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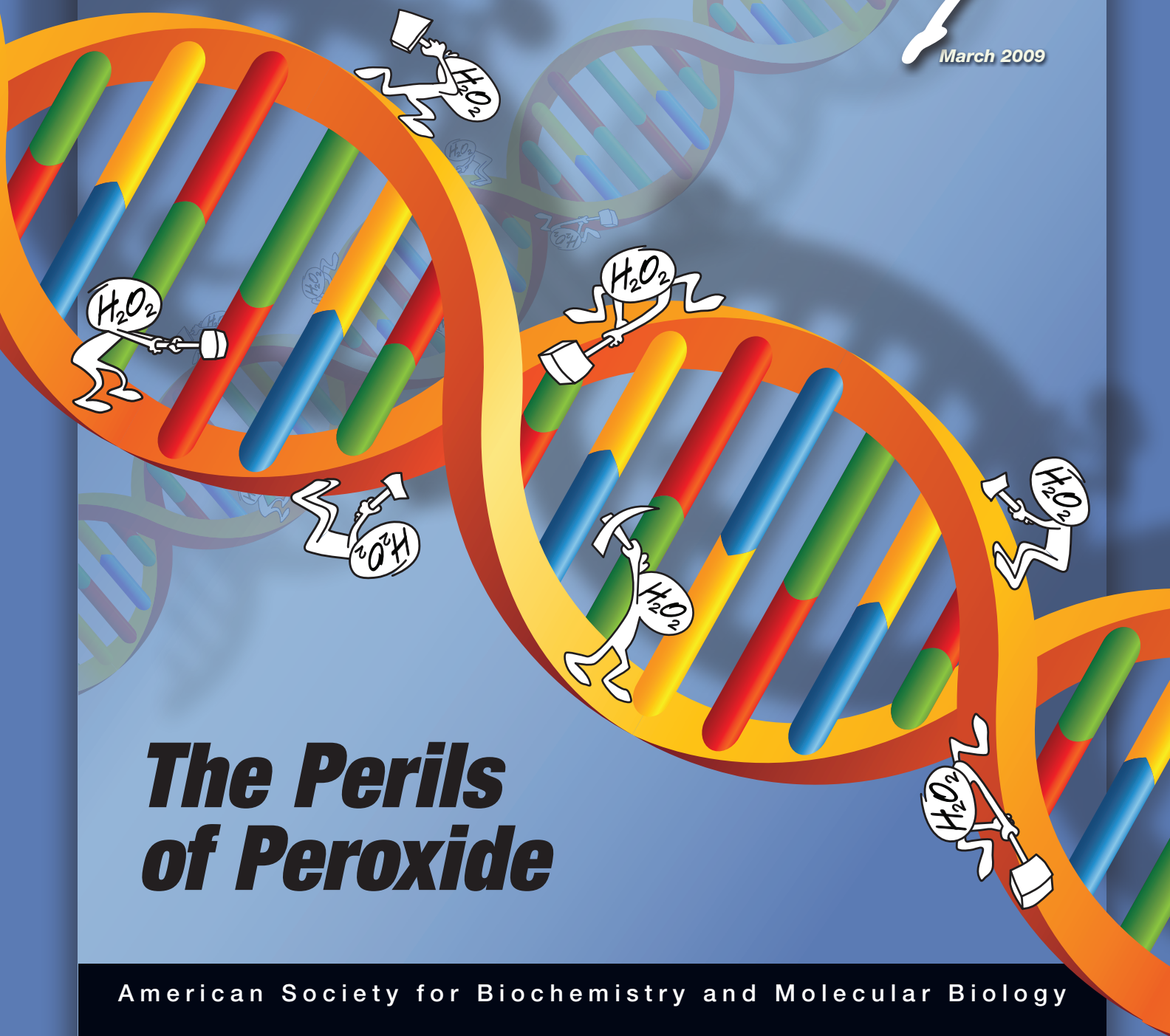
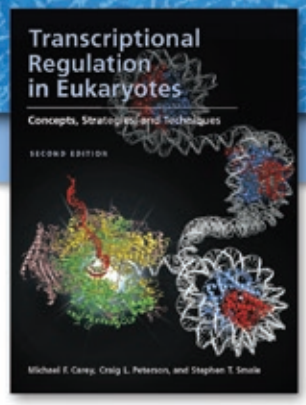


The Perils of Peroxide

American Society for Biochemistry and Molecular Biology

Transcriptional Regulation in Eukaryotes

Concepts, Strategies, and Techniques, Second Edition



By Michael F. Carey, *University of California, Los Angeles;* Craig L. Peterson, *University of Massachusetts Medical School, Worcester;* and Stephen T. Smale, *University of California, Los Angeles*

Strategies for studying gene regulation mechanisms have changed dramatically over the past several years in light of the emergence of complete genome sequences for many organisms as well as the development of or improvements to technologies such as chromatin immunoprecipitation, RNA interference, microarrays, and proteomics.

The first edition of the highly successful *Transcriptional Regulation in Eukaryotes,* written by Michael Carey and Stephen Smale at UCLA, provided a comprehensive source of strategic, conceptual, and technical information for investigating the complexities of gene regulation at the level of transcription.

With the ever-increasing importance of genome data and the appearance of new and better techniques, the second edition of this book has added a third author, Craig Peterson at the University of Massachusetts Medical School. In addition to a new chapter on the in vitro analysis of chromatin templates for DNA-binding studies and transcription, this second edition has been extensively rewritten and updated to discuss new advances in the field and their impact on gene regulation mechanisms. The second edition retains the approach of the first in covering both the conceptual and practical aspects of how to study the regulation of a newly isolated gene and the biochemistry of a new transcription factor.

Transcriptional Regulation in Eukaryotes serves as both a powerful textbook and manual for advanced instruction in molecular biology which

- supplements clearly written text with extensive illustrations
- puts methods in the context of underlying theory
- gives expert recommendations on experimental strategies
- encourages creativity in investigative design
- explains protocols for essential techniques step by step, with extensive advice on troubleshooting
- provides the latest methods in use in the field

This important and unique book is essential reading for anyone pursuing the analysis of gene expression in model systems or disease states, providing underlying theory and perspective to the newcomer and the latest techniques to the expert.

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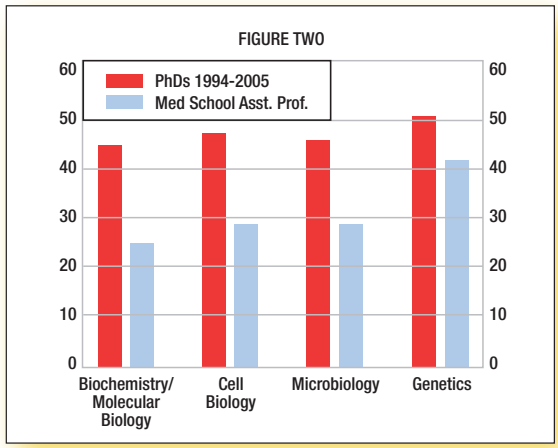

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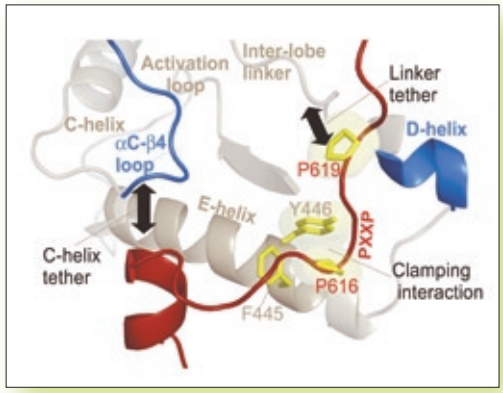

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podcast summary

This month's *JBC* Podcast features interviews with authors from the recent *JBC* Thematic Series: *Metals in Biology*.

You can listen to the podcast at www.asbmb.org/Interactive.aspx and you can view the Thematic Minireview Series at www.jbc.org/thematics/metal.

ASBMB today

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ASBMB Today
Nicole Kresge *Editor*
nkresge@asbmb.org
Nick Zagorski *Science Writer*
nzagorski@asbmb.org
Nancy J. Rodnan *Director of Publications*
nrodnan@asbmb.org
Barbara Gordon *Executive Director*
bgordon@asbmb.org

Magazine design & production: Amy Phifer

For information on advertising contact
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2008 APEX AWARDS FOR PUBLICATION EXCELLENCE

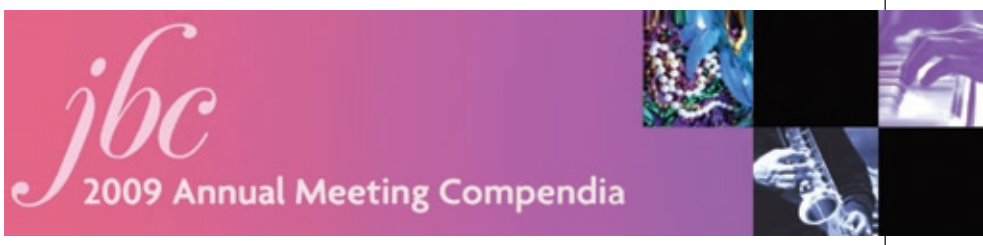
from the **editor**

JBC Annual Meeting Thematic Compendia

BY NICOLE KRESGE

At last year's annual meeting in San Diego, ASBMB introduced a special compendium of recent *Journal of Biological Chemistry* articles entitled "RNA-mediated Regulation and Non-coding RNAs." The compendium was assembled and distributed at the meeting to highlight the exciting RNA-themed symposia that were being presented, as well as the excellent RNA-related research being published in the *JBC*. The compendium was eagerly snapped up by enthusiastic meeting attendees, and we received much positive feedback and many new RNA-related submissions to the *JBC*. As a result, ASBMB has decided on a repeat performance.

This year at the New Orleans meeting in April, however, ASBMB will present not one, but eight compendia, each containing anywhere from 10 to 15 *JBC* articles published between 2007 and 2008 that reflect the various symposia themes. The included articles were selected by *JBC* associate editors based on both their high impact and their connection to the topics discussed at this year's meeting.



Four of the compendia will be available in hardcopy at the annual meeting. These include "Chromatin Structure and Transcription" by Joel Gottesfeld, "Protein Folding & Aggregation" by Norma Allewell, "Membrane Dynamics" by Robert Simoni, and "Signaling and Cancer" by Xiao-Fan Wang. All four of these compendia will also be available for viewing this month on the *JBC* website "Thematic Reviews" page (jbc.org/meeting2009). In addition, ASBMB will offer four "virtual" compendia on this page: "The Biological Chemistry of RNA" by Martha Fedor, "DNA Replication & Repair" by Robert Lehman, "Proteolysis" by Judith Bond, and "The New Metabolism" by Richard Hanson.

We believe these *JBC* compendia will offer an excellent primer to the themes discussed at this year's annual meeting, and we encourage you to take a look at these compilations. You won't be disappointed!

Nicole Kresge

letters to the editor

Recent NIH Reforms

To the Editor,

The recent reforms that will be implemented at NIH are generally a positive first step in alleviating the research funding crisis in the U.S.; however, I believe that the reforms will not be enough. The reforms, once enacted, will hopefully help young investigators receive their first major grants and ward off the loss of a generation of PIs that fail to achieve tenure. The reforms also have some parts that will help the top researchers at large research institutes and research one universities maintain their funding.

On the other hand, I believe that the reforms will do little to fix the funding crisis for mid-career researchers at smaller to medium-sized Ph.D.-granting schools. These smaller schools provide many of the domestic students who go on to graduate school/postdocs at the larger universities. The lack of funding is causing once very productive research labs to close their doors and not provide significant hands-on training to future scientists (undergrad, grad, and postdoc). The funding problem at the smaller schools is leading many of the top undergraduates/graduates to choose not to go into science research. This erosion of domestic talent has been occurring for years, but it is happening more frequently now. The impact of this current funding situation has not been fully felt yet, in my opinion. As the number of domestic grad students diminishes, research groups will need to rely more and more on international students to fill their classes and research labs. If the percentage of international graduate students continues to grow, I fear that the American public will grow tired of their tax money being used to educate these students and thus devalue the contribution that science makes in their lives.

