' empty pipelines). There are no data indicating that increasing the size of a pharmaceutical company leads to increased ability to make pharmaceuticals. In fact, there are worrying suggestions that it may often do the opposite. Innovation usually scales inversely with bureaucratic complexity. If a merger or acquisition is proposed solely for the purpose of acquiring a drug that one company makes, longer term issues of research complementarity or synergy of talent might get secondary consideration, leading to internal culture wars and strategic paralysis.

Recent history may bear this out. Despite more than a decade of mergers and acquisitions, big pharma actually makes no more drugs per company today than it did in 1995 (although one has to be careful to take into account drug approval rates by regulatory agencies, which also change with time). Larger companies also have a tendency to be more conservative, so the worry is that

innovation could suffer as firms merge. Biopharmaceuticals, the newest trend in the industry and the source of about 50 percent of its profits last year, originated in biotechnology companies, not pharmaceutical houses. The notion that proteins such as antibodies could be profitable drugs was resisted for years by big pharma, which is now scrambling furiously to catch up.

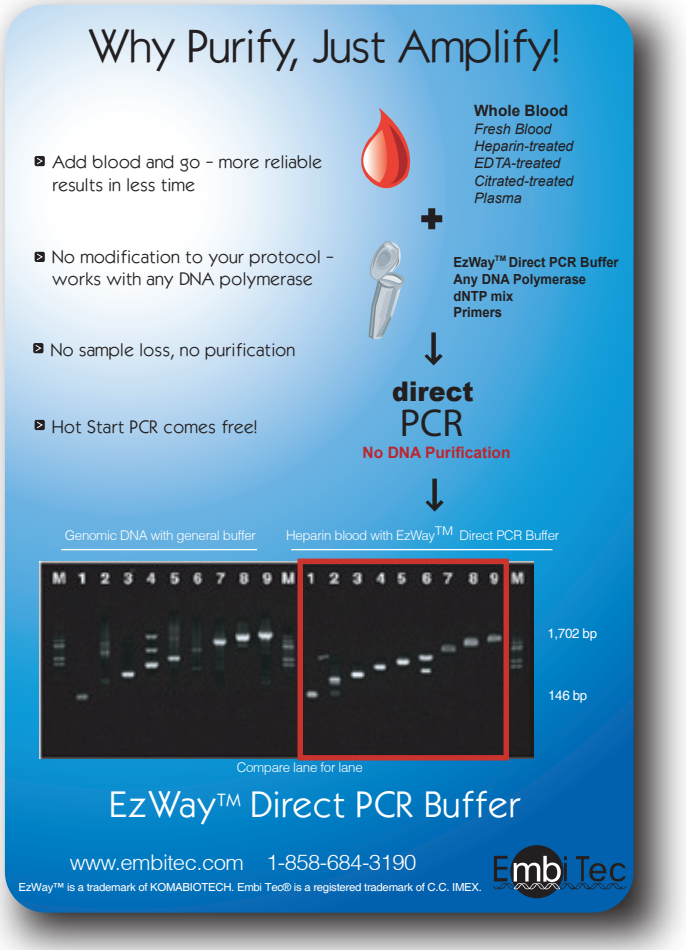
Of course, giant pharmaceutical companies can buy innovation, new targets, and even lead compounds from small biotech companies—and frequently do. That may well be the future: big pharma outsourcing target discovery and some other aspects of innovation to smaller, independently-operating biotech arms, with the parent company focusing on chemistry, testing, and marketing. It might not be a terrible model, but I still think we'd end up with fewer drugs, since the large pharmaceutical companies actually used to discover the bulk of them, and there are a lot of weak biotechnology companies out there.

Industry analysts love to tout mergers and acquisitions as tools to raise share prices, and if stockholders clamor for their advice to be followed, it can seriously affect those share prices. I've never understood why analysts seem to exert such influence on the market. I've known a few, and I have to say I was not that impressed. It seems crazy that part of the financial health of companies whose output is so important to human health should rest with people who are not scientists or business executives, who don't have the public welfare in mind, and whose track record is spotty, to say the least.

I'm not trying to bash the pharmaceutical industry here. I have enormous respect for it and for the people who work in it; most of them are motivated by a sincere desire to improve the health of mankind. It's that respect that leads to my concern for the industry's own health. Some mergers and acquisitions are good ones, of course, but I remain unconvinced that, overall, a few huge drug companies will innovate better than a larger number of smaller ones, even with the help of biotech partners.

The notion that something can be too big to succeed shouldn't be that foreign because it even applies to people. There's a famous example of an individual who became so big and lumbering that he was easily bested by a smaller, more nimble adversary. You'll find his story in Chapter 17 of the First Book of Samuel. His name was Goliath.

*adapted with permission from *Genome Biol.* (2009) **10**, 103.



FASEB Follows New Legislation, Works to Reduce Regulatory Burden

BY CARRIE D. WOLINETZ AND JENNIFER A. HOBIN

Bills on Animal Research, Gender Equity in Science, and International Science

FASEB is watching two recently reintroduced bills and one new bill in the House that could affect biomedical researchers. The Great Ape Protection Act (H.R. 1326) would eliminate the use of chimpanzees and other great apes in research. In the previous Congress, the bill had few sponsors and was referred to three separate committees. The new version of the bill has 44 co-sponsors and has been referred solely to the House Energy and Commerce Committee, increasing its chance of passage. FASEB opposes the measure because of the importance of chimpanzees in ongoing research. The legislation has the strong support of the Humane Society of the United States.

Another bill that has resurfaced in the 111th Congress is the Fulfilling the Potential of Women in Academic Science and Engineering Act (H.R.1144), whose main sponsor is Rep. Eddie Bernice Johnson of Texas, and aims to promote gender parity in STEM at the university faculty level. The legislation, which has been referred to the Science Committee, would direct federal agencies to: (1) hold workshops with study section members and department chairs on gender bias and (2) develop policies to extend research grant support and/or hire interim technical help during times of family leave.

Finally, the Science Committee is considering the International Science and Technology Cooperation Act (H.R. 1736), which would establish a new committee under the National Science and Technology Council. The mission of this committee would be to (1) coordinate interagency activities related to cooperative international research and training; (2) establish priorities to align international science activities with foreign policy goals; and (3) identify opportunities for new international science and technology cooperative research and training activities. None of the three bills has yet been introduced in the Senate.

Encouraging OMB to Reduce Regulatory Burden

FASEB sent a letter to the Office of Management and Budget (OMB) in response to an OMB request for information intended to inform the development of a set of recommendations for a new Executive Order on federal regulatory review. Responding to a directive from President Obama, OMB's recommendations are to offer suggestions related to the disclosure and transparency of regulations, the role of cost-benefit analysis in the development of regulations, public participation in agency regulatory processes, and identification of methods to ensure that regulatory review does not produce undue delay, among other issues.

In its letter, FASEB expressed concern that the cumulative burden of regulations is having a deleterious effect on scientific productivity. Citing research conducted by the Federal Demonstration Partnership, FASEB noted that scientists devote 42 percent of the time they spend on federally funded research to administrative and regulatory activities. In addition, federal agencies and institutions spend $85 million on administrative tasks directly linked to those projects.

FASEB encouraged OMB to make every effort to ensure accountability and transparency in research while minimizing the administrative burden regulations place on the scientific community. The Federation encouraged OMB to review proposed regulations to determine whether or not the costs they impose are balanced by meaningful improvements to the current oversight system. Where new regulations are necessary, FASEB stated that they should be based on sound justification. In addition, they should be harmonized with existing regulations in order to avoid unnecessary duplication, confusion, and inconsistency.

FASEB also encouraged OMB to solicit input from the scientific community when making regulatory decisions related to science. The full letter may be found at tinyurl.com/d8aezn.

Carrie D. Wolinetz is Director of Scientific Affairs and Public Relations for the Office of Public Affairs at FASEB and can be reached at cwolinetz@faseb.org. Jennifer A. Hobin is a Senior Science Policy Analyst for FASEB OPA. She can be reached at jhobin@faseb.org.

Showcasing the NSF

BY ALLEN DODSON

Speaker of the House of Representatives Nancy Pelosi repeated her familiar refrain, "science, science, science, and science," at the 15th annual Capitol Hill Exhibition held by the Coalition for National Science Funding (CNSF). The presence of such a prominent policymaker at the event was less familiar but was welcomed as a hopeful sign after years of flat budgets at the National Science Foundation (NSF).

ASBMB was one of 31 professional societies, organizations, and institutions that participated in the March 24th exhibition. As part of this effort, the Society brought the following NSF awardees to Washington to meet with their Congressional delegations and to explain the importance of the NSF:

- **Rasul Chaudhry** (Oakland University in Michigan) has a grant from the NSF's Office of International Science and Engineering to collaborate with researchers at the University of Rajshahi in Bangladesh. This work examines the effects of the pesticide carbofuran on local crops.
- **Michael Harris** (Case Western Reserve University's School of Medicine) has an NSF award to study the nucleophilic activation of water in enzyme catalysis using mass spectroscopy.
- **Lee Swem** (an NSF-supported postdoctoral fellow at Princeton University) presented the poster for ASBMB's exhibit, describing his work on drugs that affect bacterial quorum sensing—cell to cell communication that helps the bacteria to react to their environment.
- **Julio Turrens** (Associate Dean at the University of South Alabama) heads the University's Research Experiences for Undergraduates program. His NSF grant has supported dozens of undergraduates for 10-week research projects on the structure and function of proteins.

The group was able to visit 13 House and Senate offices, representing five states, to emphasize the value of continued support for the NSF.

Though the NSF is a smaller agency than the NIH—its budget in 2009 is $6.5 billion compared to the NIH's $30.3 billion—it bears a heavy burden. ASBMB estimates that 15 percent of our members receive direct support from the NSF, but that number merely scratches the surface of the agency's impact. NSF funding is a major source of support for research in chemistry, physics, the social sciences, and basic biology. These projects ultimately produce the new technologies and methods that make advances in biomedical research possible. In addition, NSF funds a number of education programs, such as the one run by Turrens, that play a significant role in preparing the next generation of researchers for careers in science.

The ASBMB delegation: (*left to right*) Julio Turrens, William Merrick, Lee Swem, Mike Harris (*back*), and Rasul Chaudhry.

Speaker Pelosi, who attended the exhibition, along with Reps. Rush Holt (D-NJ), Bart Gordon (D-TN, Chair of the House Science Committee), and Vern Ehlers (R-MI), has received much of the credit for the recent attention to NSF in the fiscal year 2009 omnibus appropriations bill and the economic stimulus package. However, she was quick to credit the advocacy community for providing the justification—showcased at the exhibition—for continued support to the agency, which she views as crucial to the nation's economic recovery. ASBMB, in turn, could not advocate for this important cause without the support of members such as the CNSF delegation who flew to Washington and the hundreds of others who have answered email advocacy alerts in support of NSF in the past. Together, we can all work for "science, science, science," and perhaps a little bit more science, in our future.

Allen Dodson is an ASBMB Science Policy Fellow. He can be reached at adodson@asbmb.org.

Email the author to join ASBMB's Local Advocacy Network for the latest updates on ASBMB's advocacy efforts.

Speaker Pelosi's prepared remarks are available online at: www.speaker.gov/newsroom/speeches?id=0177.

House, Senate Pass Budget Resolutions; Obama Budget Priorities Largely Intact

BY PETER FARNHAM

The first week of April saw action in both the House and Senate on the annual budget resolution, a spending blueprint that Congress is supposed to pass each year by May 15. The House passed its version of the resolution on April 2 on a near party line vote (no republicans voted for the resolution and only a few democrats voted "no"). The Senate followed suit that same afternoon, also adopting its version of the resolution with no GOP votes.

The budget resolution is not a binding document in large part. It sets broad spending goals by category (called "functions"). The two functions of most interest to biomedical research are Function 250, "science, space, and technology," and Function 550, "health." The amounts included in these functions are not binding. The only number in the resolution that is binding is the overall total for discretionary spending, which includes all funds the federal government spends (including funds for defense, which is about half of discretionary spending) that are not mandated by law; that is, the amounts that cover spending on everything in the federal government except Social Security and other entitlements, and interest on the national debt.