I believe that the most essential goal that NIH must achieve in the next one to two years is to return funding success rates back to the 25–33 percent region (the success rate reported on the NIH website does not count resubmissions of grants proposals in a calendar year). While there are efforts to increase the funding rate at NIH (across the board cuts on grants for example), the major strategy endorsed by ASBMB, ACS, and other scientific societies is to request more and more funding from the government. President-elect Obama has stated that he intends to increase federal funding for research; however, a great deal of that money appears to be slated for energy issues (rightfully so) and not necessarily for PI-initiated, basic research projects like those at NIH. As a father of three children, I am very concerned about simply throwing more money at the problem given the troubling and growing debt of this country (currently $10 trillion, with almost $50 trillion including the promises of Medicare and Social Security). **I believe that the implementation of some policy changes at NIH could significantly increase the funding success rate at NIH and thereby fix funding problems at other agencies.** For example:

1. **Reduce the amount of an average award.** During the time when the NIH budget was being doubled, the leaders at NIH decided to increase the amounts of the awards rather than to increase the percentage of funded proposals. This decision was probably correct because NIH should fund only the best proposals. However, this model would only work if the NIH budget increased by significant amounts forever. When the large budget increases stopped, the funding crisis started. The average amount of R01s in 1997 was $282,000 (direct and indirect), while in 2007 the average was $432,000. While the average R01 funding levels increased, a modular budget system was implemented for grant proposals that requested less than or equal to $250,000 per year in direct costs only. The modular budgets do not require PIs to provide as much budget justification as in the past, and panel members do not have enough information to make informed decisions about justified costs. The modular budget scenario has led to SRAs and research officers at research institutes to advise most applicants to request the maximum $250,000 direct costs every year (else the panels would not view the proposal as serious), regardless of whether the money can be justified. During the same time, award amounts at other funding agencies did not grow to similar levels, yet researchers with grant proposals from NSF, AHA, and others have clearly demonstrated that they can be very productive. A substantial decrease in the amount of

CORRECTION: In an article titled "ASBMB Members Elected as AAAS Fellows" in the February 2009 issue of *ASBMB Today*, we mistakenly omitted **Craig C. Malbon** of the State University of New York, Stony Brook from our list of fellows. Malbon was elected to the AAAS Section on Pharmaceutical Sciences.

R01 award amounts (and making sure that the requested funds are fully justified) will free up significant money to increase the funding success rate at NIH.

2. **More information for the panels to assess grant proposals.** In addition to providing more detailed justification for requested funds, panel members should be provided with information about all funding in a research lab. Many PIs request funds well over the $250,000 direct cost level, yet PIs are not required to report postdoctoral or predoctoral fellowships (or training grant fellowships) that have been awarded to students in their labs. Since 70–75 percent of the costs of most typical grants are associated with personnel, this information is necessary to evaluate proposed budgets. While some attention is paid to budgets after the science review stage at NIH, the panel members who have current on-going research are in the best position to evaluate costs to conduct most research projects.

3. **Cap indirect costs to a max of 45–50 percent.** It is shocking to me that some institutes can charge indirect costs of over 100 percent, particularly for RO1s. Some funding agencies have capped indirect cost rates, and I suspect that not a single PI (research facility) has ever declined a grant that was awarded. While indirect costs are vital for the infrastructure in research labs, excessive indirect costs pull funds away from the pool of money that could be used to fund more grant proposals. The last time that the NIH budget doubled, research institutions across the country decided to add several new, soft money research positions, causing the total number of NIH RO1 applications to skyrocket. A lot of these individuals have lost their positions over the last few years. I believe that a significant reduction in the indirect costs rate would minimize this effect in the future.

4. **Reduce or eliminate tuition charges for research assistants.** PIs at many universities are forced by their administrators to request funds for tuition of the RAs on grants (on top of large indirect costs percentages). The addition of tuition and fees to the stipends results in graduate students costing PIs as much or more than postdoctoral associates. At other schools, PIs do not have to request tuition and fees for the RAs, and their schools grant tuition/fee waivers. There needs to be some consistency on this practice; however during this time of low funding success rates, NIH should strongly consider not allowing for tuition costs and force universities to cost share these expenses, perhaps by using some of the indirect costs money.

5. **Evaluate PIs with multiple major grants more carefully.** A quick scan of the CRISP databank will reveal a large number of investigators with multiple R01s and other grants (PO1s, etc). Many of these PIs deserve to have multiple grants and produce large amounts of significant research and graduate top researchers. However, there are also too many who have more than two RO1s who do not publish much, do not graduate many students, etc. While many are funded because the research is outstanding, some of the grants are funded because of the "circle the wagon" mentality mentioned below. In the past, leaders at NIH indicated that careful scrutiny would be placed on PIs with multiple RO1s; however, I believe that more should be done on this front.

6. **Suspend Pioneer and similar awards until the funding success rates are increased.** I believe that the aim to increase grants like the Pioneer award is not wise at this time given the current funding success rates. People who get these awards typically already have significant federal funding. There are only a handful of people who can justify more than or equal to $1 million of direct costs a year. When funding success rates return to a healthy level, initiatives like the Pioneer program should be re-implemented.

7. **If efforts to increase the funding success rates are not implemented, I suggest that the make-up of the panels be changed more frequently and that SRAs be moved to different panels more frequently.** This recommendation is in contrast to one of the new NIH reforms. While I understand the idea of keeping some consistency in panels, this consistency can also be a problem for any researchers not closely related to the panel members. When funding rates are low, there is a "circle the wagons" mentality at the panels, and I have personally witnessed it. If a proposal is truly heads and shoulders above others, different panel members will be able to identify it. In my experience, some of these "highly meritorious" grant proposals were categorized as this because of the rather stagnant panel make-ups. I have heard comments like "while the proposal is fundamentally flawed, this PI is smart and will figure it out" far too often on panels. By the same line of argument, SRAs should be moved frequently from panel to panel. Consistency on panels is important, but fairness trumps consistency. An SRA is an administrator and should not be tied to any given panel for too long.

These seven suggestions are offered as a discussion starting point for our community to fix the funding situation in biomedical sciences. However, most of these suggestions focus on the RO1 mechanism, and revisions in other funding mechanisms are undoubtedly needed. I believe that the ultimate goal of this endeavor should be to increase the funding success rate. While I am cautiously optimistic about the new administration and our funding situation, I believe that we should explore any and all ways to remedy the problem and not only rely on massive spending increases from Congress.

Michael W. Crowder
Miami University, Oxford, OH

Why We Said "Yes, Thank You"

BY GREG PETSKO

By the time you read this, the United States Congress will almost certainly have passed some form of economic stimulus package. President Obama has requested something in the neighborhood of $850 billion to rebuild our crumbling, antiquated infrastructure of roads, bridges, and schools; modernize our primitive electrical grid; and do a variety of other things aimed at putting people back to work and preventing others from losing their jobs. Economists are divided over whether this is too much or not enough government spending, but there seems little doubt that something close to this will pass. The version already approved by the House of Representatives (with not a single Republican vote in its favor) contains, as a specific line item, $3.5 billion in one-time stimulus money for the National Institutes of Health (NIH), the country's leading funding agency for biomedical science.

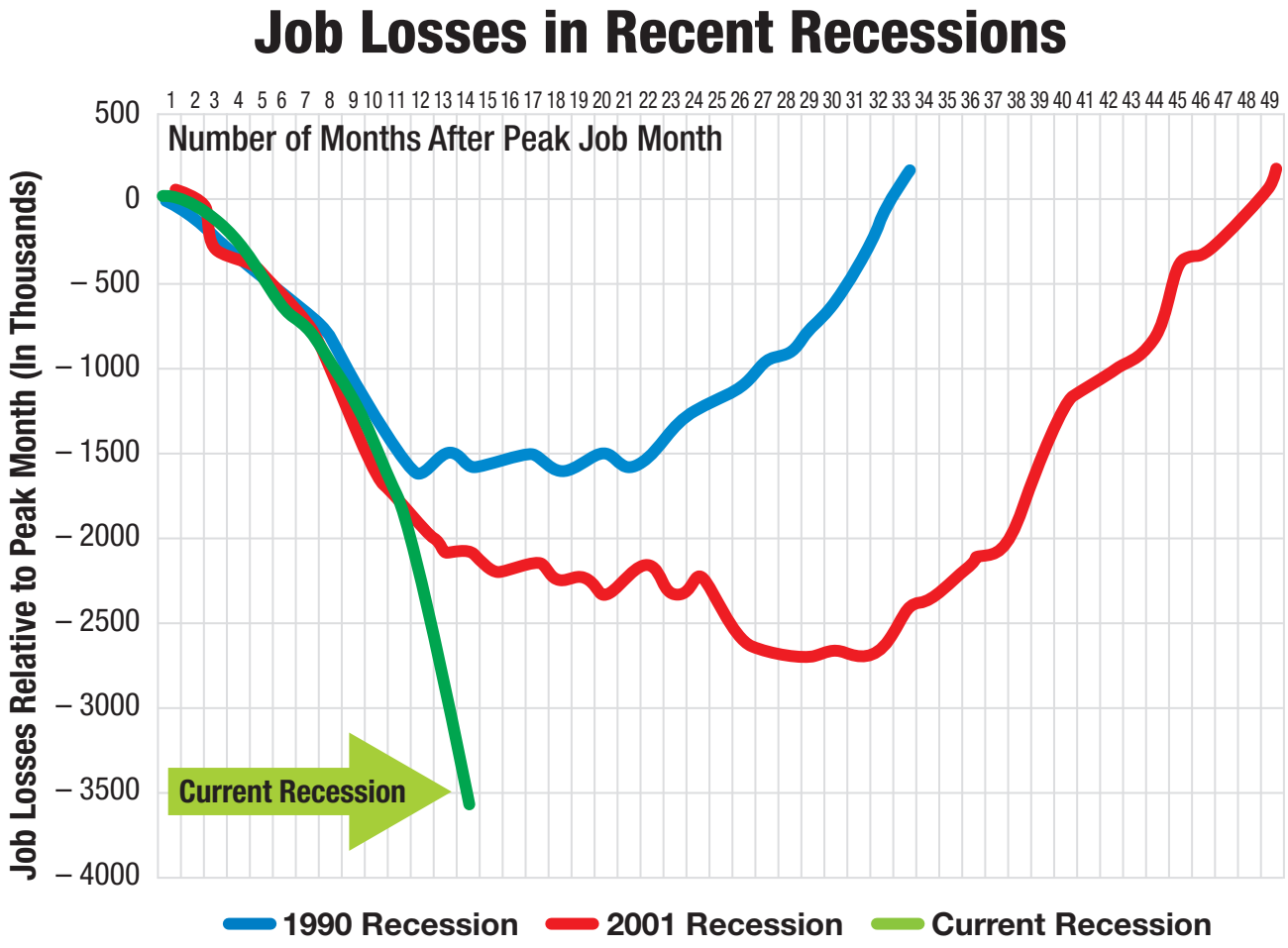
The Senate is considering its own version of the bill as this is being written. That version now contains an amendment proposed by Sen. Arlen Specter (R-PA), a longtime friend to biomedical research, that would increase that $3.5 billion to $10 billion, spread over two years.

You might think that the prospect of an injection of money equal to about a third of the NIH yearly budget would be greeted with shouts of joy by the life science community, but the chorus of approval was surprisingly muted, and many prominent scientists expressed—mostly privately—strong reservations about the amendment. Many scientific societies hesitated to offer public support for Specter's amendment when it was announced (or even for the more modest House stimulus); some still haven't done so. The American Society for Biochemistry and Molecular Biology was an exception: we came out early with a strong expression of support and were strong in our gratitude to Sen. Specter for his action. But since the whole idea of a stimulus for NIH has been controversial, especially within the scientific community, I want to tell you why we supported it.

Many scientific societies hesitated to offer public support for Specter's amendment when it was announced.