The non-defense discretionary total in the House budget resolution is $533 billion for fiscal year 2010, which begins on October 1 of this year. The overall House-approved budget is for $3.45 trillion. As can be seen, the amount of money that is available to Congress to spend on non-defense discretionary items is less than 14 percent of the total budget.

The House resolution also includes a statement that the "resolution builds on significant funding provided in the American Recovery and Reinvestment Act (the President's stimulus package) for scientific research."

The House budget resolution also largely protects the increases President Obama seeks for his trinity of priorities—health care, education, and energy. House Budget Committee Chairman John Spratt (D-SC) notes: "…the President's budget launches initiatives to make our economy more productive and our people more competitive: first, in education and in Pell Grants in particular; next, in health care for the millions uninsured; and finally, in alternative energies to reduce our dependence on foreign oil and the depletion of our environment. This mark upholds those priorities."

In the Senate, Budget Chairman Kent Conrad (D-ND) also "preserves the major priorities in President Obama's budget." The resolution provides an overall figure of $3.5 trillion, including $525 million in non-defense discretionary spending. The Senate budget resolution also specifically singles out the National Institutes of Health, noting that the Senate "continues to support funding for NIH in 2010 including support for cancer research." Readers will recall from the last issue of *ASBMB Today* that the President's budget summary referred to $6 billion in cancer research at NIH, although there were no details provided as to what this figure meant at the time. The Senate budget resolution sheds no light on the matter either.

The differences between the House and Senate ver-

sions must be ironed out, as with all legislation. The Congress is in recess for the Easter and Passover holidays for most of the first half of April, but the staff is ironing out differences between the two resolutions, and once the Congress returns later in the month, an agreement is expected soon thereafter.

The budget is expected to be approved by both Houses handily once differences are ironed out. Although the GOP still has enough strength in the Senate to filibuster the resolution if it chooses to do so (assuming all GOP senators remain opposed), the majority has indicated its willingness to use the reconciliation process to pass the bill. Under reconciliation, only a simple majority of 51 senators is needed to pass the bill, rather than the 60 needed to pass a bill if a filibuster has been launched. The process was intended as a mere book-keeping process when it was adopted as part of the Budget Act of 1974; its purpose is to reconcile existing law with the new spending plan laid out in the budget. But it has been used by both parties to pass large, difficult bills that are important to the particular administration's priorities (Presidents Reagan and Clinton both used it to advance their agendas during their presidencies).

There would be little the GOP could do to oppose this use of the reconciliation process.

The budget resolution also does not require a president's signature, and he cannot veto it. However, he retains the right to veto any legislation put forth intended to advance the goals of the budget resolution. In a Congress solidly under the control of the President's own party, however, this is an unlikely scenario.

Peter Farnham is Director of Public Affairs at ASBMB. He can be reached at pfarnham@asbmb.org.

ASBMB Members Visit the Hill: Second of Two Hill Days a Big Success

On March 25, ASBMB members came to Washington to lobby for the budget of the National Institutes of Health, making it two "Hill Days" in a row (see Allen Dodson's story on p. 7 about the NSF-focused hill day on March 24). The NIH hill day was organized by the staff of the Coalition for the Life Sciences, of which ASBMB is a new member (the CLS was once known as the Joint Steering Committee for Public Policy, and ASBMB renewed its membership last fall after a five-year hiatus).

ASBMB members attending the hill day under ASBMB's sponsorship were William Merrick, Case Western Reserve University Medical School (and deputy chairman of the Public Affairs Advisory Committee); his colleague at Case Western, Michael Harris; Bettie Sue Masters, University of Texas, San Antonio Health Sciences Center; and Leslie Parise, University of North Carolina.

Visits were arranged with the staff of 31 House and Senate members, and ASBMB members met with more than half the representatives involved during the course of the day. A high point of the day was a personal meeting with Rep. David Price (D-NC) who dropped by unexpectedly at a meeting with a member of his staff. He stayed and chatted for several minutes, making it very clear that he continued to support NIH and would work on behalf of NIH, although progress would be difficult due to budgetary constraints.

In fact, Price's comments about NIH were very typical of the day; virtually no one had anything other than praise for NIH's work and mission. The only cautionary points made were related to the difficult budgetary situation the nation faces, which constrains the amount of resources available to the agency this year. Furthermore, most Representatives and Senators were aware of the impact of the $10 billion in stimulus money that NIH will be receiving in 2009 and 2010. However, no one raised this money as a reason not to fund NIH further in the regular appropriations process, either this year or in future years.

The luncheon briefing featured David Botstein, Princeton University, who presented a talk about his research under the aegis of the Congressional Biomedical Research Caucus. Rep. Bart Gordon (D-TN), chairman of the House Science Committee, attended the caucus as well.

The Coalition for Life Sciences was organized in 1991, and current members, in addition to ASBMB are the American Society for Cell Biology, The American Society for Clinical Investigation, the Genetics Society of America, the Howard Hughes Medical Institute, the Society for Neuroscience, and the Society for Science and the Public.

Hill visits are an excellent way to advocate for issues of concern to biomedical research. ASBMB will be participating in and organizing several more hill days this year. If you are interested in coming to Washington to spend a day advocating for biomedical research, please contact the ASBMB Office of Public Affairs at 301-634-7147, or email ASBMB's Director of Public Affairs, Pete Farnham, at pfarnham@asbmb.org.

Barbas and Hruby Win Cope Scholar Awards

BARBAS

HRUBY

Carlos F. Barbas III of The Scripps Research Institute and Victor J. Hruby of the University of Arizona are the recipients of 2009 Arthur C. Cope Scholar Awards. The awards, given by the American Chemical Society and sponsored by the Arthur C. Cope Fund, are intended to recognize and encourage excellence in organic chemistry.

Barbas was nominated "for exceptional creativity and pioneering studies in organic chemistry, particularly in the areas of organocatalysis and the application of organic chemistry to chemical biology." In his research program, Barbas designs zinc finger protein-based transcription factors for the directed regulation of gene expression and gene discovery; programs complex reaction mechanisms into antibodies and uses them to treat cancer; and develops new approaches to catalytic asymmetric synthesis with DNA, proteins, and small molecules (organocatalysis).

Hruby, who is a Regents Professor Emeritus of Chemistry at the University of Arizona, was honored for his groundbreaking contributions in organic chemistry related to design, synthesis, and evaluation of conformationally constrained amino acids and their incorporation into biologically relevant peptides. His research centers on biologically active peptides and peptide mimetics with an emphasis on hormones and neurotransmitters that affect human behavior.

Carlson Receives 2009 Genetics Society of America Medal

Marian B. Carlson, Professor of Genetics & Development and Microbiology at the Columbia University Medical Center, received the 2009 Genetics Society of America Medal. The medal recognizes outstanding contributions to genetics over the last 15 years and was given to Carlson in recognition of her research on understanding metabolic and growth regulation by protein kinases and critical aspects of eukaryotic gene expression.

Carlson's research focuses on the Snf1/AMP-activated protein kinase (AMPK) family. She is particularly interested in the regulation of the Snf1 pathway, with respect to both catalytic activity and subcellular localization of the kinase, and in the mechanisms by which Snf1 kinase regulates transcription. Carlson has identified the first upstream kinases for the Snf1/AMPK family and is currently investigating the roles of these kinases in responding to different stress signals. She has also identified the LKB1 tumor suppressor kinase, which is associated with a hereditary cancer syndrome, as an upstream kinase in the AMPK cascade.

Bond to Become Vice President-Elect for Science Policy

ASBMB Past-President Judith S. Bond, Professor and Chair of Biochemistry and Molecular Biology at the Pennsylvania State University, was elected FASEB Vice President-Elect for Science Policy. Bond will begin her term on July 1, 2009, will serve as Vice President-Elect through June 30, 2010, and will then take office as FASEB Vice President for Science Policy on July 1, 2010. In these positions, Bond will serve as a spokesperson for FASEB on matters of science policy.

The focus of research in Bond's laboratory is the structure, function, and regulation of proteolytic enzymes. She is particularly interested in the function, mechanism of action, regulation of biosynthesis, oligomeric assembly, and post-translational processing of secreted and cell surface mammalian metalloproteases called meprins. Bond was president of ASBMB from 2004 to 2006 and is currently an associate editor of the *Journal of Biological Chemistry.*

DeBose-Boyd and Spies Named Early Career Scientists

DEBOSE-BOYD

PHOTO: L. BRIAN STAUFFER, UIUC NEWS BUREAU

SPIES

Russell A. DeBose-Boyd, Associate Professor of Biophysics and Molecular Genetics at the University of Texas Southwestern Medical Center, and Maria Spies, Assistant Professor of Biochemistry and Biophysics in the School of Molecular and Cellular Biology at the University of Illinois at Urbana-Champaign, were named Early Career Scientists by the Howard Hughes Medical Institute. The pair is among 50 scientists given six-year appointments to the prestigious institute along with $1.5 million toward research. All of the researchers selected for these appointments have only been leading a lab for two to six years.

Debose-Boyd studies the regulation of HGM-CoA reductase, an enzyme that produces an intermediate in the synthesis of cholesterol. The cholesterol-lowering statins block HGM-CoA reductase, but, paradoxically, they also inhibit its degradation. As more enzyme accumulates, more statins are needed. By studying HGM-CoA reductase, Debose-Boyd hopes to improve the effects of statins or find alternatives to the drug.

Spies' lab studies DNA helicases and how they function in DNA repair. Specifically, she focuses on how different helicases perform a diverse set of activities, how they utilize unique structural features incorporated into otherwise conserved motor cores, and how other players in the genome maintenance pathways modulate activities of selected helicases, adapting them to desired cellular tasks.

Conn Selected for Media Award

P. Michael Conn, Associate Director and a senior scientist at the Oregon National Primate Research Center, was selected to receive the American College of Neuropsychopharmacology (ACNP) Media Award for his book *The Animal Research War.*

The award was established in 2002 to "honor a member of the print or electronic media who has made a major contribution to the education of the public about mental illness and substance abuse research, and the positive impact of research on treatment." It is intended to reflect the appreciation that members of the ACNP feel toward outstanding leaders in the media who inform and educate the public about the brain and scientific research in this field.

Conn, who is also Professor of Physiology and Pharmacology and Cell Biology and Development at Oregon Health and Science University, co-authored *The Animal Research War* with James V. Parker. The book tells the story of the impact of animal extremism on scientific discovery and the changing view of the public toward animals. It has received positive reviews in *Science* and the *Journal of Clinical Investigation* and has been referenced on National Public Radio's Science Friday/Talk of the Nation, and has also been referenced in the *LA Times*, *The Washington Post*, *The Scientist*, and the *American Scientist*.

Elgin Honored with Education Award

Sarah C. R. Elgin, the Viktor Hamburger Professor in Arts & Sciences at Washington University in St. Louis, was selected to receive the second Elizabeth W. Jones Award for Excellence in Education. The award, given by the Genetics Society of America, recognizes individuals or groups who have made a significant and sustained impact on genetics education. According to the Genetics Society, Elgin is "an indefatigable leader and innovator in science education for students of all levels."

Elgin has been an active proponent of science education at the K-12 level. In the early 1990s, she initiated a science education partnership between Washington University and the public schools in her St. Louis community to implement a novel "hands-on" science curriculum for grades K-8 and to bring hands-on DNA science to the high school genetics curriculum. Elgin was also awarded a Howard Hughes Medical Institute Professorship in 2002, which she used to develop a course that couples the expertise of Washington University's world-renowned Genome Center with the enthusiasm and interest of undergraduates for the field of genomics. Additionally, Elgin and her husband endowed the Elgin Fund for Summer Student Research at Pomona College, and she has served for three years as a founding co-Editor-in-Chief of *Cell Biology Education* (now *CBE-Life Sciences Education*).

Losick, Shapiro, and Mori to Receive Gairdner International Awards

LOSICK

SHAPIRO

MORI

Richard Losick, Lucy Shapiro, and Kazutoshi Mori have been named as recipients of the 2009 Gairdner Awards, Canada's most prestigious international award. Over the past 50 years, some 298 scientists have won Gairdner Awards; among them, 73 scientists have gone on to win the Nobel Prize.

Both Richard Losick and Lucy Shapiro won the award "for their discovery of mechanisms that define cell polarity and asymmetric cell division, processes key in cell differentiation, and in the generation of cell diversity." Losick is a Harvard College Professor and the Maria Moors Cabot Professor of Biology at Harvard University.

Shapiro is the Director of the Beckman Center for Molecular and Genetic Medicine at Stanford University and the D. K. Ludwig Professor of Cancer Research at the Stanford University School of Medicine.

Mori, of the Department of Biophysics, Graduate School of Science at Kyoto University, received the award, along with Peter Walter of the University of California, San Francisco, "for their dissection and elucidation of a key pathway in the unfolded protein response, which regulates protein folding in the cell."

The awardees are selected by two separate judging panels made up of Canadian and international medical researchers. A Gairdner Award comes with a cash prize of $100,000 CAD. Recipients also take part in academic and public lectures and forums held across Canada before they receive their awards at a dinner in Toronto on October 29.

The First Hundred Years Are the Hardest

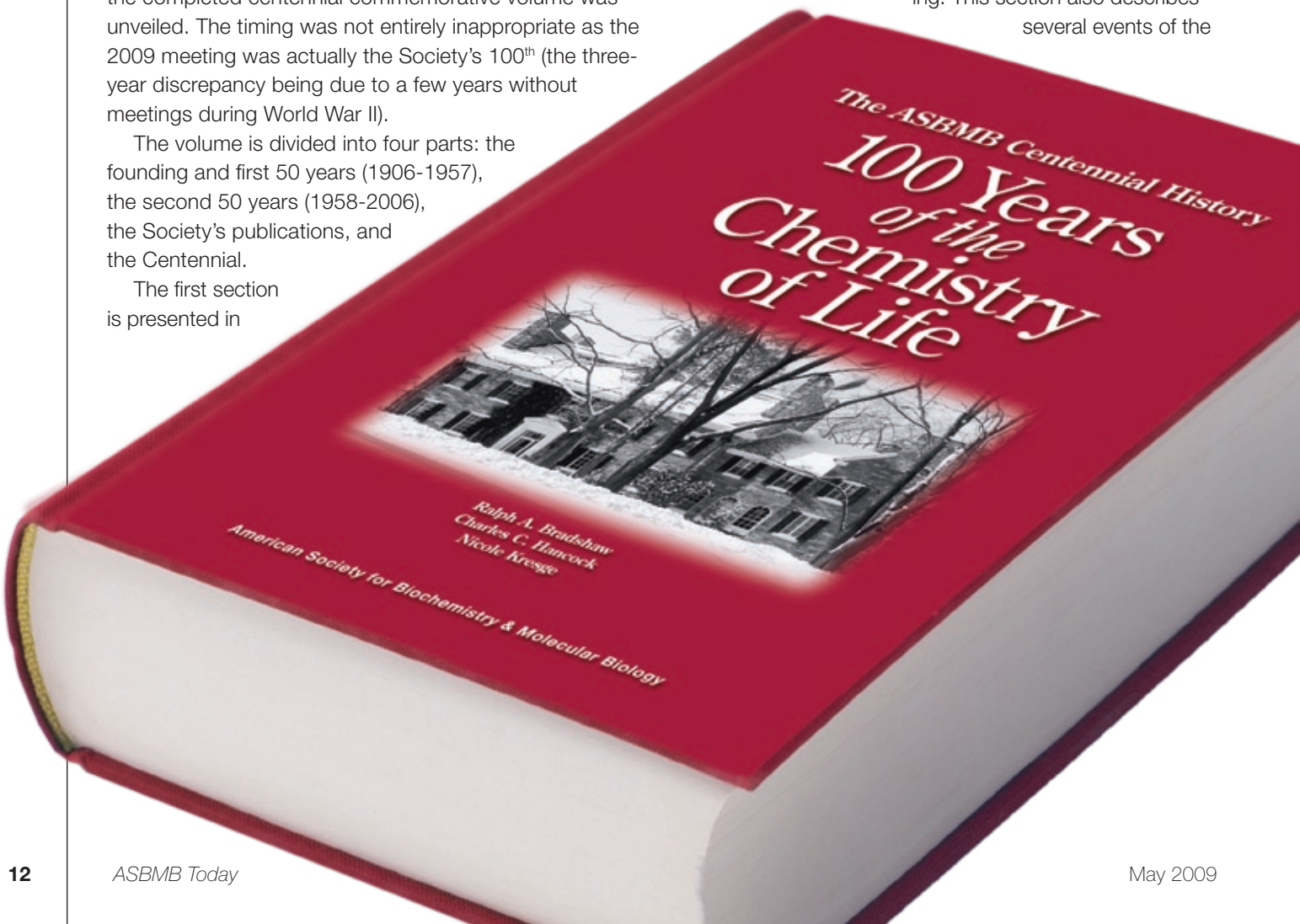
BY RALPH A. BRADSHAW, CHARLES C. HANCOCK, AND NICOLE KRESGE

ASBMB Founder John J. Abel

They say that the first hundred years are the hardest, although most of us don't get to take advantage of the next hundred. But the ASBMB has—it first celebrated its 100th birthday at the ASBMB annual meeting in San Francisco in April 2006, and then again on December 28, 2006 (the actual anniversary of its founding was December 26th) in New York City and has moved into its second century with typical enthusiasm and gusto. However, the Society still has one more present to open: a book entitled, "The ASBMB Centennial History: 100 Years of the Chemistry of Life." This project, which has been in the works for several years, reached fruition at the Society's annual meeting in New Orleans this past April when the completed centennial commemorative volume was unveiled. The timing was not entirely inappropriate as the 2009 meeting was actually the Society's 100th (the three-year discrepancy being due to a few years without meetings during World War II).

The volume is divided into four parts: the founding and first 50 years (1906-1957), the second 50 years (1958-2006), the Society's publications, and the Centennial.

The first section is presented in a chronological fashion that details the Society's early growth and partially reflects a previously published history of the first 25 years by Russell Chittenden. It contains copies of many of the documents that were essential to the founding of the Society, including a letter from ASBMB founder John Jacob Abel proposing the formation of a new society, the Society's first membership ledger, and the front and back of the program from the first annual meeting. This section also describes several events of the



1950s, including the purchase of the Beaumont House (and grounds), which eventually became the Society's headquarters, the establishment of an Executive Officer, which greatly impacted how both the Society and the *Journal of Biological Chemistry* were run, and the start of the International Union of Biochemistry (now IUBMB) and the U.S. National Committee for Biochemistry.

Part two of the book takes a look at the second half century through the Society's activities, including its meetings, its awards, and the committees formed to address both social and scientific issues that did not exist in the earlier period.

The third part of the book centers on the Society's publications—the *Journal of Biological Chemistry*, the *Journal of Lipid Research*, *Molecular and Cellular Proteomics*, and *ASBMB Today*—and also looks at its partnership with Cadmus Communications. Because detailed histories covering the first 75 years of the *JBC* are available, the *JBC* chapter places more emphasis on recent accomplishments such as the Journal's pivotal role in initiating electronic publishing.

The final section of the book recounts the Society's centennial celebrations, including the 2006 annual meeting and a commemorative ceremony and plaque dedication in New York City. The book concludes with a look at the ASBMB of tomorrow and the Society's coming opportunities and challenges.

The book includes a timeline that illustrates ASBMB member involvement in major scientific breakthroughs, photographs and biographies of ASBMB's Presidents, and an appendix listing ASBMB's Nobel Laureates along with brief descriptions of their prize-winning research.

This commemorative book was written and assembled by Ralph A. Bradshaw, Society Historian; Charles C. Hancock, Past-ASBMB Executive Officer; and Nicole Kresge, Editor of *ASBMB Today*. They gathered information from many sources, including the Society's archives at the University of Maryland, Baltimore County, to produce the volume. Several chapters were also contributed by friends and members of the Society.

The book celebrates one of the more remarkable stories in the pursuit of scientific wisdom. The ASBMB, which began life as the American Society of Biological Chemists, has had an admirable record of supporting both biochemistry and biochemists and thus being one of the most accomplished learned societies in existence today. The foresight of the 26 founders, led by John Jacob Abel, in breaking from the Physiological Society and striking out on their own, has certainly been rewarded. This 100-year history of the ASBMB is dedicated to that spirit and to all the biochemists that the Society has served well in this period. We hope you will enjoy the stories and pictures that document this 100-year history.

If you would like to purchase a copy of this limited-edition book, visit: www.asbmb.org/historyorder.

Power to the Postdocs

BY NICK ZAGORSKI

As Jonathan Wiest, Associate Director for Training and Education at the Center for Cancer Research (CCR) at the National Cancer Institute (NCI), addresses the sea of intent faces during his opening remarks at this year's CCR Fellows & Young Investigators Colloquium, he takes a moment to emphasize that their eyes may be focused on the wrong person. "Look all around you," he says to the gathered audience of postdocs and research fellows (with a smattering of post-baccalaureates as well). "This is your future; these are the people who will be your colleagues, your collaborators, and your connections for the next 30 years. This colloquium is not about me; it's about you."

It's a point that's plainly obvious once stated, but one that's often overlooked in a scientific world where the only future many can focus on is the immediate future. But although it's definitely important for young investigators to reach out to established and senior scientists to help them take their next few steps, it's equally as vital to cultivate relationships with peers and gain valuable resources down the road—and perhaps more often than you think. As Wiest notes, "after all these years, it's still surprising how small the scientific community is." And in the backdrop of the city referred to as "the sweetest place on Earth," over 400 young NCI researchers have come to do just that.

Specifically billed as an event "by the NCI fellows, for the NCI fellows," the Ninth Annual CCR-FYI Colloquium (held March 18-20 in Hershey, PA) brought these trainees together in a "retreat"-style setting where they could network with their colleagues and invited guests to foster employment contacts, research collaborations, or even just new friendships. Along the way they could listen to excellent scientific presentations, take in career-related panel discussions, see some of their friends' posters, speak with some of the reps at the career fair, and maybe even catch a few minutes of "March Madness" with some of their newly made friends.

Wiest notes that this colloquium illustrates the strong, working relationship the NCI has with its fellows. "We truly value our young investigators; they are our most precious resource, and the NCI does its best to empower them," he says. "But we know we can't just hold their hands the whole time, because they need to build their independence." And allowing the fellows, specifically the FYI Steering Committee (a body of fellows that acts as an advocacy group and leadership liaison for their young investigator peers), full control in planning, organizing, and moderating this colloquium provides a great example of that empowerment.

This year the fellows behind the colloquium, during a 10-month brainstorming and organizing process that could best be described as a labor of love, delivered a sterling event that provided something for everyone. There were five keynote lectures on emerging areas of cancer research (cancer metabolism, small and micro RNAs, cancer stem cells, and T-cell homeostasis); six workshops on diverse topics such as effective publishing strategies, guides to transitioning to patient-oriented research, careers in industry, non-benchwork career options, and a virtual tour of some NCI core facilities like the Cancer Biomedical Informatics Grid; and 40 oral presentations and over 140 posters from some of NCI's best and brightest.

"This year, in addition to events that appeal to all the attendees, we wanted to include some sessions that really impact first and second year fellows," says Krista Zanetti, one of the six members of the colloquium planning committee that devoted so much of their energy to bring this colloquium together. "We wanted to help them figure out what they want to do and how to go about doing it early on, so they can get the most out of their five-year fellowship and really excel at their chosen path."

Undoubtedly, though, the most memorable segment of the event was the screening of the documentary "Dear Talula: An Intimate Portrait of a Breast Cancer Survivor," a poignant film that chronicles both the major events and everyday experiences of a young mother rising up to meet the challenges of her cancer diagnosis head on (www.deartalula.com). "Many of these fellows have been doing basic research for years now and may have lost sight of the human aspect of cancer," says Wiest. "This film was a great reminder that cancer has, or will, touch all of us directly."