Objections to a specific stimulus for biomedical research have been based on two arguments: first, that it smacks of "pork barrel spending," and second, that a bolus of short-term money exacerbates the disturbing trend at NIH of moving away from individual investigator-initiated research and towards government-initiated "big science" projects.

I think the first objection is easily answered. Although a great deal of pork barrel spending is wasteful, that cannot be said of stimulus money for NIH. Federal spending on biomedical research is actually a strong generator of economic prosperity. The "multiplier effect" for every dollar spent by NIH is calculated to be about 2.5, by which I mean that $10 billion in stimulus is expected to generate about $25 billion in growth. A lot of that comes in the form of jobs, the major focus of the whole stimulus package. Most research money is spent on hiring technicians, paying the salaries of postdocs, and funding graduate student education. Many grant applicants have people



lined up waiting to be hired, if only the money were available. And most of what isn't spent on salaries tends to go for scientific supplies and equipment. Even conservatives should be able to support that spending because scientific supplies and equipment are two of the increasingly rare items that are manufactured to a large extent in the United States. Buying U.S.-made products preserves and creates U.S. jobs.

But the second objection is not so easily answered. I have gotten into trouble for saying this in the past, but I believe it to be true, and I think it bears repeating: we did not manage the recent doubling of the NIH budget well at all. By "we" I mean all of us: the bureaucrats at NIH, university administrators, and the scientific community. As money poured into the agency, administrators created numerous new initiatives and large-scale programs, without much thought to increasing the number of recipients of investigator-initiated research grants (RO1s). Meanwhile, university and hospital administrators built new buildings and hired lots of new people on the assumption that increased NIH budgets would pay for this expansion. And we scientists didn't help matters: during the doubling, established investigators wrote more grants and bigger grants, resulting in the shocking statistic that, though the NIH budget doubled over a five-year period, the number of funded investigators increased only slightly. In short, everybody behaved as though the doubling would never end, even though such booms are invariably followed by busts.

When the bust came, it hit hard. The big projects continued to need feeding when the doubling stopped and were rarely phased out or cut back significantly during the latter part of the Bush administration, when NIH budgets actually fell in inflation-adjusted dollars. Why should they have been? If you're a scientific administrator, what are you going to protect: a bunch of small research grants or some big program that you started? Besides, big science is easier to explain to Congress and to sell to the public. "The Cancer Genome Project" sounds so much more exciting than "Mechanisms of Enzymic Proton and Hydride Transfers" (which happens to be the title of one of my grants). This is not to say that all big science projects are wasteful or overhyped; many are not. But

in all the excitement to start bold new initiatives, the backbone of American science, the individual research grant, was forgotten. No one was protecting it, so pretty soon the success rate for approved applications at many of the NIH Institutes fell below 15 percent, and huge amounts of good science weren't being funded.

There was another unintended consequence of the doubling and the new initiatives it spawned. Gradually at first, but at an increasingly accelerated rate, the setting of priorities for biomedical research began to shift away from the study section to scientific administrators or a small number of scientists who could influence them. Of course, broad science policy must come from the government, since the public puts us in the lab and has the right, through their elected representatives, to tell us their concerns and ask us to work on things that matter in their daily lives. But traditionally, the details of how those large objectives could be met were left to the scientific community to hammer out in open competition among individual grants. Post-doubling, more and more of these decisions seemed to come from above.

My predecessor, ASBMB President Heidi Hamm, was among the first to sound the warning call about the slow and continual drying up of the RO1 pool. I've spent a good bit of time in this letter explaining the history of recent NIH funding because the perception that it was the rapid doubling of the NIH budget that, paradoxically, led to the funding crunch in which we now find ourselves, is the main reason for the objections to the $10 billion stimulus that Sen. Specter has proposed. The last thing we would seem to need, the argument goes, is another sudden infusion of money, especially short-term money. It would just encourage NIH officials (and some of our colleagues) to create more big new initiatives that would further crowd out the individual investigator. We'd be better off without it.

But, it wasn't the doubling itself that caused problems; it was how we responded to it. If we learn from past mistakes (and we must have the courage to admit that mistakes were made, even if only to ourselves), we don't have to repeat the boom-to-bust whiplash that has so demoralized researchers. We can, as a community, influence how that money is put to use. We—and here the scientific societies especially have a duty to speak up loud and clear—can insist that NIH use the stimulus to shift us back towards a better balance between big and small science, centers, NIH-initiated programs and initiatives, and the individual research grant. Yes, the stimulus money is only good for two years, and Sen. Specter has proposed some ways to spend this money in that amount of time (Peter Farnham's article elsewhere in this issue details Specter's proposals), but here are a few things we can do with short-term funding that would make a big difference:

- **Shared Instrumentation. It creates jobs and improves infrastructure. The Obama administration should love that.**
- **One-time Research Grants. There are hundreds of excellent RO1s sitting on program directors' desks at NIH that just missed being funded because there wasn't enough money to pay for them. Rather than creating a class of new "challenge grants," simply fund many of these R01s now, for two years only, with no renewal. If the language of the bill doesn't allow anything to be paid beyond one year, then award the money for one year only, but double the requested budget and allow a one-year, no-cost extension.**

I could think up several more, but you get the idea. All it takes is a little creativity to ensure that Sen. Specter's stimulus money goes where it is needed: to individual research scientists. Do you have an idea of your own? Good—send it to your favorite NIH director or program officer.

Thus, the main reason the ASBMB came out in support of the Specter amendment is that, if it passes, the money can actually help fix the problems that those who are objecting to it are most worried about. But there are three other important reasons for supporting the inclusion of NIH in the stimulus package. One is to stake our claim that science is an important part of the economy and in many ways is the engine that drives economic progress. The second is that, when a friend tries to help you out by giving you what you've been clamoring for, it is at best ungracious and at worst an embarrassing slap in the face to say, "Thanks, but no thanks." The final reason is that it is a good thing, not a bad thing, to make the stimulus bill bigger.

I do understand the risk of a huge increase in government spending. It is certainly inflationary, perhaps seriously so. And it raises the deficit at exactly the time we don't need a bigger national debt. And I am very concerned about the size of the stimulus bill as a whole. Not that I think it's too big; I think even at $900 billion, it may well not be big enough.

At the risk of being wonkish, here's the problem. We are in an almost unprecedented combination of a huge output gap (the difference between the current Gross Domestic Product and what it should be if we had full employment and normal industrial output) plus a liquidity trap (a situation in which the nominal interest rate has been lowered nearly to zero to avoid a recession, but the liquidity

in the market that should be created by these low interest rates does not stimulate the economy because credit is so tight that borrowers prefer saving rather than making long-term investments). The output gap on the whole isn't frightening, at least not yet; by some measures, it was larger in the 1980 recession, when unemployment was in the double digits. But when you add in the credit crunch, you have a situation like that of Japan in the early 1990s.

There are three ways to keep recessions from spiraling into depressions: spending and investment, tax cuts, and monetary policy. Monetary policy is useless here because the real interest rate is already effectively zero; there's nothing left to cut. Tax decreases, paradoxically, actually make things worse: in a situation like we're in now, people generally save a hefty percentage of the cut, so money goes out of circulation, which increases the liquidity problem.

So the only thing left is spending. Since consumers aren't spending and businesses aren't investing, the spending has to come from the government. Classical Keynesian theory suggests, by my calculation, that the stimulus needs to be at least $1.3 trillion—some liberal economists put the figure at over $1.5 trillion. Of course, that's inflationary, but the Fed has plenty of room to raise interest rates to keep that moderate.

If this stimulus bill gets reduced to below $800 billion, I would be very worried that it will be ineffective. The result would be a deflationary spiral. That's exactly what happened in Japan in 1990, when the Liberal Democratic Party failed to inject enough money fast enough into the economy. The result was a lost decade and a slump they are still not completely out of. The Japanese equivalent of the Dow Jones Industrial Average is still about one quarter of what it was at the height of their real estate bubble in the late 1980s. That would correspond to a Dow of 3500 here.

So regardless of whether the Specter Amendment stays in the final stimulus bill or not, I think it's clear that spending on scientific research isn't just good for us; it's good for everyone. This issue will come up again. And when it does, we will be there with our strong expression of support. Now you know why.

Biosecurity Comes to the Forefront

BY CARRIE D. WOLINETZ

The National Science Advisory Board on Biosecurity (NSABB), which is charged with the oversight of dual use research (life sciences research that can be misused for harmful purposes), released a report in December recommending both voluntary and mandatory biosecurity education for federally funded scientists. However, the report was overshadowed at the meeting by a new task given to NSABB: the consideration of personnel reliability programs (PRP) for users of select agent pathogens. PRP are psychological evaluation protocols, designed to allow access to only the most trustworthy individuals and are currently used for access to nuclear weapons. The Department of Defense and some national labs have recently implemented PRP, which include requirements like regular psychiatric exams, interviews with acquaintances, and drug testing, for use with select agents, in response to the Bruce Ivins case. The NSABB is examining whether such a program could be utilized for the extramural community, although many members of the Board expressed concern about the cost and practicality of implementing PRP among the thousands of select agent licensees. The NSABB report on PRP is expected by their May 2009 meeting.

Around the same time the NSABB was meeting, a congressionally appointed commission examining the risks associated with weapons of mass destruction released their report, *World at Risk*. A number of recommendations in the report concerned mitigating the risk of biological weapons, including strengthening the Select Agent Program and increasing the oversight of high-containment labs, particularly for Biosafety Level (BSL)-3 and -4 facilities. A number of high-profile biosafety violations, as well as controversy over the construction of new BSL facilities, have dominated the news headlines and likely influenced the Commission's focus. The report caught the attention of the Senate Committee on Homeland Security and Governmental Affairs, which held a hearing in December with the chairs of the Commission: Senators Bob Graham and Jim Talent. Following the hearing, Homeland Security Committee Chairman Joe Lieberman (ID-CT) and Ranking Member Susan Collins (R-ME) vowed to introduce legislation in the new Congress "to tighten oversight of high-containment laboratories around the country that could handle deadly biological pathogens."

Interestingly, a biosecurity bill had already been introduced in the previous Congress by Senators Edward Kennedy (D-MA) and Richard Burr (R-NC). The Select Agent Program and Biosafety Improvement Act of 2008 (S. 3127) would have reauthorized the Select Agent Program. It called for an evaluation of the program by the National Academies and an examination of the oversight of BSL-3 and -4 facilities. The legislation was primarily introduced for discussion purposes and never progressed through the Senate. It is unclear whether Senators Lieberman and Collins would modify the existing legislation or draft their own. One of the possibilities suggested at the hearing and in subsequent press reports is that in a Lieberman-Collins proposal, oversight of the Select Agent Program and high-containment laboratories might move into the Department of Homeland Security. Such a shift could have major consequences for scientists working with pathogens.

Not to be left out, the Bush administration also responded to the growing tide of biosecurity concerns, issuing an Executive Order on January 9th titled, "Strengthening Laboratory Biosecurity in the United States." The order called for the formation of a Working Group, headed by the Secretaries of HHS and DoD (or their designees), to issue a review of current biosecurity laws and regulations, particularly those relevant to the control of dangerous pathogens and BSL facilities. Unless specifically rescinded by President Obama, the Working Group will move forward and will release their report sometime this summer. FASEB's Science Policy Committee and staff are closely monitoring all of these ongoing activities and will be prepared to respond should policy changes be introduced.

Carrie D. Wolinetz is Director of Scientific Affairs and Public Relations for the Office of Public Affairs at the Federation of American Societies for Experimental Biology (FASEB). She can be reached at cwolinetz@faseb.org.

Stimulus Bill Has Good News for Science

BY PETER FARNHAM

The National Institutes of Health would receive a $10 billion increase over two years if the Senate version of the American Recovery and Reinvestment Act—the so-called "stimulus" bill—is adopted by the Congress and sent to President Obama's desk. After a week of painful negotiations in early February, the Senate is expected to pass its version of the bill, setting up a likely contentious conference with the House to hammer out a bill on which both chambers can agree.

Work began on the stimulus bill shortly after the new year, and the House completed work on its version in late January, developing an $819 billion package that includes billions of additional dollars for science programs at a host of agencies, including NIH and the National Science Foundation. NIH would increase by $3.5 billion over the two-year life of the bill, and NSF would receive an additional $3 billion, a whopping 50 percent increase.

Once the House completed work on the bill, it went to the Senate, where the bill ran into considerable opposition over its size. While House Democrats enjoy a large enough majority to pass legislation without assistance from Republicans, the rules are different in the Senate. Virtually any important piece of legislation requires 60 votes to pass; filibuster rules allow the minority to prevent final passage of a bill if they can muster 41 votes. There are 58 Democratic senators, two short of the total needed for a filibuster-proof majority.

Thus, Majority Leader Harry Reid (D-NV) needed to pick up at least two GOP votes in order to assure passage of any stimulus bill. This of course gives enormous leverage to any Republican willing to play ball with Reid. Senators Susan Collins and Olympia Snowe, both Republicans from Maine, as well as Arlen Specter (R-PA) will most likely provide the votes Reid needs.

The Senate bill started growing almost immediately, ballooning to well over $900 billion before a centrist coalition of about 20 senators, led by Susan Collins and Ben Nelson (D-NE) began to hammer out a package that trimmed spending by about $100 billion, a level that a bare filibuster-proof majority is expected to approve the week of February 9. The size of the bill is similar to what passed in the House a week earlier, but the mix is different in significant ways.

Among the increases accepted in the Senate package was the Specter amendment to increase the funds going to NIH by $6.5 billion over the $3.5 billion already in the House version of the bill.

Specter's staff began talking up this amendment to the biomedical research community before the bill ever came over to the Senate from the House. The amendment would distribute $7.85 billion to research programs. These are mostly in the form of so-called "challenge grants," consisting of $500,000 grants over two years to focus on "specific scientific challenges identified by NIH." An additional $1.35 billion would be distributed at the discretion of the Office of the Director. $500 million would go to support buildings and facilities, and $300 million would support shared instrumentation. ASBMB announced its support for the bill on January 28, making it one of the first scientific societies to do so. Other societies quickly followed suit.

It was unclear exactly when Specter would offer his amendment, but he finally did so on February 3. He had planned to offer it during the Appropriations Committee markup but withdrew it for procedural reasons. It was then adopted by voice vote during late evening floor debate. It was one of the few spending amendments that were accepted; many were being voted down as the size of the package grew to over $900 billion.

It then became clear that the package had gotten too big to pass and that some cuts were necessary. Thus, Collins and Nelson began their efforts to trim the overall size of the package. Finally, they announced late in the day on February 6 that they had succeeded. Reid is expected to garner just enough votes to pass the bill when it comes up for a vote the week of February 9.

In an op-ed piece in the *Washington Post* on February 9, Specter said that in his view, the Collins/Nelson alternative "is the only [stimulus] bill with a reasonable chance of passage in the Senate." Actor Patrick Swayze, who suffers from pancreatic cancer, weighed in on the NIH increase on February 8, also in the *Washington Post*, publishing a column urging Congress to support the amendment.

NSF Fares Well, but…

While the overall news for NSF is good, it is not as good as it might have been. The House version of the bill increased the NSF budget by over $3 billion, and this is the figure that

the Senate started with when it began deliberations on the bill the week of February 2. However, one of the first steps it took was to cut the increase to $1.4 billion. While disappointing, this still represented a huge increase for the agency on a percentage basis.

But during deliberations of the Collins/Nelson group, word leaked that they were proposing that NSF be zeroed out of the stimulus bill—the agency would thus get no new money. FASEB, ASBMB, and a host of other science groups thus launched an 11th hour lobbying campaign, mobilizing their grassroots networks to encourage the Senate to keep the money in the bill. We are pleased to note that when the Collins/Nelson package was agreed to, NSF was still on track to receive an additional $1.2 billion, roughly a 20 percent increase.

Conflict of Interest Language

There have been a variety of other proposed amendments to the stimulus bill, most of which will probably be defeated during floor consideration.

Sen. John McCain (R-AZ) has proposed an amendment that would require recipients of stimulus funds to disclose whom they hired to lobby on these issues and how much the lobbyists were paid. It is unclear whether groups like ASBMB and FASEB would be covered by this language.

Sen. Charles Grassley (R-IA) proposed another amendment to the stimulus package that would attach disclosure requirements to all NIH grants (not just stimulus-funded "challenge" grants) above $250,000. The PI would be required to report to NIH:

1. The amount of the primary investigator's significant financial interest, estimated to the nearest $1,000; and
2. A detailed report on how the grantee institution will manage the primary investigator's conflict of interest.

It is unclear whether Grassley's staff has actually defined crucial terms in this language, such as "significant" and "manage."

Sen. Grassley is also proposing an amendment to crack down on pornography-watching at the NSF. An investigation discovered that six NSF employees had been watching internet porn on their office computers during work time. Though the employees in question are guilty of falsifying timesheets—an offense for which they will be terminated if it has not happened already—Grassley apparently feels that the porn problem might be more pervasive. He is calling for a variety of accountability, investigative, and oversight measures and wants $3 billion in NSF operating funds frozen until these measures are implemented.

Rocky Conference Expected

Assuming the stimulus bill passes the Senate, it will head into what is likely to be a very difficult conference. Specter's staff considers it likely that an effort will be made to drop the Specter amendment, particularly since education funding took a large hit in the compromised Senate version (this is a known favorite program of Rep. Dave Obey, chairman of the House Appropriations Committee). Former Appropriations Committee staffers with whom this writer is acquainted say that it will be almost impossible to complete a thorough conference on a bill of this size, given the many differences between the two versions. Thus, splitting the difference on many of the provisions would be the most likely scenario. If this were to happen, we could see NIH come out of conference with an increase somewhere around the $6.5 billion level. NSF would come out with just over a $2 billion increase.

There is still considerable doubt that the package as a whole will accomplish what it is intended to do—stimulate the economy enough to turn around a widening recession—with economists arguing among themselves over whether the package is too small or too large. There are also arguments about the mix—is enough of the spending truly stimulative, or have powerful special interests simply used the opportunity presented by a bad recession to promote spending on their own agenda? Which of these visions is accurate will become clear in due course. However, it is clear now that regardless of the outcome of the impending conference on the bill, science is positioned to do very well. As we go to press, the stimulus bill has passed.

NIH will receive $10 billion, and the NSF will receive $3 billion.

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

asbmb member spotlight

Beckwith Wins Waksman Award

Jonathan Beckwith, American Cancer Society Professor in the Department of Microbiology and Molecular Genetics at Harvard University, will receive the 2009 Selman A. Waksman Award in Microbiology from the National Academy of Sciences.

Beckwith is being honored for fundamental contributions to gene regulation, protein targeting and secretion, disulfide biochemistry, and also for the development of gene fusions as an experimental tool. The Waksman Award, established by the Foundation for Microbiology, recognizes excellence in the field of microbiology and includes a prize of $5,000.

Beckwith uses genetics, biochemistry, and bioinformatics to study the properties and evolution of enzyme systems in bacteria that are important for protein folding, protein translocation, and responses to oxidative stress. For these studies, he and his colleagues are defining the pathways of electron transfer that confer a reducing environment on the cytoplasm and an oxidizing environment on extra-cytoplasmic compartments. These include the glutathione/glutaredoxin and thioredoxin pathways of *E. coli.* He is also studying the mechanisms by which the enzymes DsbC and DsbD correct proteins that are misfolded as a result of formation of incorrect disulfide bonds.

Chu to Deliver Eweson Award Lecture

Charleen T. Chu has been named a Dorothy Dillon Eweson Lecturer on the Advances in Aging Research for 2009, sponsored by the American Federation for Aging Research (AFAR). The Eweson Lecture Series on Advances in Aging Research was established in 1997 to enhance awareness of "cutting-edge" research in aging and age-related conditions at the forefront of scientific or medical specialty disciplines.

Chu's lecture, entitled "In the PINK1: Mitochondrial Kinases and Autophagic Neurodegeneration," will be presented at the "Presidential Symposium on Resolving Cell Death and Inflammation: Implications in Disease," on April 20 in New Orleans, LA as part of the American Society of Investigative Pathology (ASIP) Annual Meeting at Experimental Biology 2009.

Chu is a neuropathology physician-scientist in the Department of Pathology at the University of Pittsburgh, with secondary appointments in Ophthalmology, Center for Neuroscience, Pittsburgh Institute for Neurodegenerative Diseases, and McGowan Institute for Regenerative Medicine. Her research focuses on neuronal cell signaling in toxin and genetic models of Parkinson disease, implicating mitochondrial kinases and reactive oxygen species in regulating autophagy as a double-edged sword.

Eichman Receives Young Investigator Award

Brandt F. Eichman, assistant professor of biological sciences and biochemistry at Vanderbilt University, has been honored with Sigma Xi's Young Investigator Award.

Eichman is recognized as a leader in research into the structural biology of cellular mechanisms that maintain DNA fidelity. The Young Investigator Award has been presented annually since 1998. Sigma Xi members within 10 years of their highest earned degree are eligible for the award, which recognizes excellence in research. It includes a certificate of recognition and a $5,000 honorarium. The recipient is also invited to present a lecture at the Sigma Xi Annual Meeting.

Eichman's research interests include structural biology, biophysics, and biochemistry of proteins and protein-nucleic acid complexes. Research in his laboratory is focused on understanding how proteins recognize and manipulate DNA structure during replication and repair processes, which are critical for the prevention of genetic disease and cancer. Eichman and his colleagues use X-ray crystallography and biochemistry to investigate the physical and mechanistic basis for the biological functions of several DNA processing enzymes.

Horwich Presented with Horwitz Prize

Arthur Horwich, Eugene Higgins Professor of Genetics, professor of pediatrics, and a Howard Hughes Medical Institute (HHMI) investigator at Yale University School of Medicine, has been awarded the 2008 Louisa Gross Horwitz Prize from Columbia University.

Horwich shares the prize with F. Ulrich Hartl, professor and director of the Department of Cellular Biochemistry at the Max Planck Institute of Biochemistry in Germany, for their collaborative work in expanding fundamental understanding of cellular protein folding, and its role in Alzheimer disease, Huntington disease, cystic fibrosis, and other life-threatening diseases.

Previously, it was thought that proteins spontaneously fold themselves into their final, three-dimensional structures. Hartl and Horwich discovered that inside cells, proteins need assistance from chaperones to guide the folding process and ensure they fold into the proper shape. In independent and often complementary work, they also established the pathway and molecular mechanisms involved in this process. Their work also demonstrated that when the protein folding pathway is imperfect, protein can accumulate in cells, leading to disease.

The Louisa Gross Horwitz Prize was established by Columbia University to recognize outstanding contributions to basic research in the fields of biology and biochemistry. Awarded annually since 1967, the prize is named for the mother of Columbia benefactor S. Gross Horwitz.

Park Recognized by *Quebec Science* Magazine

Morag Park, scientific director of the Canadian Institutes of Health Research's Institute of Cancer Research, was recently recognized by *Quebec Science* magazine for her research. The February issue of the magazine contained its "Top Ten Discoveries of 2008," which included Park's work on the cellular environment surrounding breast cancer tumors.

"We know that this environment is pivotal for cancer initiation and progression; different patients have distinct tumor microenvironments at a gene level," explains Park. "Our findings show that the gene profile of these distinct microenvironments can be used to determine clinical outcome—who will fare well and who will not."

Park and her colleagues identified a panel of 26 specific genes that could be used to accurately predict clinical outcome. She intends to use these results to produce a reliable functional test that can be performed on patients and expects it to be ready for clinical trials at the end of 2009.

Park's research interests focus on the molecular mechanisms of oncogenic activation of receptor tyrosine kinases and mechanisms for cell transformation using hepatocyte growth factor (HGF) as a model. She has demonstrated that the activity of the HGF receptor is frequently altered in human cancer and has proposed new models for its mechanism of oncogenic activation.