Hopefully, adds Robert Wiltrout, director of CCR, this colloquium will also serve as an illustration that the NCI,

Recipients of the 2009 Travel Awards for excellence in scientific presentations at the NCI Colloquium. *Left* to *Right*: Tiffany Wallace, Luhua Zhang, Kimberly Shafer-Weaver, Sam Hong, Patricia Tsang, Tai Chi Cheuk.

and to a broader extent NIH as a whole (as other institutes have similar colloquia), is more than just a funding agency. As he looks around during one of the mentored lunches (the meals are structured to allow fellows to sit at tables with one of the keynote speakers or workshop presenters and pick their brain) and reflects on another successful colloquium—though there will inevitably be a few complaints about the food—Wiltrout says, "one of the most exciting things for me is when I get comments from invited guests who rave about this colloquium and say, 'I wish our institute did something like this.' And that reinforces the idea that NCI can and should set an example in post-doctoral training and mentoring."

Although many people may comment on the slow pace of government, Wiltrout stresses that "the NCI is not afraid to evolve and change on the fly to adjust to changing times, just like this colloquium has changed and grown every year." And these times, as both Wiltrout and Wiest noted in their opening remarks, include a post-doctoral workforce of which only one-third wish to pursue a career in academia—and, of those, less than half will ultimately find success. To maximize these odds, NCI is undergoing a "Renaissance in Training."

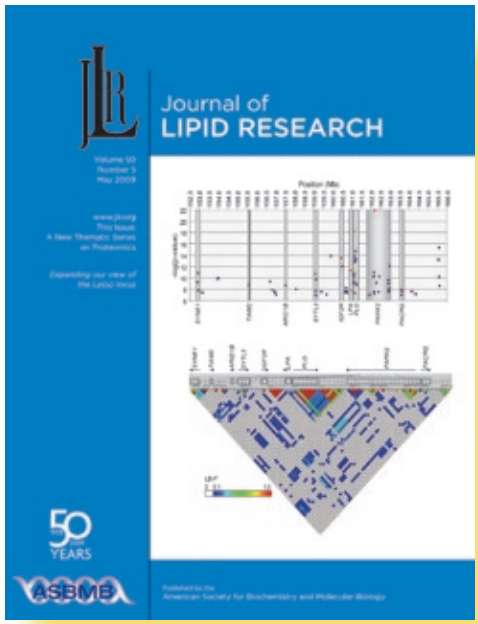
For example, realizing that research should not be carried out in individual silos, CCR created four Centers of Excellence, designed to bridge traditional lab boundaries. Each of the four centers (Chromosome Biology, Immunology, AIDS & Cancer Virology, and Integrative Cancer Biology) serves as a hub to promote interactions among investigators across NIH and externally to help accelerate discovery and delivery of therapies in these fields of research. Wiltrout notes these centers will help train young investigators to address their scientific pursuits through collaboration and multidisciplinary approaches; "it's part of my hope that when our fellows talk about NCI mentors, it's always in the plural."

As with the colloquium though, the Steering Committee, working with the Office of Training and Education, also contributes heavily throughout the year to support their fellows' training by organizing career fairs, networking lunches with invited speakers, and grant-writing workshops, among other initiatives. But they note more help is always welcome and needed and, much like CCR empowered fellows with a large say in their NCI training program, the FYI Steering Committee tries to empower their colleagues to help as well, by joining up with one of the many groups and committees across NIH's campus or volunteering in some other capacity—such as, perhaps, helping plan next year's colloquium.

Nick Zagorski is a science writer for ASBMB. He can be reached at nzagorski@asbmb.org.

Premiering in May: A New *JLR* Thematic Review Series on Proteomics

BY MARY L. CHANG



The May issue of the *Journal of Lipid Research* marks the beginning of a new Thematic Review Series on proteomics in the study of lipids. The series is being coordinated by Jay W. Heinecke of the University of Washington, an associate editor of the journal.

In the introduction to the new series, Heinecke will review two mass spectrometry (MS) methods that have greatly advanced the study of proteins involved in lipid metabolism and biology. The first, matrix-assisted laser desorption ionization (MALDI), is the chief method used to examine solid-state biomolecules. Matrix material that can absorb the frequency of a rapidly pulsing laser is co-crystallized with a protein product of interest so that when a laser strikes the compound, the matrix absorbs energy and causes the protein product to enter the gaseous phase. MALDI is extremely useful in that it is so sensitive it can detect subpicomolar quantities of an analyzed substance, and when used with time-of-flight (TOF) MS, many samples can be analyzed in a short time if a high-throughput liquid chromatography system is employed. Furthermore, MALDI-TOF-MS can be used, via peptide mapping or peptide mass fingerprinting, to identify unknown proteins. A second technique, tandem mass spectrometry (MS/MS), can detect post-translational modifications of proteins. Heinecke will describe how MS/MS can detect the oxygenation of thiol residues and how this modification is related to the regulation of matrix metalloproteinases by myeloperoxidase.

The May issue of *JLR* will also contain the first review in the series. This review, by Tomas Vaisar of the University of Washington, will cover lipid-associated proteins and discuss the difficulties related to, and approaches for, successful proteomic analysis of these complexes. Vaisar will look specifically at the proteomics of two groups of lipid-protein complexes. Integral membrane proteins (like transmembrane phospholipids) have been extensively researched in the past, and there are many well-validated protocols for their analysis. However, less analysis has been done on plasma lipoproteins (such as HDL and LDL), and, because of the unique structure of these compounds, investigators will have to be innovative in their analysis. Vaisar's review will also discuss the steps of isolation, solubilization, delipidation, digestion, and MS analysis for both types of lipid-protein complexes.

Eicosanoids are oxygenated essential fatty acids that act as signaling molecules and play important roles in inflammation and immunity. The June issue of *JLR* will feature a review about "-omics" analysis of eicosanoids by Matthew W. Buczynski, Darren S. Dumlao, and Edward A. Dennis of the University of California, San Diego. They will look at how characterization of eicosanoid biosynthetic pathways has allowed for the unique integration of genomics, metabolomics, and proteomics in studying the pathology of diseases associated with eicosanoids. This review will provide a systematic overview of phospholipase A2, cyclooxygenase metabolites (including prostaglandins), cytochrome P450 metabolites, 5-lipoxygenase metabolites (including leukotrienes), and other lipoxygenases, as well as products of eicosanoid catabolism.

Four more reviews are planned for this series and will appear in *JLR* in the coming months.

Mary L. Chang is Managing Editor of the *Journal of Lipid Research*. She can be reached at mchang@asbmb.org.

Getting Off of the Ground!

BY DANIEL M. RABEN

Last month in the Lipid News column, we announced the inauguration of the ASBMB Lipid Division. This month, I thought I would outline some of our "works in progress."

The Lipid News Column

First, I would like to discuss this monthly column in *ASBMB Today*. If anyone has a topic they would like to see addressed, they can contact me directly. Additionally, I am hoping to engage our overseas colleagues by encouraging them to contribute to this column; the topics will vary, but they will all highlight the research and issues in different countries.

The ASBMB Annual Meeting

The presentation of lipid research has been a major component of ASBMB's annual meetings. Starting in 2010, the members of the Lipid Division will be intimately involved in selecting the organizers for the lipid theme. We hope that this will serve as a mechanism for enhancing the impact of the entire lipid community.

Lipid Division Committees

Additionally, we have begun to organize some important Lipid Division committees:

- A steering committee is in place and has been crucial to getting this division started.
- The fundraising committee has been tasked with raising funds to support awards at our meetings. I am pleased to announce that Rob Stahelin (Indiana University School of Medicine-South Bend) has agreed to chair this committee.
- We are in the process of forming an Awards Committee, which will be responsible for organizing Lipid Division awards.

NIH Panels

Many scientists have expressed concern that the breadth and depth of various lipid fields are not adequately represented on NIH study panels. We are currently assessing the lipid representation on the various study panels. Our data will be available on the Lipid Corner website as soon as this assessment is complete. We hope then to bring this data to the attention of NIH.

Lipid Corner Website

Finally, I encourage you to visit our website at www.asbmb.org/lipidcorner. I have started a thread in the Forum titled "Issues for and about the Lipid Division." If there are any issues or concerns you would like to raise, please post them there. This will allow for an open discussion among members of the entire lipid community. Please also feel free to contact me directly if you have an issue you would like to discuss in a less public venue.

We are excited about the formation of the ASBMB Lipid Division and have high hopes that it will bring recognition to the lipid community on a national and international level.

Daniel Raben is director of the ASBMB Lipid Division and also a professor in the Department of Biological Chemistry at The Johns Hopkins University School of Medicine. He can be reached at draben@jhmi.edu.

Visit the ASBMB Lipid Division Website at www.asbmb.org/lipidcorner

UAN Announces 2009 Award Winners

BY WEIYI ZHAO

The ASBMB Undergraduate Affiliate Network (UAN) is a national organization comprised of university-based chapters dedicated to the advancement of undergraduate research, research-based undergraduate education, and K-12 outreach in biochemistry and molecular biology. This year the UAN was able to offer several awards and scholarships designed to support undergraduate and K-12 research and community engagement in the study of biochemistry and molecular biology.

Please join the ASBMB in congratulating the following 2009 award winners.

UNDERGRADUATE RESEARCH AWARD WINNERS

Undergraduate Research Awards in the amount of $1,000 are awarded to UAN student members conducting research under the direction of a faculty member who is an ASBMB member. The award is to be used for the purchase of research supplies. Awardees are expected to present their findings at the next ASBMB annual meeting and/or a regional ASBMB UAN meeting. This year's awardees are **Christopher Doucette** of Wesleyan University and **Daniel Laurent** of the University of Wisconsin, La Crosse.

OUTREACH SUPPORT AWARD WINNERS

The Outreach Support Award provides UAN Chapter winners with $250 to hold outreach events in K-12 schools in their region to promote Science, Technology, Engineering, and Mathematics (STEM) education and careers in biochemistry and molecular biology. The recipients of the 2009 Outreach Support Award are: **College of the Holy Cross**, **Tennessee Technological University**, **Seattle University**, and **Western Illinois University**.

7-12 TEACHER SUMMER RESEARCH AWARD WINNERS

Totaling $12,000 per team, the purpose of this award is to promote research-based educational activities by building connections between teachers and students in secondary schools and colleges. A secondary purpose of this award is to provide grades 7-12 students with role models and to present UAN faculty members and their students with meaningful service-learning opportunities. Each project pairs one grade 7-12 school teacher and a grade 7-12 student with a UAN faculty mentor and a UAN student. This Award is being piloted in 2009. The following winning teams will work together for two years (two summers and one academic year):

Stan Richter—Detroit Lakes High School and
Joe Provost—Minnesota State University Moorhead

Anne Mach & **Miranda Sanchez**—
La Crosse Central High School and
Todd Weaver & **Sarah Schreiner**—
University of Wisconsin La Crosse

John Spengler—Pine Creek High School and
Mike Taber & **Neena Grover**—Colorado College

Rachel Gruner & **Rachel Jones**—
Robious Middle School, and
Ellis Bell, **Hugo Guterres**, & **Farren Billue**—
University of Richmond

2009 OUTSTANDING REGIONAL UAN CHAPTER AWARD

This Award aims to recognize UAN chapters that have demonstrated leadership in their educational activities in the areas of biochemistry and molecular biology, exhibited exceptional commitment to increasing public scientific awareness, demonstrated interaction with other campus activities and events, participated in regional and national meetings, and showed sustained chapter activity. The three chapters receiving the award this year are **Colorado College**, **Tennessee Technical University**, and the **University of Delaware**.

2009 UAN TRAVEL AWARD WINNERS

Travel awards in the amount of $400 are used to support UAN students and faculty members attending the ASBMB Annual Meeting. The following recipients attended this year's Annual Meeting in New Orleans. All UAN Student Travel Award recipients also participated in the 13th Annual ASBMB Undergraduate Student Poster Competition.