Berkhout Awarded *Retrovirology* Prize

Ben Berkhout, professor and head of the Laboratory of Experimental Virology at the University of Amsterdam, has been awarded the 2008 M. Jeang Retrovirology Prize.

Berkhout was honored for his multidisciplinary approach to RNA research, which has provided additional important building blocks for many aspects of our current knowledge on HIV-1 replication. Berkhout's research has extended our insights into the mechanisms of transcription, reverse transcription, drug-resistance, and RNA interference.

The Retrovirology Prize, awarded annually, recognizes an outstanding mid-career retrovirologist aged 45 to 60. The prize, which consists of a $3,000 check and a crystal trophy, is partly sponsored by the Ming K. Jeang Foundation and alternates between HIV and non-HIV research. The winner is selected by *Retrovirology's* editors from nominations submitted by the journal's editorial board.

In an interview published in the journal *Retrovirology*, Berkhout says, "It really is a fantastic surprise. As an editorial board member of *Retrovirology*, I know from previous years how fierce the competition is for the Retrovirology Prize. It is rather enjoyable being recognized at this level by my colleagues."

Enwonwu and Rasenick Named Global Health Research Ambassadors

ENWONWU

RASENICK

Cyril O. Enwonwu, professor of biomedical sciences in the School of Dentistry at the University of Maryland, and Mark Rasenick, Director of the Biomedical Neuroscience Training Program at the University of Illinois Chicago College of Medicine, have been named Global Health Research Ambassadors in Research!America's Paul G. Rogers Society for Global Health Research.

Enwonwu and Rasenick are two of 23 new ambassadors, all of whom are foremost experts in global health research. They include experts in pediatrics, nursing, and dentistry who specialize in critical areas, including neglected and emerging tropical diseases, tuberculosis, and polio. The ambassadors are selected by an advisory council comprised of leaders in science, public policy, and communications. Together with 50 of their peers, these new ambassadors will advocate for greater U.S. investment in global health research.

The Rogers Society, named for the Honorable Paul G. Rogers, former Florida Congressman, renowned champion of health research and Research!America chair emeritus, works to increase awareness, of and make the case for, greater U.S. investment in research to fight diseases that disproportionately affect the world's poorest nations. The Society was established in 2006 by Research!America with funding from the Bill & Melinda Gates Foundation. Research!America works with the Ambassadors to maximize the effectiveness of their outreach to policy makers, opinion leaders, and the media.

"We have a new Congress and a new administration. Now is the time when we can make a difference for global health research. These Ambassadors will be exceptional leaders in advocacy. Their example will serve as an inspiration for every global health researcher," said the Hon. John Edward Porter, chair of the Rogers Society Advisory Council and Research!America board chair. "Paul Rogers' spirit lives on through the work of each of these Ambassadors. As he often said, 'Without research, there is no hope.'"

Retrospective: Dennis Shields (1948-2008)

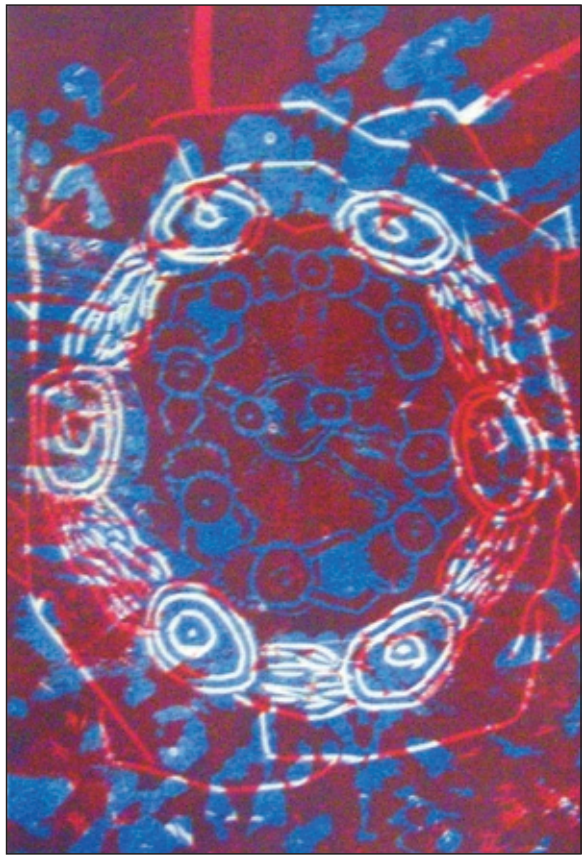
BY JOHN J. M. BERGERON AND TOMMY NILSSON

The sudden loss of Dennis Shields, a dear friend and colleague to many of us working in the fields of biochemistry and cell biology, is an important reminder of the human element of science as well as the unpredictability of life. Below, we have tried to encapsulate some of Dennis' scientific work and a sense of Dennis as a person to remind us of who he was and what he did. This retrospective is neither complete in words nor in content but is a tribute to his memory.

Dennis was a member of the editorial board of *The Journal of Biological Chemistry* and a prominent molecular cell biologist whose interests ranged from the fundamental mechanisms of transcription to the mechanisms of processing of polypeptide hormone precursors. This led to a deep interest in the regulation of secretion via different phospholipids regulating Golgi apparatus structure and function. As a professor in the departments of Developmental and Molecular Biology as well as Anatomy and Structural Biology at the Albert Einstein College of Medicine, Dennis Shields was a passionate advocate for the primary importance of basic biomedical research as the critical route to the mechanistic insight essential for therapeutic applications to human disease.

Dennis' interest in the beauty of the inner workings of microstructures is illustrated by the woodcuts he made as a graduate student (Figs. 1 and 2), showing his early artistic renditions inspired by electron micrographs of a bacteriophage and a microtubule.

Inspired by the early work of Widnell and Tata,[1] who were the first to document distinctive RNA polymerase activities (now known as RNA polymerases I and II), Dennis together with his Ph.D. supervisor, Jamshed Tata at the National Institute for Medical Research in London, delineated the sensitivities of these distinct RNA polymerase activities to both thermal inactivation and the fungal toxin alpha amanitin.[2-4] During his subsequent postdoctoral training with Günter Blobel at The Rockefeller University in New York, Dennis studied polypeptide hormones biosynthesized by the endocrine pancreas. At that time, insulin was known to be synthesized as a larger form, termed proinsulin by Don Steiner and colleagues.[5] However, Dennis Shields was able to demonstrate the synthesis of a still larger form, when islet mRNA (from fish islets) was translated in a wheat germ cell-free system in the absence of microsomal membranes. He dubbed that larger precursor "preproinsulin." Strikingly, translation in the presence of microsomal vesicles from canine pancreas yielded correctly processed proinsulin from which the presequence had been properly removed and which was co-translationally translocated into the lumen of microsomal vesicles, yielding proinsulin. These data indicated that the initial events in polypeptide hormone synthesis are similar to those for other more classical secretory proteins, and suggested that the mechanisms of protein translocation across the ER membrane have been highly conserved during evolution. In effect, plant ribosomes, fish mRNA, and mammalian microsomal membranes were all able to collaborate to accomplish protein translocation across the ER membrane in what has now been unraveled as a



ABOVE: A woodcut based on an electron micrograph of a bacteriophage done by Dennis Shields in 1973. BELOW: A woodcut based on an electron micrograph of a microtubule done by Dennis Shields in 1973.

multi-step chain of events.[6-8]

Dennis' next major scientific contribution was made shortly after his recruitment to The Albert Einstein College of Medicine. There, Dennis was the first to discover that different somatostatins were expressed by the endocrine pancreas. Clever molecular biology enabled the Shields lab to uncover the Golgi apparatus/secretory granules location of the proteinases responsible for processing somatostatin from its inactive precursor form to its biologically active form, as well as to define the importance of the prodomain in sorting prosomatostatin towards dense core secretory granules.[9-11] Their data also showed that prosomatostatin processing in anglerfish or rodents is not necessarily dependent on a specific protease found only in somatostatin-producing cells, suggesting that proteolytic cleavage is not restricted to cells that process endogenous hormones. This prediction was later proven true with the discovery of the widespread neural and endocrine processing enzymes PC1/3 and PC2.

The last phase of Dennis' career involved deciphering how the complexity of the Golgi apparatus efficiently regulates secretory cargo processing and transport. The Shields lab provided evidence of the importance of phospholipases in secretory vesicle generation from the Golgi apparatus. This developed into an interest in the regulatory role of phospholipase D, phosphatidic acid, and phosphatidyl inositol 4,5 bisphosphate in Golgi apparatus structure and function.[12,13] Ongoing studies are now uncovering the relevance of this work to neurological disease, cancer, and apoptosis. For apoptosis, the Shields lab has presented compelling evidence for a role of p115, a Golgi-tethering molecule involved in COPI vesicle function and Golgi function, thus bringing molecular insights into an under-appreciated role of the Golgi apparatus in this critical cellular process. His latest paper on apoptosis appeared in *JBC*[14] and was selected as a Paper of the Week. It details, mechanistically, the need for a fragment of p115 produced by caspase cleavage in the Golgi apparatus, to enter the nucleus to trigger apoptosis.[15] This, as many of his other discoveries, has provided fundamental insights into novel aspects of Golgi function. He leaves us with a legacy of novel, yet to be fully explored research avenues: the role of clathrin in Golgi reassembly, the role of phosphoinositols (PI4P and PI4,5P), phospholipase D and phosphatidic acid in Golgi function, and the role of the Golgi apparatus in apoptosis.

Dennis' success reflects the personal qualities he brought to research. He mastered a combination of boldness and courage necessary to allow scientific curiosity to dictate research direction with the integrity, diligence, and experimental rigor needed to generate high quality data. For this, he represents the very best of role models, for us as well as for new generations of biochemists and molecular biologists ready to carry the torch to illuminate the paths of scientific research.

But beyond these attributes we admired in the scien-

tist are the qualities that drew us to him as a human being. Dennis was a fun-loving individual with an endearing self-deprecating style who, despite his absolute commitment to quality science, never made the mistake of taking himself too seriously. His decency, warmth, and kindness put him at the center of a close and loving family and a circle of strong, lifelong friendships. Dennis' personal life was as exemplary as his scientific one. While we pay tribute to his science and the progress yet to come from his achievements, it is the man himself we mourn and miss. Dennis is survived by his loving and caring wife Toni, his children Rebecca, Jacqueline, and Matthew, and his son-in-law, David.

John J. M. Bergeron is a professor at McGill University in Montreal and can be reached at john.bergeron@mcgill.ca. Tommy Nilsson is a professor at The Research Institute of the McGill University Health Centre and the Department of Medicine, McGill University, Montreal.

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Annual Meeting Events for Early Career Scientists

BY NICOLE KRESGE

The ASBMB annual meeting in New Orleans is just around the corner, and in addition to a great lineup of scientific talks and award lectures, we've planned several events that are geared toward early career scientists—undergraduates, graduate students, and postdoctoral fellows. Many of the events are free, while others require advance registration and a nominal fee. (Registration for these events can be done on the Experimental Biology website: eb2009.org/Registration.htm.)

Graduate/Postdoctoral and Graduate Minority Travel Award Symposium

The events start on Friday, April 17 at 5:00 pm with an invitation-only Graduate/Postdoctoral and Graduate Minority Travel Award Symposium. This symposium will honor the recipients of the ASBMB 2009 Graduate/Postdoctoral and Graduate Minority Travel Awards. The program features a special plenary lecture by 2008 ASBMB Award for Exemplary Contributions to Education recipient Michael F. Summers of the University of Maryland, Baltimore County. Summers' talk is titled, "Research, Mentoring, and Diversity. Which is more Important?"

This lecture will be followed by a poster session in which all travel award recipients will present their work.

Graduate and Postdoctoral Professional Development Session

Our early career scientist events in New Orleans continue on Saturday with the graduate student and postdoctoral fellow professional development session from 9:00 am to 5:00 pm. This special pre-meeting program features a morning panel and discussion session on career options, followed by a networking luncheon. The afternoon session includes oral presentations by a selection of this year's travel award recipients, followed by a series of career and professional development-related workshops targeting graduate students or postdoctoral fellows. (See box for program details.)

The program is open to all graduate students, postdoctoral fellows, and their mentors. Registration for the session is $20 for ASBMB members and $25 for non-members. Recipients of ASBMB Graduate Minority and Graduate/Postdoctoral Travel Awards do not have to register for this event—it is included as part of the award.

13th Annual Undergraduate Student Research Poster Competition

On Saturday afternoon, 150 undergraduate students will present their research at the 13th Annual ASBMB Undergraduate Student Research Poster Competition. The event, which will be held from 1:00 pm to 4:30 pm, is a great opportunity for students to meet fellow undergraduate meeting attendees and to make friends and contacts before the meeting starts. The poster session will also contain a networking break during which students can visit with prospective graduate school representatives and enjoy light refreshments. Prizes for students making the best poster presentations at the competition will be awarded on Sunday, April 19, at the ASBMB Award for Exemplary Contributions to Education Lecture.

How to Publish in the *Journal of Biological Chemistry* Workshop

The *Journal of Biological Chemistry* (*JBC*) is hosting a lunchtime workshop on Sunday, April19 from 12:30 pm to 2:30 pm for authors interested in submit-

ting their work to the *JBC* for the first time. This workshop will be led by *JBC* associate editors and will describe the submission and review processes, and give tips on how best to prepare a manuscript for submission to the *JBC*. Registration for this workshop is still open, but spaces are limited. The fee is $15 for ASBMB members and $20 for all other meeting registrants; lunch is included.

Scientific Thematic Receptions

ASBMB is hosting several scientific thematic receptions immediately after the afternoon symposia on Monday, April 20. These receptions will occur on the ASBMB third floor foyer from 5:50 pm to 6:30 pm and provide a great opportunity for younger scientists to meet the speakers, network with other meeting attendees, and enjoy light refreshments.

Minority Scientists Networking Luncheon

On Tuesday, April 21, from 12:30 pm to 2:00 pm, the ASBMB Minority Affairs Committee is hosting a networking luncheon. The luncheon will be in the La Louisiane A Ballroom and will provide a chance for young investigators and students to come together with PIs, industry professionals, and educators for discussions on various topics, such as career opportunities, mentoring options, and issues facing minority scientists today.

Women Scientists' Panel and Networking Event

And finally, on Tuesday, April 21 from 6:15 pm to 8:00 pm, ASBMB is sponsoring the Women Scientists' Panel and Networking Event. This event will begin with a panel of women scientists from the New Orleans area (Diane A. Blake, Tulane University School of Medicine; Mary Clancy, New Orleans University; Fiona M. Inglis, Tulane University; Sunyoung Kim, Louisiana State University Health Sciences Center) who will discuss how their personal and professional lives and their scientific programs have been affected by the past several years of natural disaster and recovery. The panel will be followed by a reception which will offer the opportunity for informal discussion and networking. The event is open to all meeting attendees.

Graduate and Postdoctoral Professional Development Session Program

SATURDAY, APRIL 18

9:00 am – 12:00 pm

Career Options: The Bench, the Boardroom, or in between?

Industry: *Ravikumar Peri*, Wyeth Research
Bioinformatics: *Chris Burge*, Massachusetts Institute of Technology
Academics at a Medical School: *Carmen Dessauer*, University of Texas Health Science Center at Houston
Academics at a Small Liberal Arts University: *Manju Hingorani*, Wesleyan University
Science Policy: *Phyllis Frosst*, National Institutes of Health
Marketing: *Jessica Homa*, ASBMB

12:15 pm

Networking Luncheon

1:30 pm– 2:00 pm

***Public Affairs—Advocacy* Presentation**

Judith S. Bond, Pennsylvania State University
Allen Dodson, ASBMB

2:00 pm – 3:00 pm

Graduate/Postdoctoral Travel Award Winner Oral Presentations

3:15 pm – 5:00 pm

Graduate Student and Postdoctoral Professional Development Panels

Panel for Graduate Students: What You Need to Know to Get Through Graduate School

CHAIR: *Kimberly Dodge-Kafka*, University of Connecticut Health Center
John Denu, University of Wisconsin Medical School
Michael Holinstat, Vanderbilt University Medical Center

Panel for Postdoctoral Fellows: The Pathway(s) to Your Own Lab

CHAIR: *Chris Heinen*, University of Connecticut Health Center
Manju Hingorani, Wesleyan University
Rick Morimoto, Northwestern University

Biochemistry Department Diversity: A Lack of Sex Appeal

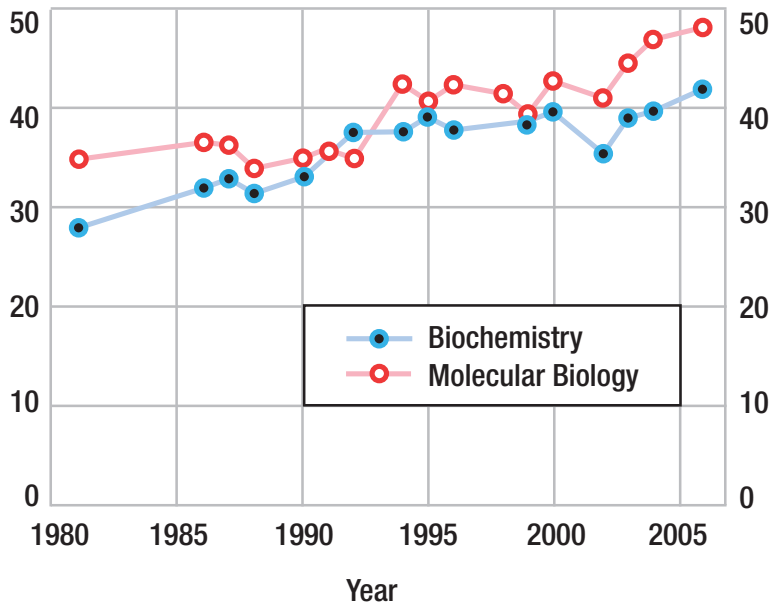
BY PHOEBE LEBOY

In the early 1970s, when ASBMB was known as the American Society of Biological Chemists, I was a member of the Society's Committee on Women. The need for such a committee was obvious; most of us had never met a woman who was a professor of Biochemistry, and there were few women with appropriate training. Change occurred rapidly. By 1981, 31 percent of U.S. doctorates in biochemistry and 37 percent in molecular biology were awarded to women. The data for recent years show that women now comprise approximately 40 percent of biochemistry doctorates and close to 50 percent of molecular biology doctorates (Fig. 1). It was not until 1978 that Mildred Cohn, the first woman president of the Society, was elected, but in the past 10 years, more than half of the ASBMB presidents have been women…and the Committee on Women no longer exists.

It is reasonable to expect that the proportion of women on the faculty of biochemistry and molecular biology departments would keep pace with their increasing numbers in the Ph.D. population. To my knowledge, there are no published data analyzing the tenured and tenure-track faculty of U.S. biochemistry departments. There is, however, an internet full of websites listing faculty in departments of major universities and medical schools, which usually display pictures of each faculty member and facilitate gender identification. In the spring of 2007, I checked the sites of 24 biochemistry departments in medical schools, identifying 569 individuals who seemed to be full-time tenured or tenure-track faculty. Among these, 113 (slightly less than 20 percent) were women. There are many biochemistry colleagues who were tenured many years ago and still retained faculty status; these would be overwhelmingly male and produce a "cohort effect," *i.e.* the gender composition of senior faculty would not accurately reflect changes of the past 30 years. Indeed the senior faculty (full and associate professors) in medical school biochemistry departments did show a smaller proportion of women than the junior faculty (assistant professor) group, but the difference was not great. Women averaged 18.7 percent of the senior faculty and 24.8 percent of the junior faculty.

During a separate study of applicants for faculty positions in the fall of 2007, Association for Women in Science (AWIS) staffers reviewed the faculty composition of two dozen departments advertising for tenure-track assistant professors in biochemistry or molecular biology. The seven medical school departments averaged 17 percent women among senior faculty and 24 percent women among assistant professors, in good agreement with our previous data. An additional 17 departments advertising a biochemistry/molecular biology position were chemistry, biochemistry, or molecular biology departments not located in medical schools. These

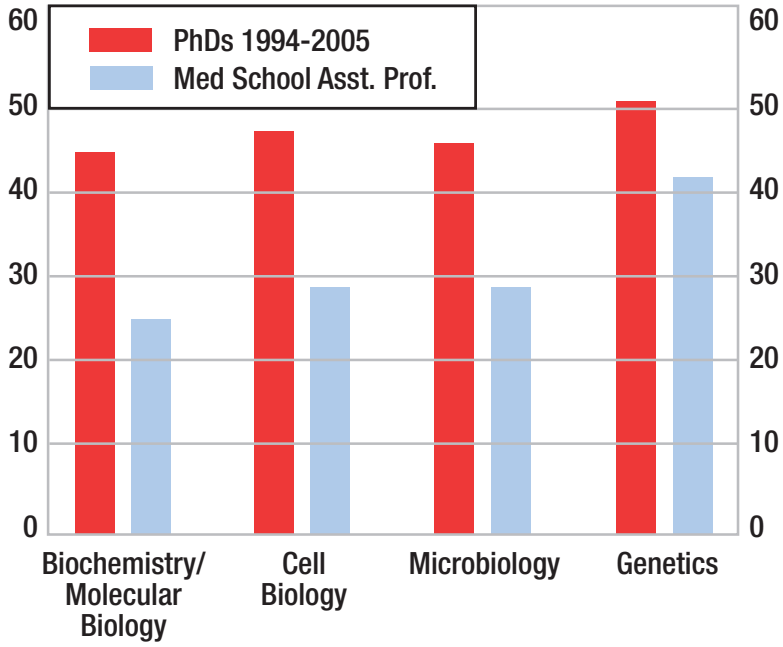
FIGURE ONE



showed slightly higher numbers of women among current faculty: 21 percent of the senior faculty and 28 percent of assistant professors.

Thus, the proportion of women biochemists in faculty positions is far below that expected by the proportion of women with Ph.D.s in biochemistry. Most strikingly, the recently hired assistant professor population, which the numbers of biochemistry Ph.D.s suggest should be at least 40 percent female (Fig. 1), was only 24–25 percent female in medical school departments and 28 percent in non-medical school departments. The discrepancy between expected and actual faculty is even greater if we include molecular biology Ph.D.s, because women have comprised more than 45 percent of molecular biology doctorates for at least 10 years.

FIGURE TWO



The disparity between women Ph.D.s and women faculty is not unique to biochemistry and molecular biology. Looking at the four most common basic science departments of 24 medical schools, all had fewer women assistant professors in 2007 than would be expected by averaging Ph.D.s awarded in the 12-year period of 1994–2005 (Fig. 2). Genetics departments, with 28 women among 68 assistant professors, seemed closest to parity, but biochemistry departments (27 women among 109 assistant professors) had the poorest showing. One clue to where the missing female biochemists might be is in data on faculty composition of medical school departments compiled by the Association of American Medical Colleges (AAMC); they include not only tenure-track faculty but also research-track and part-timers and come up with 34 percent women among assistant professors in biochemistry departments.

While common to many disciplines, the disconnect between the Ph.D. pool and faculty composition is not seen in all sciences; both physics and engineering departments in research universities seem to hire junior women faculty in proportion to their availability in the Ph.D. population. Why such a disparity between Ph.D.s awarded to women and faculty composition in our discipline? There are probably still some cases of outright discrimination in hiring, but it is not likely that senior biochemistry faculty in over 30 different departments, not noted for their unanimity of opinion on most other matters, have banded together in a deliberate effort to exclude women from their faculty ranks. The existing literature on academic employment in science, engineering, technology, and math departments (often referred to as STEM departments) suggests more subtle factors are at work.