Pablo Apablaza—Montclair State University
Chloe Benson—Colorado College
Kelsey Bohn—Western Illinois University
Eric Brandt—University of Michigan, Dearborn
Jenny Canine—Minnesota State University, Moorhead
Rachel Chikowski—University of Richmond

Jennifer Chmielowski—Western Illinois University
Cheerena Clay—Hampton University
Sarah Connor—Washington and Lee University
Brad Falk—University of Richmond
Jarrett Failing—North Dakota State University
Andrew Haak—Minnesota State University, Moorhead
Jason Hocking—University of Wisconsin, La Crosse
Casey McCormick—Tennessee Technical University
Derek Janssens—Grand Valley State University
Robert Jones—University of Michigan, Dearborn
Jessica Karr—Texas State University—San Marcos
Adam Kerrigan—College of the Holy Cross
Craig Kutz—Minnesota State University, Moorhead
Brittany Lekies—Viterbo University
David Nemer—University of Notre Dame
Ka Yang—Adelphi University
Daniel Osipovitch—University of New Haven
Matthew Richards—University of Delaware
Alex Ritter—Concordia College
James Ruble—Grand Valley State University
Kyle Schneider—Grand Valley State University
Jessica Stevens—Marymount Manhattan College
Ryan Wilson—University of Delaware
Meghan Woods—University of Delaware
Daniel York—College of the Holy Cross

Join the ASBMB UAN today and qualify for the 2010 UAN Awards! Apply now and pay only $100 (a 50 percent discount) in application fees. For more information and to obtain an application, visit: www.asbmb.org or contact Weiyi Zhao at wzhao@asbmb.org.

Weiyi Zhao is the ASBMB Manager of Education and Professional Development.

How to Enhance Your Postdoctoral Experience

BY FABIAN V. FILIPP

At the seventh annual National Postdoctoral Association meeting in Houston, Texas this past March, plenary speaker Peter S. Fiske spoke to a packed auditorium about career planning and the job hunting process. His talk, titled "Putting Your Science to Work: Creating New Options and Opportunities via the Postdoc," attracted approximately 300 postdoctoral fellows, eager to learn how to leverage their degrees in a faltering economy. In the interview below, Fiske talks about the postdoc experience and how to make the most of it.

ASBMB: *What makes postdoctoral training a special period?*

PSF: Postdoctoral appointments were always intended as short periods of transition between graduate school and "academy" when they were first started at Johns Hopkins about a century ago. Today, mostly due to economic forces, the postdoctoral years have evolved and expanded. In the life sciences, the postdoctoral experience can be as long, or even longer, than the graduate school experience, making it a very attenuated traineeship. Ironically, when my father obtained his Ph.D. in 1960, he had only one publication to his name but standing faculty offers at Harvard, U.C. Santa Barbara, and the U.S. Geological Survey. Back then, once you had an appointment as assistant professor, you were supposed to learn how to publish and how to get your first grant. Today the bar is set much higher—a postdoc, today, is what an assistant professor used to be.

ASBMB: *What kind of career training is required to make the postdoctoral fellowship an effective experience?*

PSF: You always have to actively work on your career, even in research science. Obviously, the postdoctoral years are a marvelous experience. I had a great time during my postdoc. It is a period after your Ph.D. giving you time to explore your own direction, but before you have lots of responsibilities that come with a faculty position like teaching. Postdoctoral fellows have also become a flexible reservoir that accommodates the surge in Ph.D.

production and the dearth of Ph.D. jobs. After spending years of talking to NIH and NSF on the subject of looking rationally at the level of Ph.D. production, I simply don't think that these funders will ever regulate Ph.D. production in any meaningful way.

Of course you want to make every career choice full of purpose and with absolute clarity. The fact is that it is perfectly okay to do a postdoc as a means of exploring whether a research career makes sense for you. I did that myself. My research advisor at the time was really put off by that! I just caution postdocs who find themselves in year three, four, or five of their appointment to question whether they really want to go on this path. The sooner you begin exploring options the better, especially while you are still a postdoc, while there is some protection. A postdoc is a great opportunity also to move your career laterally. I went from geochemistry to planetary science. Once you have an assistant professorship you don't have the flexibility to move around intellectually that much anymore.

ASBMB: ***The requirements in the academic job market are very different from those in the industrial or private sector. Is it possible to prepare for the next step during your postdoc?***

PSF: Anyone's career options, whether for an academic career, an industry career, or for a career in public policy, critically depend on the professional network they develop. An important thing that should be on every postdoc's mind is how they develop their professional network, who they are getting to meet, who they are getting to work with, and what opportunities are being created as a result. The worst situation that postdocs can find themselves in is one in which they feel very much like graduate students: they are stuck in a research group, they have no collaborations on the outside, and they lack interactions with people in other universities or industry. If you find yourself caught in a very small environment, you need to bust out! Strictly speaking, postdoc programs are supposed to be developmental assignments as well as "regular jobs." Sometimes postdocs find their PIs are very uncooperative in that regard and very inflexible about giving them time to explore or develop other collaborations. But those outside collaborations are going to be absolutely critical for the postdoc's ability to transition to the next step, whatever that may be.

ASBMB: ***How can one enhance the mentoring experience?***

PSF: The term "mentor" is a very mythologized term in academia. Certainly most academic professors feel they are very good mentors, just as most parents feel they are very good parents. However, when you talk to the children, the evaluations are much more mixed! [Mentoring] is a very personal relationship, and in a way, that can pose as many problems as benefits. It is very difficult for a mentor not to see a bit of him/herself in you. This transference is part of the bond. And when you choose pathways and activities that your mentor might not agree with, it can set you up for a lot of conflict or frustration. Choosing your own path is exactly what you should be doing as a postdoc. The National Academy of Sciences came out with a book called *Adviser, Teacher, Role Model, Friend*, a very small volume that was supposed to summarize the Academy's view of what advisors should do for their students and their postdocs. The problem I had with that approach is that, while you would like to be "advisor, teacher, role model, and friend," as a PI you are also going to be "boss, jerk, and a guy who tells people to work harder!" It is just too much in a work relationship to try to pack all those personal expectations into mentoring.

Collaborations are the way that you will build your career: by branching out and working with other people. That brings in a second very important component, the network. A lot of young scientists have an incomplete view of networking. They view it as very shmoozy. And yet networking is a very important part of being a successful scientist. We do networking as young scientists all the time; we just don't tend to call it that. When you go to a meeting and present a poster, it is not just scientific communication, it is networking! I try to unpack the whole term "networking" and frame it in terms of relationships. Networking is nothing more than making relationships; in particular, relationships with people who share your personal and professional interests. From time to time, you might talk to these people about career transitions that you make. Practically speaking, anyone you know is part of your network. However, within this set there is a certain subset of people who will be extremely valuable to you. Those are the people in the career field that already interests you, and who are willing to give you help. Let's say you are a graduate student in biochemistry; you are debating whether you want to do a postdoc, but you are also really interested in learning more about intellectual property and law in the biotech industry. You know someone who works in marketing at Bayer ,who knows and works with the people in the intellectual property office. [This person] will be delighted to introduce you and arrange an informational interview with the people in the intellectual property office at Bayer. That is a great example how networking works.

ASBMB: *At the seventh annual NPA Meeting, the University of California was often cited as a model system for postdoctoral training. What is the University of California doing right in its postdoc programs? Where do you see opportunities to improve the training experience of postdocs?*

PSF: I love to see postdoctoral associations and societies. Regular seminar series in professional development, outside speakers, and panel discussions with alumni are always valuable and very informative for postdocs, and they do not cost much money. Postdocs could organize these things for themselves if their institutions are willing to let them. What it takes is the institution creating a culture whereby postdocs are genuinely understood as not just a flexible labor force but actually developing scientists. In my MBA program, we had classes on negotiating, leadership skills, extemporary speech, and business etiquette. MBA programs realized that their students needed to be armed with those skills in order to be successful professionals around the world. Similarly, research institutions need to understand that postdocs need to be armed with the exact same set of skills. It is a convenient rationale for an institution or a PI to simply say "the best students understand all this and do not need any help in this regard; the ones who don't get it are beyond saving." That kind of rationale conveniently lightens the workload on their side. Nevertheless, we are talking about an academic institution: the university. The fundamental reason for its existence is the production of new minds and intellectual leaders. As difficult as it is to run a research group today and balance a load of grant applications and publications, postdocs still need to be considered by their PIs as special; and their institution needs to uphold that when conflicts arise between PIs and postdocs.

Regular seminar series in professional development, outside speakers, and panel discussions with alumni are always valuable and very informative for postdocs.

ASBMB: *You took some dramatic shifts in your personal career. What lessons did you learn from that?*

PSF: Every career is going to come with some degree of setback. I have not had nearly as many as others. Often, when you become very invested in a certain pathway, setbacks can be very devastating. And yet that disappointment, that setback, is itself the seed for a new opportunity that you simply had not considered before. One thing I am concerned about is that graduate students and postdocs are steeped into what can sometimes be a very conservative intellectual culture, where risk-taking is considered dangerous and frowned upon. And yet that risk-taking is exactly what we need for science and what people need for their own professional development. The biggest opportunities for me have come when I have found the courage (or foolishness) to take a risk. Frankly, grad students and postdocs are smart people; they know risk and they know the consequences—they are not deluded. The best thing that you can do is to offset those risks by creating other options. As one very dear mentor of mine said, the definition of mental health is the feeling that you have options. One of the ways that you can create the most options is by having a strong professional network made up of people who know you and think highly of your work and who are willing to help you when those transitions are necessary. A strong network provides a level of safety and will keep you alive, even if you fall off a professional tightrope.

In the course of doing my Ph.D., I did some "extracurricular research," initially to the frustration of my advisor, but eventually he got onto the idea. And that extracurricular research actually led to my postdoc in the Livermore lab: a wonderful three-year postdoc. At the end of it, I was certain I was leaving science and never coming back. I went to Washington, D. C. for a year on a science policy program called the White House Fellowship. About six weeks into my life in Washington, I realized that I did not want to spend the rest of my career there. So I made my way back to Lawrence Livermore National Laboratory in the Bay area as a member of the technical staff for four years. After that, I left to start my first company. That was probably my biggest professional risk. But I am glad I did it.

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Science in the Obama Administration: Are We Coming Out of the Dark?

BY SQUIRE J. BOOKER

In 1991, Gloria Estefan released the single "Coming Out of the Dark," a future number one hit on the Billboard Top 100. This single was in response to a near-fatal collision between her tour bus and a truck, which almost ended the singer's acclaimed career. In the chorus of the song, which is primarily a tribute to her husband's support during a difficult period of physical and emotional rehabilitation, she celebrates, "…Coming out of the dark, I finally see the light now, and it's shining on me…"

Few will argue against the notion that science in the United States has endured a perilous, if not a near fatal, period during the last eight years. After an era in which the budget for NIH was nearly doubled between 1998 and 2003, funding increases for science became stagnant in many disciplines, whereas in others funding was decreased, especially after accounting for annual rates of inflation. More dishearteningly, many expressed concern that fundamental scientific values were under attack and that the opinions of internationally recognized scientific experts were neglected, if not disrespected. Indeed, the downturn in the perceived value of science and scientific expertise left many scientists demoralized and resentful.