Some of the factors keeping down numbers of faculty women operate at the recruitment and hiring stage. While we now advertise our faculty vacancies, it is common for faculty search committees to actually "search" and ask friends and colleagues about their favored protégées. Unless a deliberate effort is made to specifically ask about women, they are often inadvertently omitted in compiling such lists because a discipline accustomed to seeing mostly male colleagues tends to think of male candidates. If the practice is to rely on the women in the applicant pool, one of our recent studies suggests that this will not produce a representative pool of women.

In late 2007, we asked 55 departments searching for assistant professors in biochemistry or molecular biology to report what proportion of their responses were from women. Although there was a disappointing lack of response from colleges and smaller universities, we had a greater than 70 percent response rate from large university and medical school departments. The medical school departments told us less than 18 percent of the applicants for their biochemistry positions were women. Among non-medical departments, the seven chemistry departments reported 21 percent women, six biochemistry departments reported 22 percent women, while four biology departments that included biochemistry

reported 26 percent women among applications.

At least two lessons can be drawn from this disturbing outcome: 1) applications received in response to ads will seriously underestimate the proportion of women qualified for the position; and 2) women are obviously disinclined to apply for tenure-track faculty positions in research universities and may be particularly reluctant to apply to medical school biochemistry departments.

Conversations with women postdocs indicate that the difficulties of obtaining grants are high among reasons for not applying, but this is also cited by most men. Many of the women talk about an additional set of concerns making faculty positions in research-intensive institutions unattractive for them. They see family-unfriendly working patterns and a culture often perceived to be excessively macho. They also see an unlevel playing field in which women are expected to assume more of the responsibilities for teaching and mentoring than their male colleagues and where junior women faculty often lack the prestige to attract the best students and postdocs.

These generalizations do not, of course, apply to all women seeking a tenure-track biochemistry position. Many women in ASBMB are finding their way to faculty jobs in research universities and medical schools, handling the rough spots with a combination of hard work and confidence driven by their personal goal to be an academic biochemist. But the data indicate that the proportion of women who believe they can achieve this goal is only half that of men. Furthermore, this gender-biased lack of confidence is based on an all-too-real perception that the path to success is still harder for a woman. The profession has two choices: examine the path to success and fix the women-unfriendly obstacles, or live with the consequences of a system which is designed to make it harder for our female ASBMB colleagues to be faculty colleagues.

Phoebe Leboy is a professor of biochemistry emerita at the University of Pennsylvania and the current president of the Association for Women in Science. She can be reached at phoebe@biochem.dental.upenn.edu.

ASBMB Roundtable: Daniel Steinberg

BY NICK ZAGORSKI

Today, the idea that lowering your cholesterol is good for your heart seems self-evident (maybe the abundance of commercials touting statin drugs or the benefits of oatmeal have something to do with it). Yet, there was a time when the notion that excess cholesterol is a major risk factor for heart disease was contentiously disputed. In fact, this fight over cholesterol, from its inauspicious beginnings in St. Petersburg, Russia nearly a century ago to the emergence of statins in the 1980s, was one of the defining hallmarks of lipid research in the 20th century. This amazing story is well-presented in *The Cholesterol Wars* (Academic Press, 2007) by one of the soldiers at the forefront, Daniel Steinberg. For more than 40 years, Steinberg fought for "cholesterol's cardiac causality" through his basic and clinical studies (first at NIH and later at UCSD) and numerous policy efforts. Steinberg, also a former editor-in-chief of the *Journal of Lipid Research* (and one of the journal's first contributors in 1959), sits down with ASBMB and talks about the fight over cholesterol.

ASBMB: ***When was the idea that high cholesterol was linked with a higher risk of atherosclerosis first proposed?***

STEINBERG: The whole thing began way back in 1913, with a series of classical experiments by Russian scientist Nikolai Anitschkow, which, interestingly, were not even intended to be about cholesterol. Anitschkow's boss wanted him to look into a hypothesis that excess protein could be responsible for the toxic effects of aging. So Anitschkow fed rabbits a diet of red meat, eggs, and milk, and found that they did indeed have deteriorating health, including arterial lesions. He then began narrowing the ingredients down to identify what was inducing this damage; first, he found the same results using just eggs, then just egg yolks, and finally purified cholesterol in oil. Unfortunately, the "protein hypothesis" was ruined, but the "lipid hypothesis" was born. And then, like Topsy, it just grew!

ASBMB: ***And along with the birth of this hypothesis came the birth of the first skeptics, correct?***

STEINBERG: Yes, a lot of people pooh-poohed these results, mainly because rabbits are natural vegetarians, and this diet would be extremely foreign to them. So other physiologists tried to replicate Anitschkow's work using models that were more accustomed to fat and protein, and back then that was dogs and rats. And those animals did not get arterial lesions following a high-cholesterol diet, which led the skeptics to say, "A-ha! The results in rabbits were just a fluke," the first in a long line of denials about the causality of cholesterol in atherosclerosis.

Now, what those physiologists didn't know back then was that dogs and rats are peculiar in that they can convert cholesterol into bile acids very rapidly, so their plasma cholesterol levels never became elevated. In later studies, researchers got around this bile conversion by depressing the activity of the thyroid gland, thus down-regulating the LDL receptor. Now they found that indeed, dogs and rats could develop atherosclerosis. In fact, high cholesterol could induce atherosclerosis in a whole host of animals: chickens, guinea pigs, even parrots. So why should humans be exempt?

ASBMB: ***At what point in your career were you drawn into this battle over the lipid hypothesis?***

STEINBERG: I first set foot in the arena in 1956, when I published my initial paper on lipoproteins. However, during my time at NIH (1951–1968), I wasn't working on atherosclerosis *per se*, though I believed that everything I was doing with lipoproteins was relevant to the disease. After I came to California in 1968, I felt that I had built up enough status in the field and I decided to get down to the "brass tacks" and start directly looking at the mechanisms involved in arterial damage.

However, I would be remiss not to point out the tremendously important role that basic science played in all this. From Schoenheimer's work proving that cholesterol turns

over in the body, to John Gofman's elegant analytical centrifuge studies highlighting the complexity of lipoproteins, Konrad Bloch's details concerning cholesterol biosynthesis, and of course Michael Brown and Joseph Goldstein's work with the LDL receptor—all these were vital in stimulating researchers and physicians alike.

ASBMB: ***Usually, it takes just one or two events to significantly turn the tide of battle; in your opinion, what was the "Washington crossing the Delaware" equivalent of the Cholesterol Wars?***

STEINBERG: I think the evidence obtained by the Coronary Primary Prevention Trial (CPPT) in 1984 really turned the corner. It was the first study of hypercholesterolemia that featured a significantly large group, some 3,600 men in 10 different centers across the U.S., in a double-blind study. And this study found that treatment with the cholesterol-lowering agent cholestyramine did reduce the incidence of heart disease by about 20 percent. The trial was followed by a Consensus Conference at NIH, which I had the privilege of helping plan and chair. After many days of looking over the broad scope of evidence, and hearing arguments from experts on both sides of the debate, the Consensus Panel agreed unanimously that lowering blood cholesterol would reduce the risk of heart attacks.

ASBMB: ***But even after the CPPT and the Consensus Panel, some people remained unconvinced?***

STEINBERG: Oh yes; there were criticisms like, "This study was only done in men, so you have no mandate to treat women," or "This study only looked at men with really high cholesterol, so you can't extrapolate the results to people with moderately elevated levels." However, as in previous cases, the skepticism about this study was just another of the many repeated retreats the critics have been forced to take over the years.

Now, I should stress, in discussing the back-and-forth over the lipid hypothesis, I don't want to give the impression that this battle has been a 50-50 split. Even before the CPPT Trial in 1984, the naysayers had been restricted to a small but vocal minority. In 1978, Norweigen physiologist Kaare Norum sent out a questionnaire to over 200 researchers, nutritionists, cardiologists, and others who work in the field of atherosclerosis which included the question, "Do you think that the evidence supports cholesterol as a major contributor to atherosclerosis and heart attacks?" Ninety-five percent said yes. I think the controversy managed to last longer than it should have because the vocal minority included some influential figures like noted British researcher Michael Oliver… though even he eventually came around.

ASBMB: ***So is the book on cholesterol, in your opinion, officially closed?***

STEINBERG: Well, for the question of whether lowering blood cholesterol levels decreases your chances of a heart attack, I think the answer of "Yes" has been proven beyond a reasonable doubt. Now, a lot of questions still remain, however. For example, mechanistically, how relevant is the oxidation of LDL? That's something I review in the special 50th anniversary issue of *JLR* (jlr.org/collections/anniversary/index.dtl).

However, a very pressing question is: how early in life should we start treating at-risk individuals? I think right now, in many cases, we begin treatment too late. Atherosclerosis actually begins in childhood with the development of fatty streaks, which themselves are benign, but eventually lead to the lesions of atherosclerosis. So by the time people begin treatment for high cholesterol in middle age, the disease has already been progressing for decades. Physicians do recommend early and aggressive medication for extremely high-risk individuals, but I believe even someone at moderate risk should consider starting treatment at 30 to prevent a heart attack at 50.

ASBMB: ***I guess that makes cholesterol treatment the new battleground?***

STEINBERG: I would say so; in fact, that debate is going on right now. The NHLBI (National Heart, Lung, and Blood Institute) has set up an expert panel to evaluate the clinical guidelines for the detection, evaluation, and treatment of high blood cholesterol in adults. I don't have any numbers yet, but the panel's evaluation should be available by the end of the year. Let us hope they opt for earlier intervention.

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

What's Going on in New Orleans?

BY ELLIS BELL

The Education and Professional Development theme at this year's meeting in New Orleans has something for everyone, with a full slate of symposia and workshops scheduled throughout the meeting.

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On Saturday morning, for faculty members whose students are participating in the Undergraduate Poster Competition, there are two workshops aimed at helping connect four-year college faculty with other important learning communities, such as the K-12 arena and community colleges. Both of these communities are key players in bringing students, particularly those from diverse backgrounds, into the sciences.

The first workshop, "Connecting with K-12: Reaching Out to High School Faculty" will be run by Margaret D. Johnson of the University of Alabama. The goals of this workshop are to provide information about funding resources and opportunities available to train high school teachers in research laboratories and to illustrate how helping students pose applicable scientific questions can motivate and encourage them to choose a career in the sciences. Information will also be available to help teachers utilize their class time and limited laboratory equipment to better demonstrate how scientific methods lead to knowledge.

The second workshop, "Connecting with Community Colleges," run by Deborah L. Neely Fisher of the J. Sargeant Reynolds Community College, focuses on the transition from community college to four-year college. Students involved in undergraduate research become better at problem-solving and analysis. They also become more engaged in their own education, improve their quality of their writing, and become better at managing their time. An initiative in the Virginia community college system called Dateline 2009 aims to have Virginia's community colleges rank in the top 10 percent of the nation's community college systems in rates of student graduation, retention, and job placement, as well as triple the number of graduates who successfully transfer to four-year institutions. Richard S. Groover, a faculty member at J. Sargeant Reynolds Community College, has been awarded a Chancellor's Commonwealth Professorship to develop and implement a system-wide model for the engagement of independent research by community college students. This session will explore the benefits of having community college students and faculty mentors, participate in undergraduate research projects, and connect with research faculty at four-year institutions.

In the afternoon, ASBMB will host be the 13th Annual Undergraduate Student Research Poster Competition, which is always a highlight of the opening day of the meeting. This year, the session will include presentations by various Howard Hughes Medical Institute "SMART" Teams, sponsored by the Center for Biomolecular Modeling at the Milwaukee School of Engineering. These teams partner with HHMI investigators on protein modeling projects.

The Classroom of the Future IV symposium on Sunday, chaired by Cheryl P. Bailey of the University of Nebraska-Lincoln, features a number of presentations on the latest pedagogical approaches for teaching biochemistry and molecular biology. This will be followed by the ASBMB Award for Exemplary Contributions to Education award lecture, given by this year's award winner, Rochelle D. Schwartz-Bloom of the Duke University Medical Center. Her talk is titled, "Science Education: A Basic Scientist's View of Translational Medicine." Awards from Saturday's Undergraduate Poster Session will also be presented at this plenary session.