The magnitude of the state of affairs on the eve of an upcoming presidential election warranted an open letter to the American people in support of then Sen. Obama, which was eventually signed by more than 75 Nobel Prize-winning scientists who are American citizens or permanent residents. Although some past presidential candidates have enjoyed similar backing by acclaimed scientists—notably John Kerry in 2004 and Al Gore in 2000—their support of Barack Obama this past year was significantly augmented. The urgency of the situation was apparent in the opening statements of the letter, which claimed, "This year's presidential election is among the most significant in our nation's history. The country urgently needs a visionary leader who can ensure the future of our traditional strengths in science and technology and who can harness those strengths to address many of our greatest problems: energy, disease, climate change, security, and economic competitiveness."[1] It was further stated, "The government's scientific advisory process has been distorted by political considerations. As a result, our once dominant position in the scientific world has been shaken, and our prosperity has been placed at risk. We have lost time critical for the development of new ways to provide energy, treat disease, reverse climate change, strengthen our security, and improve our economy."[1]

Learning from Problems of the Past Administration

The problems of the past administration with respect to its relationship with science were many; however, one of the gravest mistakes was the perception that the administration was distorting or misusing science for political gain. A number of transgressions were outlined in a 2004 statement entitled "Restoring Scientific Integrity to Federal Policy Making," which was signed by more than 62 scientists, including several Nobel Laureates, leading medical experts, and university presidents.[2] The statement claimed, "When scientific knowledge has been found to be in conflict with its political goals, the administration has often manipulated the process through which science enters into its decisions. This has been done by placing people who are professionally unqualified or who have clear conflicts of interest in official posts and on scientific advisory committees; by disbanding existing advisory committees; by censoring and suppressing reports by the government's own scientists; and by simply not seeking independent scientific advice." Some of the findings were rebutted by the administration, and a revised, but still critical, version of the letter was eventually released.[3]

In addition, notable scientists took issue with the administration's lack of support of condom use in protection from HIV/AIDS, its views on human involvement in climate change, and its ban on federal support for embryonic stem cell research using stem cell lines created after 2001, despite the wide belief in the scientific community that embryonic stem cells have the potential to impact significantly on a number of diseases or conditions.[4] Many scientists warmly welcomed the words of President Obama's inauguration speech on January 20, 2009, "We will restore science to its rightful place."

President Obama's Policy for Science and Innovation

So, what's in store for science under the Obama administration? The major elements of the Obama-Biden science policy are:

1. **restoring integrity to U.S. science policy to ensure that decisions that can be informed by science are made on the basis of the strongest possible evidence;**
2. **doubling the federal investment in basic research by key science agencies over a 10-year period, with a special emphasis on supporting young researchers at the beginning of their careers, and backing high-risk, high-return research;**
3. **making a national commitment to science education and training by recruiting some of America's best minds to teach K-12 math and science, by tripling the number of the National Science Foundation's Graduate Research Fellowships;**
4. **encouraging American innovation to flourish by making the R&D tax credit permanent, streamlining our patent system, eliminating the capital gains tax on start-ups and small businesses, and promoting the deployment of next-generation broadband networks; and**
5. **addressing the "grand challenges" of the 21st century through accelerating the transition to a low-carbon, oil-free economy, enabling all Americans to live longer and healthier lives, and protecting our country from emerging threats to our national security.**[5]

All indications suggest that the administration has gotten off to a solid start, which is undoubtedly fueled by President Obama's strong scientific advisory board. President Obama expeditiously chose John Holdren, a physicist and expert in energy, as his Science Advisor and Director of the White House Office of Science and Technology Policy, as well as Steven Chu, Nobel Prize winner in physics as the Energy Secretary.[6] He has reversed the executive ban on some of the limitations on using federal taxpayer dollars for embryonic stem cell research and has ushered through Congress a massive economic stimulus bill, which includes over $21 billion for research and development projects over the next two years. Excitingly, Nancy Pelosi, the Speaker of the House, recently stated to a group of academic leaders, "if you want to know our domestic agenda, it is science, science, science, and science."[7] With this seemingly renewed focus on science and technology, a developing challenge will be to ensure that Americans are suitably equipped to take full advantage of emerging and/or expanding resources in this area.

The executive summary of a 2006 report entitled *Beyond Bias and Barriers: Fulfilling the Potential of Women in Academic Science and Engineering*, by the Committee on Maximizing the Potential of Women in Academic Science and Engineering of the National Academies of Sciences and Engineering and the Institute of Medicine, warned that the United States would have to pursue the innovative capacity of all sectors of society, regardless of sex, in order to compete and maintain scientific leadership amid increasing economic and educational globalization.[8] The report further concluded that, although the percentage of women majoring in STEM (Science, Technology, Engineering, Mathematics) fields is increasing, the percentage of women on science or engineering faculties is relatively small and that they typically receive fewer resources than their male counterparts. It was further stated that the small proportion was not due to a lack of talent but was instead due to unintentional biases and outmoded institutional structures that hindered the access and advancement of women.

Obama and Biden agreed with the report's conclusions and with the premise that the leadership of the United States in innovation is the key to its prosperity and national security. They argued that the workforce in STEM will need to be increased significantly, engaging "not just women and minorities but also persons with disabilities, English language learners, and students from low income families."[9]

Squire J. Booker is an associate professor of chemistry and an associate professor of biochemistry and molecular biology at The Pennsylvania State University. He is also Deputy Chair of the ASBMB Minority Affairs Committee. He can be reached at sjb14@psu.edu.

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Mastering Microscopes

BY BRET L. JUDSON

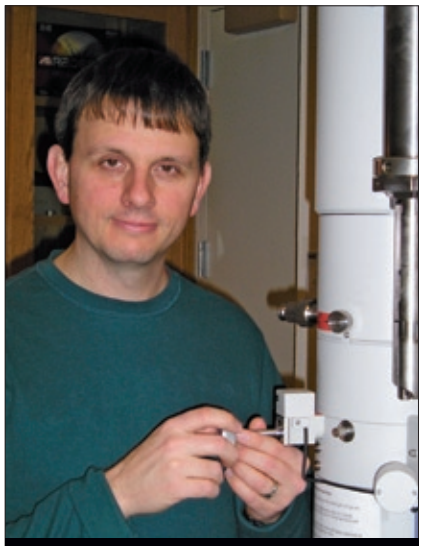
I never imagined that I would one day find myself running an imaging facility for an Ivy League university. In high school, I had envisioned a career in law enforcement and was intent on going to college for that. Shortly after high school, however, I enlisted in the army and spent a few years at Fort Knox and Fort Campbell. I realized that a career in the military was not for me, but it was a time for me to do many things that I would not have the chance to do again, like jumping out of airplanes and driving track vehicles. After the army, I spent one year at a local community college before transferring to the State University of New York at Binghamton, where I started my biological studies.

I entered college, as many biology undergraduates, with an idea of being "pre-med." I envisioned myself finishing undergraduate work, going on to medical school and so on. I quickly realized that this was not the path for me. I ended up taking a course load that favored botany, and I also served as an undergraduate teaching assistant for a few semesters. During my senior year, I took a lecture/laboratory course in phycology that utilized microscopy for a large portion of the class. If I had to pinpoint a time when my interest was piqued, that would be it. I realized that I really enjoyed working on and with microscopes.

I ended up enrolling in the biology department for my Masters degree with my phycology professor as my thesis advisor. I spent the next two years doing primarily ultrastructural (TEM and SEM) studies on *Jania,* a coralline alga. My Masters project was technically challenging because the alga was calcified. This challenge honed my research and troubleshooting skills, both of which would serve me well in the future, especially when dealing with technically complex microscopes. I also realized that I really enjoyed teaching, and between undergraduate and Masters work I spent a total of nine semesters teaching.

I decided to take a break from graduate work after spending a semester in the Ph.D. program at SUNY-Binghamton. To my very good fortune, an opportunity presented itself at the Upstate Medical Center in Syracuse, NY. The position involved a study investigating the role of inhaled particulate matter in the death of Londoners who expired during the Great Smog event of December 1952. This was a very exciting project, and I spent the next two years doing primarily x-ray microanalysis using the SEM on lung tissue from archival tissue specimens. This position made me realize that I could use the research skills I'd learned through undergraduate and graduate work with something I really liked, *i.e.* microscopy, to earn a living. This particular project ended in a key publication on inhaled particulate matter and an invited poster at a conference in London, England.

Shortly before my grant-funded position in Syracuse ended, a position working in the laboratory of William Brown at Cornell University became available. The position was two-fold: half of my time would be spent as the lab manager for Bill, and the other half would be devoted to maintaining the departmental transmission electron microscopy facility. This was a very exciting position for me as I could continue doing research but could also train users and collaborate with others using TEM. Shortly after I started in this position, Bill Brown



Judson

Bret Judson attended the State University of New York at Binghamton, where he earned his bachelor's and master's degrees. He then worked on an American Lung Association-funded study at the Upstate Medical University in Syracuse, NY for two years, after which he took a position at Cornell University, where he was the laboratory manager for a research lab and also the manager of the departmental transmission electron microscope facility. After more than four years at Cornell, Bret accepted a position as the manager of the W. M. Keck Bioimaging Laboratory at Arizona State University. In the spring of 2008, Bret returned to Cornell University, where he is currently the Director of Imaging for the newly founded Weill Institute for Cell and Molecular Biology.

and Tony Bretscher jointly purchased a confocal microscope for their labs, and I was placed in charge of this as well. Light microscopy began to excite me as much as electron microscopy. I ended up as a co-author on several publications from Bill's lab and taught countless people confocal and transmission electron microscopy.

After over four years in Bill's lab, an exciting opportunity opened up at Arizona State University. The position was for a manager for the W. M. Keck Bioimaging Laboratory in the School of Life Sciences. This position would involve light microscopy only but would also have a teaching component, a graduate level lab course in microscopy. I decided to accept the position, and my wife and I moved to Arizona in the summer of 2006. Was it hot? Yes, but at least it was a dry heat. I certainly enjoyed my surroundings, especially learning about unfamiliar plants and animals and hiking a variety of landscapes that were quickly accessible. The school was a newly founded multidepartmental endeavor with many new faculty members. The lab's user base was very cosmopolitan, coming from all over campus and off-campus as well. I had many exciting times in the lab, and teaching the lab course was certainly a highlight of my time there. The only unfortunate part for me was that the electron microscopy component, which I really enjoyed, was missing. But I was still able to have many stimulating conversations about electron microscopy as my co-worker David Lowry, the electron microscopy facility manager, was just down the hall.

Shortly before I left Cornell University, ground had been broken for a new building just adjacent to my old laboratory. This new building was to be one of the cornerstones of Cornell's new life sciences initiatives. Housed in this building would be an institute founded primarily for cell biology. I was approached about the possibility of coming back to Cornell University a short time after having moved to Arizona. Cornell had hired a director for the new institute, Scott Emr, and Tony Bretscher, my next-door lab PI from my previous position at Cornell, was named the associate director. I was very excited at first, but the thought of moving back across the country so soon after relocation was difficult to imagine. Also, the 330-plus days of Arizona sunshine would be sorely missed. I had many fruitful discussions with Scott and Tony, and after a visit back to Cornell in the fall of 2007, we decided to make the trip back to Ithaca. The new position would be Director of Imaging for the recently endowed Joan and Sanford I. Weill Institute for Cell and Molecular Biology housed in the newly opened Weill Hall. This exceptional position would combine both light and electron microscopy.

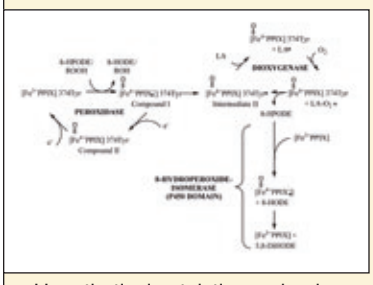
> *"There are many exciting opportunities in the world of research, and I encourage everyone to pursue that which they truly enjoy."*

I returned to Cornell University in early 2008, and the future looks very promising. I have gone back to teaching and training both light and electron microscopy and have already had many interesting collaborations. I was also able to pick up on some projects where I had left off. The possibilities of collaborative and independent studies are what interest me most about my current position. Additionally, I enjoy the troubleshooting and maintenance aspects of my position.

As a new undergraduate in biological sciences, I did not envision myself one day running an imaging facility; in fact, I am not sure it even occurred to me. I do remember one of my first days on campus walking outside of the biological sciences building and seeing a sign for the electron microscopy facility, and maybe it was then that a spark was ignited. My position today involves everything I enjoyed in school, teaching, and research. There are many exciting opportunities in the world of research, and I encourage everyone to pursue that which they truly enjoy.

Two Hemes Are Better than One

Psi factors are fatty acid-derived molecules, generated by enzymes known as psi factor producing oxygenases (Ppos), which regulate the balance between sexual and asexual life cycles in many fungi. Of the three Ppos in *Aspergillus nidulans*, PpoA is intriguing because it's predicted to contain two distinct heme domains: an N-terminal peroxidase domain and a C-terminal P450 heme thiolate domain. In this article, *A. nidulans* PpoA was cloned and expressed in *Escherichia coli* to better characterize its biochemical properties. Biochemical and site-directed mutagenesis studies revealed that PpoA uses both domains to catalyze two separate reaction steps; the peroxidase domain first oxidizes linoleic acid to (8R)-hydroperoxy-octadecadienoic acid (8-HPODE), and then the C-terminal thiolate domain isomerizes 8-HPODE to 5,8-dihydroxy-octadecadienoic acid (5,8-DiHODE). This mechanism is quite different than that of a related fatty acid dioxygenase in *Gaeumannomyces graminis*, which has only one predicted heme domain and converts the 8-HPODE intermediate to (7S,8S)-DiHODE. PpoA is similar to other enzymatic partnerships in which separately expressed fatty acid dioxygenases and cytochrome P450s form bioactive products; in PpoA, though, the roles of fatty acid peroxide production and its isomerization are combined in a single fusion protein, making this enzyme unique.



Hypothetical catalytic mechanism of *A. nidulans* PpoA.

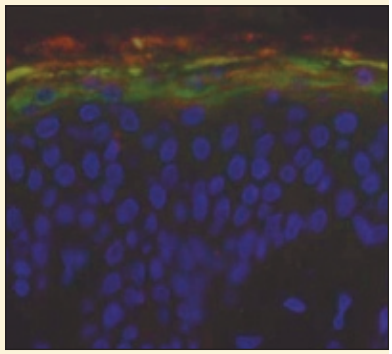
Identification of PSI Factor Producing Oxygenase A (PpoA) from *Aspergillus nidulans* as a Fusion Protein of a Fatty Acid Heme Dioxygenase/Peroxidase and a Cytochrome P450

Florian Brodhun, Cornelia Göbel, Ellen Hornung, and Ivo Feussner

J. Biol. Chem. 2009, published online March 13

jbc

Getting under BH's Skin



Immunofluorescence staining of human skin tissue shows the co-localization of bleomycin hydrolase (*red*) and filaggrin (*green*) in the upper layer of the epidermis.

The natural ability of our skin to remain hydrated is due to the presence of numerous hygroscopic amino acids known as natural moisturizing factors or NMFs. Concentrated in the epidermal upper layer, these NMFs arise from an insoluble protein known as profilaggrin, which during the course of epidermal progression is first broken down into smaller filaggrin filaments, that are subsequently deiminated (creating citrulline side chains), and then further broken down to peptides and finally individual amino acids. The proteases responsible for most of these processing steps remain unknown, but in this study, the researchers employed some elegant biochemical analyses to identify bleomycin hydrolase (BH) as an essential component of the final step that generates the free amino acids. Immunohistochemical analysis also revealed that BH and filaggrin co-localized in the granular layer of the epidermis, which, together with some previous genetic studies, confirms the role of BH as an NMF protease. This study provides valuable insight on a protein that has been well-known for its ability to detoxify bleomycin-based cancer drugs, but whose normal function has remained somewhat elusive.

Neutral Cysteine Protease Bleomycin Hydrolase Is Essential for the Breakdown of Deiminated Filaggrin into Amino Acids

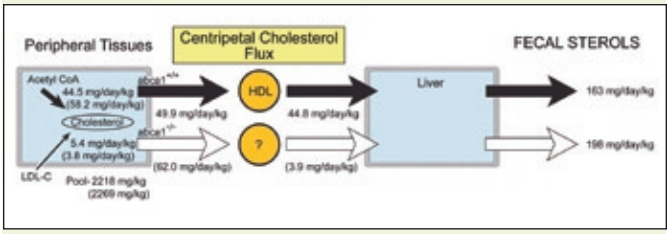
Yayoi Kamata, Aya Taniguchi, Mami Yamamoto, Junko Nomura, Kazuhiko Ishihara, Hidenari Takahara, Toshihiko Hibino, and Atsushi Takeda

J. Biol. Chem. 2009, published online March 13

jbc

The Conundrum of Cholesterol Transport

The cells in our body continually replace, or "turn over," the cholesterol present in cell membranes, shuttling the cholesterol to the liver where it can be converted to bile acids and excreted from the body. For a while, it had been envisioned that the ATP-binding cassette transporter A1 (ABCA1) was a key component enabling this reverse cholesterol transport, but recent data suggest otherwise. In this study, the researchers use mouse models to definitively quantify that functional ABCA1 is not required for cholesterol turnover in peripheral organs or in cholesterol excretion. The sterol pool in the peripheral organs of both control and *abca-* mice was consistently around 2200 mg/kg, and though there was a marked reduction in the rate of cholesteryl ester movement through HDL to the liver in *abca-* mice (3.9 mg/day/kg versus normal rate of 44.8 mg/day/kg), neither the total centripetal efflux of cholesterol nor the rate of fecal sterol excretion was reduced in these animals. So, although ABCA1 still has critical cellular functions such as removing cholesterol from macrophages, it appears to play no role in controlling reverse cholesterol transport.



Flow chart comparing centripetal cholesterol transport in normal and ABCA1-deficient mice (*abca-* numbers in *parentheses*).

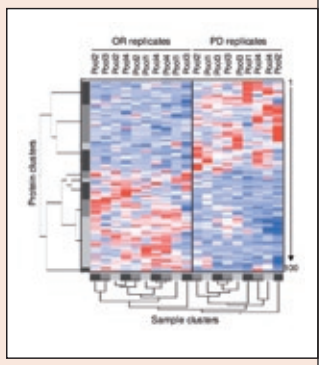
ABCA1 Plays No Role in the Centripetal Movement of Cholesterol from Peripheral Tissues to the Liver and Intestine in the Mouse

Chonglun Xie, Stephen D. Turley, and John M. Dietschy

J. Lipid Res. 2009, published online March 12

Breast Cancer Biomarkers

Tamoxifen is an anti-estrogenic agent that has achieved great success in the treatment of breast cancer; however, in about 50 percent of cases of recurrent disease, tamoxifen provides no benefit due to intrinsic resistance, and many of the patients who do respond will eventually develop progressive disease due to acquired tamoxifen resistance.



Hierarchical clustering of objective response (*OR*) and progressive disease (*PD*) breast tumor samples.

Therefore, identifying proteins that associate with tamoxifen resistance would be a vital step toward better response prediction. In this study, the researchers undertook a comparative proteome analysis of over 5,000 pooled tumor cells obtained through laser capture microdissection (LCM) that contained both tamoxifen-sensitive and tamoxifen-resistant tumors. They identified 100 differentially abundant proteins between the two tumor types and verified 47 of those through targeted nanoLC-MS/MS. One of the most promising candidates was EMMPRIN, which was more prevalent in therapy-resistant tumors and significantly associated with an earlier tumor progression following first-line tamoxifen treatment. EMMPRIN and the other differentially expressed proteins may hold potential as biomarkers to identify tamoxifen resistance in recurrent breast cancer.

Identification of a Putative Protein Profile Associating with Tamoxifen Therapy Resistance in Breast Cancer

Arzu Umar, Hyuk Kang, Annemieke M. Timmermans, Maxime P. Look, Marion E. Meijer-van Gelder, Michael A. den Bakker, Navdeep Jaitly, John W. M. Martens, Theo M. Luider, John A. Foekens, and Ljiljana Pasa-Tolic

Mol. Cell. Prot. 2009, published online March 27

Benjamin Neel: Phosphatases and Disease

BY NICK ZAGORSKI

Every once in a while, Ben Neel likes to joke that he peaked too early. As a vivid example, he recalls an incident from 1983. Neel, then conducting the medical portion of his MD/PhD degree at Cornell Medical School in New York (having just completed his PhD at nearby Rockefeller University), had traveled to Boston to visit his future wife, who was a graduate student in the computer science department at MIT. One day, as they were leaving her departmental building, which just happened to be located directly across from the newly formed Whitehead Institute, a postdoc in Robert Weinberg's lab (the pioneering researcher who first isolated the *ras* oncogene and Rb tumor suppressor gene) approached him and asked, "Hey, didn't you used to be Ben Neel?"

The basis for that playful ribbing stemmed from Neel's recent groundbreaking graduate studies at Rockefeller under William S. Hayward on slowly transforming RNA tumor viruses. Unlike rapidly transforming viruses, such as the noted Rous sarcoma virus (RSV), which helped spur two different Nobel prizes in medicine, and which drive an efficient transformation of normal cells into cancerous ones, avian leukosis virus (ALV) and other slowly transforming viruses don't have any specific "transforming genes," like *src* in RSV, that can induce rapid cell growth. However, ALV-infected cells could still become cancerous after a few months, indicating some mechanism of activation.

So what was the activating factor? Neel notes that Hayward proposed the idea that ALV was integrating near cellular genes, inducing an overstimulation of expression and transforming the cells, which was an unusual theory back in the 1970s. "Science had not yet clearly shown that bona fide tumors could arise solely from activated cellular oncogenes," Neel says. "Researchers were intent on uncovering how the cellular genes could get into viruses and help inform the molecular basis for viral oncogenesis; they hadn't yet demonstrated that the cellular genes themselves were a rich source of cancer in their own right."

But there were some recent studies to support the idea of cellular transformation. For example, Hidesaburo Hanafusa, the head of Rockefeller's viral oncology lab where Neel and Hayward worked, had demonstrated that RSV particles missing part of their *src* gene, and thus supposedly defective, could still induce cancer in chickens by means of recombining the remaining viral *src* with cellular *src* to create a fusion gene. Soon thereafter, George Vande Woude at the National Cancer Institute showed that simply attaching the long terminal repeats (LTRs) that flank retroviral genes onto a normal cellular gene could be sufficient to promote transformation.

So when Neel heard Hayward's idea, it seemed intuitively correct. "When I started in the lab, Bill actually gave me two projects," Neel notes. "One was the work with slow virus activation, and the other involved identifying the numerous small RNAs that were packaged into retroviral particles. But when Bill started explaining his model, I focused my

energies into those studies because I realized the tremendous implications if we could prove it."

In examining numerous ALV-infected cells, Neel, Hawyard, and collaborator Sue Astrin at Fox-Chase soon found a connection: the cells that eventually became cancerous all had similar sites of viral integration. "These slow viruses were inserting themselves next to a normal gene, thus placing it under control of the highly active viral promoter and ratcheting up its expression, which in turn caused transformation," he says. "What's more, in all of the tumors, the gene in question was *c-myc*, which happened to be very similar to a viral 'transforming gene.'" As Neel notes, the other shoe had now dropped.

This discovery helped change scientific thinking on these cellular "oncogenes" and the origins of cancer. "In fact, I realized that this model of 'promoter insertion' could be generalized for other events, like cancer arising because genes switched promoters via a chromosomal translocation," Neel says. "I actually wrote that theory into the first draft of our paper, but Bill made me take it out because it was too speculative."

Still, it was certainly an impressive way to begin a research career, especially considering that it really began by accident. (When he arrived at Rockefeller, Neel didn't have any specific labs in mind and interviewed with several investigators; then one day several students from Hanafusa's lab came up to him and said they had heard he had joined their group. "I actually hadn't, but it seemed as good a lab as any, so I decided to pick it.") Now, just a few short years later, Neel stood on the campus of MIT wondering if he really was washed up before 30.

"There you have it," he says wryly, "My first two papers were my best, and it's been all downhill since."

A Plethora of PTPs

Despite his assertions, however, it is an injustice to consider Neel, currently the Director of the Ontario Cancer Institute as well as a Professor of Medical Biophysics at the University of Toronto, solely for his work done as a graduate student. Admittedly, after finishing his residency and beginning a postdoc with Raymond Erikson in 1985, Neel experienced some difficulties—more of his postdoctoral projects failed than succeeded—that may have reinforced his belief that his best days were behind him. But since beginning his own lab at Harvard in 1988, Neel has become recognized as a leader in the field of signal transduction, particularly in regard to protein-tyrosine phosphatases (the enzymes that remove the phosphate modifications attached by kinases). "Coming from a background of identifying and analyzing oncogenes, it was a natural progression for me to begin looking into the functional aspects of the proteins encoded by these oncogenes," Neel says.

> **"Researchers were intent on uncovering how the cellular genes could get into viruses and help inform the molecular basis for viral oncogenesis; they hadn't yet demonstrated that the cellular genes themselves were a rich source of cancer in their own right."**

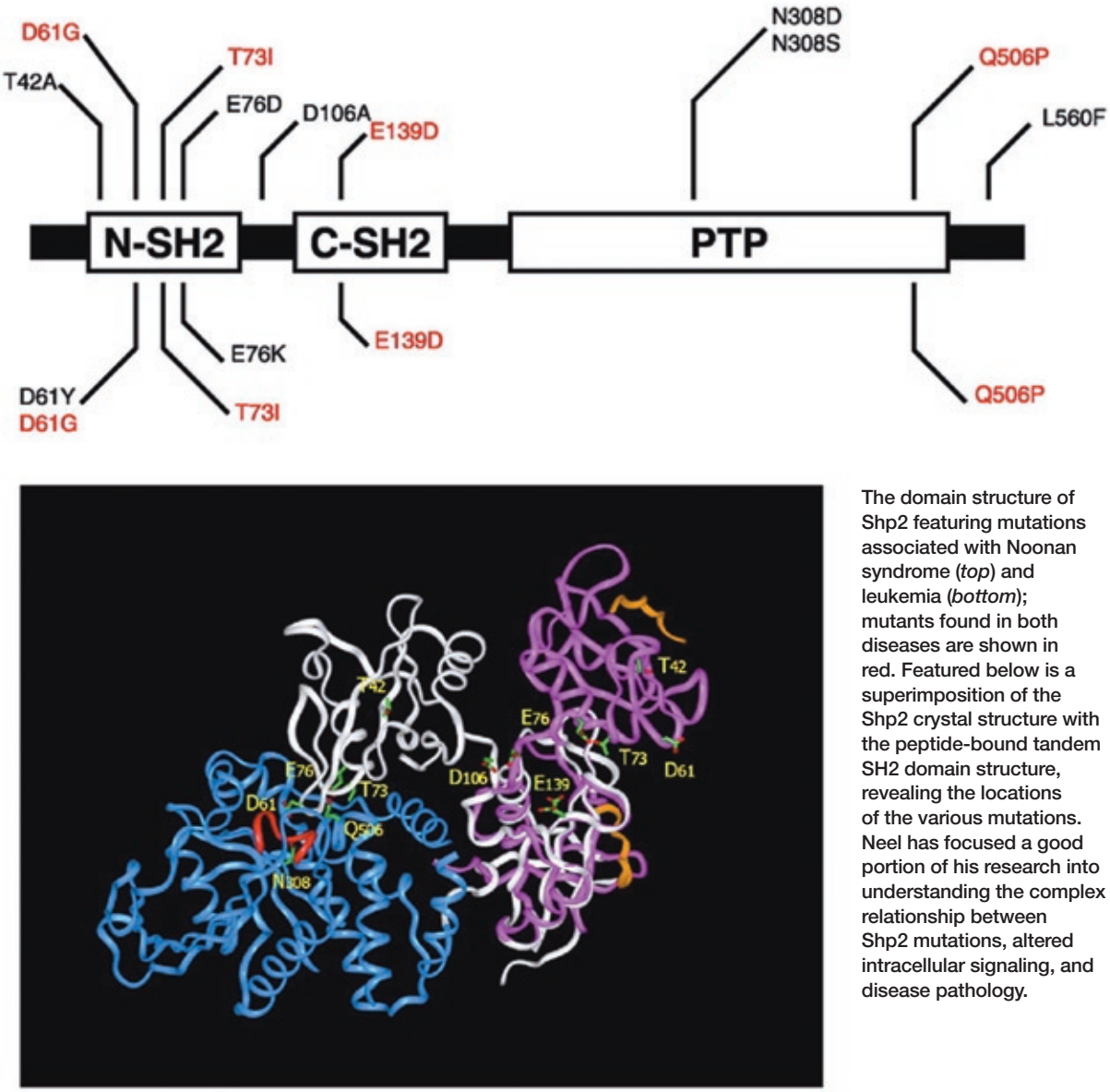
For example, Neel has contributed much to our knowledge of Protein tyrosine phosphatase-1B (PTP1B), such as his group's findings that this phosphatase localizes on the endoplasmic reticulum and is a major mechanism by which receptor tyrosine kinases are inactivated (following their endocytosis). In addition, along with Barbara Kahn at Beth Israel Deaconess Medical Center, he's been elucidating PTP1B's importance in regulating glucose homeostasis and its association with diabetes and obesity; and Neel and his postdoc Mohamed Bentires-Alj also recently demonstrated that PTP1B was involved in Her-2/Neu-induced breast cancer.

Another significant part of Neel's work has been studying *src* homology domain-containing phosphatase 2 (SHP2), a ubiquitous phosphatase that activates the Ras/Erk signaling pathway and is a vital component of many developmental processes. As such SHP2 is connected with several

human diseases, including Noonan syndrome and the clinically related LEOPARD syndrome, inherited disorders that result in numerous growth defects (Noonan syndrome is one of the leading contributors to congenital heart disease). Following up on the work of Bruce Gelb and Marco Tartaglia, which identified that dominant SHP2 mutants were responsible for these disorders, Neel helped show that these conditions were in fact brought on by different biochemical mechanisms: Noonan syndrome arises from SHP2-hyperactivating mutations; whereas in LEOPARD, the mutations create an inactive form of SHP2, revealing that Noonan and LEOPARD are distinct disorders that manifest in a similar manner.

As he reflects back on his academic career, though, Neel notes that unlike his PhD project, which he knew would be significant, the work done in his own lab has usually produced studies that didn't seem important at the time but have ended up being some of his most relevant work.

"In retrospect, one of our most important studies was carried out by Alana O'Reilly in 2000 on Shp2 activating mutants," he says. Initially, that project started out simply as an effort to test some predictions about SHP2 activity that were suggested by the crystal structure recently solved by



The domain structure of Shp2 featuring mutations associated with Noonan syndrome (*top*) and leukemia (*bottom*); mutants found in both diseases are shown in red. Featured below is a superimposition of the Shp2 crystal structure with the peptide-bound tandem SH2 domain structure, revealing the locations of the various mutations. Neel has focused a good portion of his research into understanding the complex relationship between Shp2 mutations, altered intracellular signaling, and disease pathology.

Harvard colleagues Scott Pluskey and Steven Shoelson. They created two "active" SHP2 mutants and examined their effect on *Xenopus* frog development; these active phosphatases could induce elongation in embryo cells similar to what would happen if fibroblast growth factor (FGF) had been added.

"Little did we realize that this paper would anticipate and explain how the SHP2 gain of function mutants that cause Noonan syndrome operated," he says, referring to one of his newest discoveries in which he uncovered the mechanism explaining the cardiac defects brought on by Noonan syndrome: an excess of SHP2 activity in the endocardium (the inner layer of the heart) causes excessive valvular mesenchyme production, resulting in defective heart valves (similar disruptions in the developing neural crest cause the facial abnormalities).

The very first paper from his group, in which they demonstrated that the expression of the retinoid receptor RAR-beta was frequently defective in lung tumors, is another fine example. "Later work showed that RAR-beta induction in response to retinoids was a good marker to test whether patients would respond to retinoid chemoprevention therapy," Neel says. "So our work had an important clinical impact, but it's something we don't get credit for because our lab has been so strongly associated with the phosphatase field."

North by Northwest

As in many cases, Neel's interest in cancer biology has a personal side; one of his major motivations for choosing medicine was experiencing many family members succumb to this disease, especially his grandmother Ida whom he was close to growing up. So in 2007, after a distinguished tenure in basic research, Neel decided to head in a new direction in order to bring back some of that personal side of science. "Having graduated as an MD/PhD, I felt I had a duty to undertake more translational research," he says. "I also wanted an opportunity to have a bigger impact than just running my own lab."

That impact would be found as Director of the Ontario Cancer Institute (OCI), Canada's largest cancer center—thus making his move quite significant at both the personal and professional levels. And it has required a bit of adjustment. "From the visits I took before moving here, I had the impression that Toronto was basically New York with a little less crime and pollution," he says. "But in my first year, I have noticed that there is definitely a different culture here." One major difference Neel highlights is that, despite its status as a metropolis, Toronto has a far less stressed atmosphere than major cities in the Northeastern United States (and having lived most of his life in Philadelphia, New York, or Boston, Neel doesn't mind this change).

And although Neel will miss the extremely high concentration of "scientific dynamism" present in Boston, he points out this can be both good and bad. "The depth and breadth of research in Boston is so staggering that it's not even the case that there's someone in every area of study; there's probably four or five people in every area of study," he says. "And it reaches a point where intellectual space can get pretty crowded." And he also adds that Toronto, which features researchers like Tak Mak and recent Kyoto Prize winner Anthony Pawson, is no slouch when it comes to hosting smart and intellectual people.

And with the numerous well-run hospitals and clinics in the city, Toronto also provides a large patient and sample population that Neel sees as a tremendous resource. "One of my main long-term goals as director is to create a platform that brings our basic researchers and clinicians together, so we can better utilize our clinical population and speed up the translation of our exciting work in cancer genetics to the patients," he says, citing the work Massachusetts General Hospital has begun in genotyping tumors to test for genes that may correlate with clinical outcome as an example. To help with this effort, Neel is refocusing and recharging the OCI to make it more interactive, a task that includes hiring several new faculty members.

On the research side of things,

Out of Focus: Immortality Denied

While phosphate-removing enzymes have been Neel's primary focus, one of his first major contributions to the signaling arena involved identifying a novel protein kinase that could be induced by serum (he and fellow postdoc Dan Simmons carried out this work during his time with Erikson). Naturally, Simmons and Neel named this protein serum-inducible kinase or SNK. "Of course, it didn't escape our attention that SNK could also stand for 'Simmons-Neel kinase,' giving us a permanent fixture in the scientific literature." Unfortunately, their immortality would be short-lived; it was subsequently discovered that SNK was just one member of a larger Polo-like family of kinases, and a few years after its discovery, SNK was renamed PLK2 so that all the Polo-like kinases would have consistent nomenclature.

Neel has continued his studies into phosphatases, and in addition to using the great clinical resources available, he is taking advantage of a local strength in proteomics to get a broader view of phosphatase substrates and binding partners in order to answer questions such as why the opposite SHP2 defects underlying Noonan and Leopard syndromes produce such similar phenotypes. Neel has also decided to use his move to Toronto and the associated clinical population to initiate a study into cancer stem cells, particularly in identifying and characterizing the native stem cell populations in solid tumors such as ovarian and lung cancers, as well as in leukemia.

Of course, he notes that when he mentioned that he would be working at the Division of Stem Cell and Developmental Biology, he too frequently heard the question: "Oh, are you moving to Canada because of Bush and the restrictions on stem cells?" Much like the question posed by Weinberg's postdoc many years ago, this one took him slightly aback; while not getting overly political, Neel thinks that some people, including scientists, have been overly dramatic about the stem cell controversy. Fortunately, Neel didn't have to worry about any political discussions because he could always reply, "No, it was just a matter of finding a great opportunity in a great location."

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www.lipidmaps.org

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www.easo.org/eco2009

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www.selectbiosciencies.com/conferences/files/Agendas2009/CP2009_Agenda.pdf

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www.bb.iastate.edu/~gfst/phomepg.html

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www.lakemedelsakademin.se/templates/LMAstandard.aspx?id=2529

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International Conference on Cytochrome P450
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www.grc.org/programs.aspx?year=2009&program=athero

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www.sebiology.org/meetings/Glasgow/glasgow.html

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www.grc.org/programs.aspx?year=2009&program=stressprot

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www.soph.uab.edu/ssg/nsfstatgen/nsfsecondannual

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www.insulinresistance.us

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NOVEMBER 12–15, 2009
SAN DIEGO, CA
www.glycobiology.org

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sapmea.asn.au/conventions/signalling09/index.html

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SAN JUAN, PR
www.glyco20.org

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www.biophysics.org/Default.aspx?alias=www.biophysics.org/2009meeting

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Saturday, October 24 — STRUCTURE
John-Marc Chandonia, Lawrence Berkeley National Laboratory
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