The EPD-sponsored events at the annual meeting continue on Monday with a workshop titled "Transitions from Academia to Industry and Back," organized by Greg P. Bertenshaw of Correlogic Systems, Inc.

On Tuesday, Lynelle Golden will chair the symposium, "Life Science Education in the 21st Century: Making the Science We Teach Reflect the Science We Practice." This is an EB-sponsored session that is co-sponsored by ASBMB.

Wednesday features an ASBMB-IUBMB co-sponsored workshop called "Defining the Core of the Discipline and Developing Suitable Assessment Tools." The workshop will feature work by Duane Sears and colleagues. Like many other scientific disciplines, biochemistry's foundation is built on

basic concepts from other areas, particularly chemistry and biology. However, biochemistry students often have heterogeneous background training in these disciplines and sometimes lack sufficient mastery of important ancillary concepts.[1] To be successful then, concept inventory (CI) development in biochemistry may depend in part on the co-evaluation of students' basic conceptual knowledge in these other areas. Inspired by CI questions that Kathy Garvin-Doxas and Michael W. Klymkowsky[2] developed to probe biology students' conceptual understanding of molecular diffusion and random movement in solution, assessment questions were devised to probe biochemistry students' conceptual understanding of the pH-dependent migratory behavior of ionizable molecules in an aqueous solution in the presence of an electric field. Preliminary results of the assessment data that will be presented at the workshop suggest that many students have difficulty coupling several basic chemical concepts related to random and electrophoretic movement of molecules that also undergo reversible ionization.

Finally, in a symposium co-sponsored with APS, ASBMB will host a panel discussion featuring several ASBMB members titled "Writing the Test Question Isn't Enough." This discussion was organized by Vikki McCleary of the University of North Dakota School of Medicine and Health Sciences and Katherine Sukalski of the University of North Dakota School of Medicine and Health Sciences.

See you in New Orleans!

Ellis Bell is currently Professor of Chemistry and Chair of the Biochemistry & Molecular Biology Program at the University of Richmond. He is also Chair of the ASBMB Education and Professional Development Committee. He can be reached at jbell2@richmond.edu.

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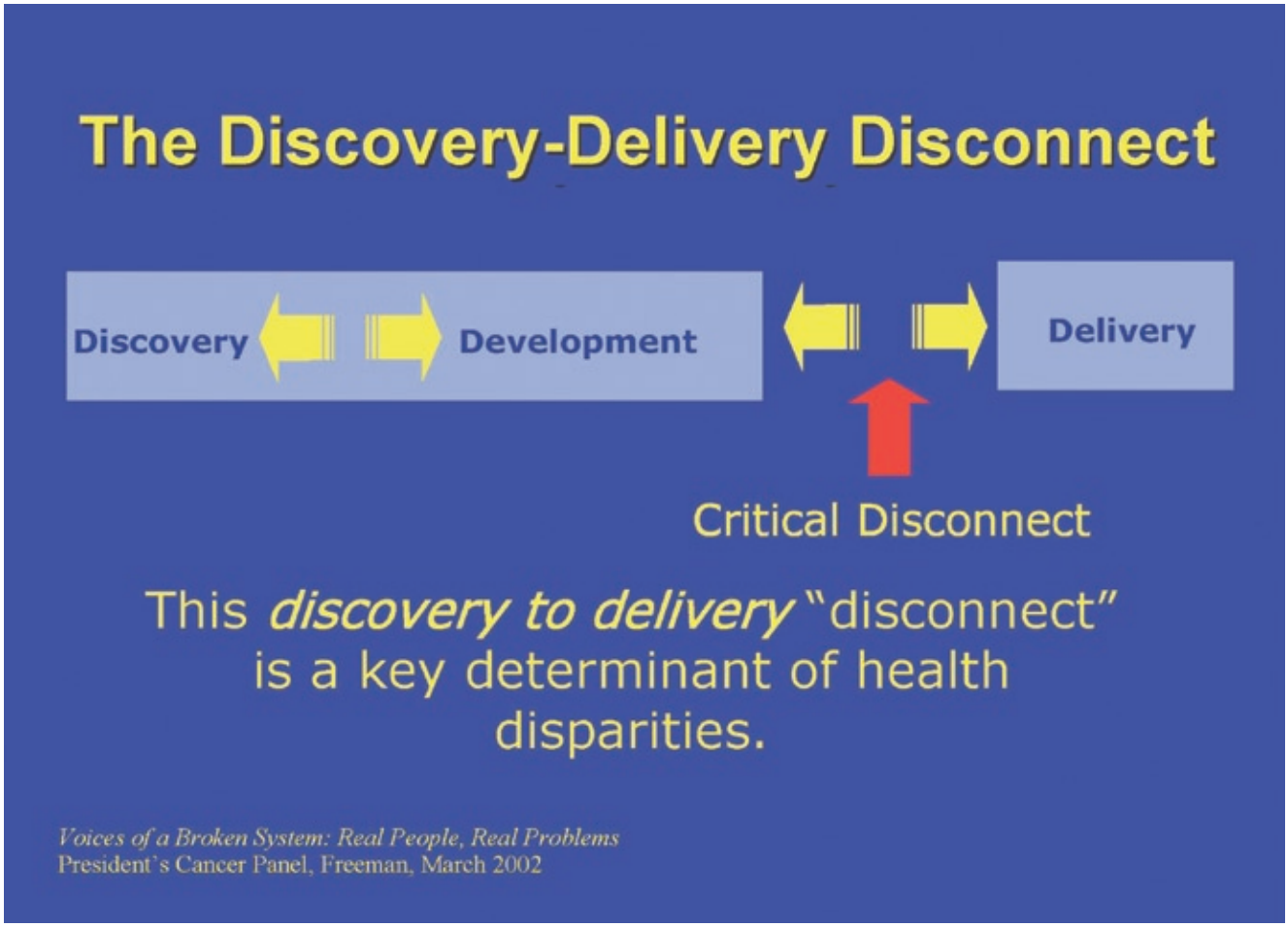
Eliminating Health Disparities

BY GEORGE C. HILL

One of the most exciting and important conferences of 2008 was the NIH summit titled, "The Sciences of Eliminating Health Disparities," which was held on December 16–18, 2008 at the Gaylord National Resort and Convention Center in National Harbor, MD.

The NIH National Center on Minority Health and Health Disparities, with the support of its NIH Institute/Center partners, convened the first government research summit on the science of eliminating health disparities, hoping to:

- **Showcase the collective contribution of NIH in the development of new knowledge in the science of eliminating health disparities;**
- **Highlight the progress of NIH minority health and health disparities research activities to improve prevention, diagnostic, and treatment methods;**
- **Increase awareness and understanding of disparities in health;**
- **Showcase best-practice models in research, capacity-building, outreach, and integrated strategies to find solutions to health disparities;**
- **Provide an exciting forum for participants to learn and network with the nation's multidisciplinary health disparities experts;**
- **Identify gaps in health disparities research;**
- **Allow participants to make recommendations that will shape the NIH health disparities strategic plan; and**



- **Establish a framework for ongoing dialogue and creation of innovative and unique partnerships to address disparities in health in all affected communities.**

The theme of this summit was the intersection of science, practice, and policy. "The elimination of health disparities will require a wide spectrum of approaches," said John Ruffin, director of the NIH National Center on Minority Health and Health Disparities. "Continual improvement and integration of different paradigms is fundamental in understanding and identifying real solutions to health disparities."

The summit highlighted many of the complex biological and non-biological factors that influence health outcomes. Sessions offered best practice models in research, training, career development, clinical intervention, community outreach, and policy being applied in communities around the nation and in different countries. "Our strategy cannot be isolated or stagnant; it will take all of us working together to eliminate health disparities," said Ruffin.

For scientists like us, in the past decade, profound advances in biomedical science have contributed to improved quality of life and longevity for many Americans. However, there is an urgent need to aggressively search for links between biomedical research discoveries and racial and ethnic disparities. Clearly, the causes of health disparities are multifactorial, but with significant advances in understanding the molecular and biochemical basis of diseases, investigating these links is growing more important. One of the goals of the conference was to further stimulate such research.

There is an urgent need to aggressively search for links between biomedical research discoveries and racial and ethnic disparities

An example reported at this summit was from D. D. De Leon of Loma Linda University and her team, who are studying the role of IGF-II in the breast cancer survival disparity among African American women. They are investigating the possibility that IGF-II is highly expressed in tumors from African American women promoting estrogen-independent breast cancer growth, which could contribute to the disparity in survival observed in African American breast cancer patients. More such approaches in research investigating the biological, molecular, and genetic differences that may be present in different populations are needed.

At the summit, the acting director of NIH, Raynard Kington, announced "the approval of an intramural research program at the National Center of Minority Health and Health Disparities to complement its extensive extramural research activities." He noted that this intramural program "will conduct state-of-the-art research focusing on the links between biological and nonbiological determinants of health and health disparities populations. It will create training and mentorship opportunities to grow intramural research focused on health disparities research, including those from health disparities populations. It will contribute a pool of early stage and seasoned investigators that will enhance the diversity of scientists and research disciplines comprising the intramural program of NIH."

Kington concluded, "As we move forward in the future in which everyone in this nation has the likelihood of a healthy and long life, we can be confident that the NCMHD intramural research program will contribute significantly toward creating that future."

The fostering of extramural and intramural research on health disparities by NIH is critical, as is the establishment of research collaborations with colleagues in ASBMB. With such efforts, we can be confident that, with appropriate investments, we will see continued progress in addressing this important health challenge for our nation.

George C. Hill is a member of the ASBMB Minority Affairs Committee and is the Levi Watkins, Jr. Professor at Vanderbilt University School of Medicine and Associate Dean for Diversity in Medical Education. He can be reached at george.hill@vanderbilt.edu.

Luck, Knowing Someone, and Doing Something For Free: *My Career Trajectory*

BY FAYE FARMER

I have only just officially had a "career" for only about five years now. In retrospect, I would ascribe 70 percent of my career to luck, knowing someone, and doing something for free. I would call my trajectory purposeful yet haphazard. Hopefully, I have managed to learn a few lessons that I will relate here.

After graduating from the University of Arizona in Tucson with a B.S. in Plant Sciences, I was accepted to serve as a Peace Corps volunteer in Lesotho (Southern Africa). After serving for two years, I worked for a year at a bookstore and then decided to attend graduate school. I entered my degree program certain of two things; 1) I did not want to pursue a Ph.D. (having a negative impression of that amount of specialization in regard to job prospects), and 2) I wanted to work in a laboratory afterwards. I graduated with an M.S. in Plant Biology from Arizona State University in Tempe. I interviewed for one laboratory position and three non-laboratory positions, thus signaling my change of heart regarding my employment desires.

I spent six months following graduation working as a manuscript editor for a researcher at a local hospital and taught introductory biology at a local community college. Through a connection I had made in graduate school, I was hired as the Laboratory Coordinator for Introductory Biology at ASU. This position allowed me to continue writing science in the form of curriculum development and grant proposals. I also started the School of Life Sciences Newsletter (now the SOLS Magazine) and opened a small student learning center for the school. I did both of these activities with no initial financial reward, but due to my commitment, I was offered a promotion to the student services office within the school.

After a year as an advisor and continuing as a contributing writer for the SOLS Magazine, I realized that my position at the school was terminal. I did not know what I wanted to do, but science writing had to be some part of it. I created a professional writing portfolio and sent it to a friend who was looking to hire a writer and editor.

I was hired into the Research Management Office at the Biodesign Institute last year. It can be best described as a "proposal machine." My office works to professionally manage the submission of proposals to sponsors. The result is a more comprehensive, holistic management of time, money, and proposal content resulting in increased funding. The office is composed of individuals who specialize in research administration and program management, in addition to editorial and content services. That last division is my responsibility. We create boilerplate or *de novo* content, editing, and formatting. We also work on whitepapers, manuscripts, and other miscellaneous presentations as needed. I am able to read and write science

Farmer

Faye Farmer is the manager of the Editorial and Content Services division of the Research Management Office at the Biodesign Institute at Arizona State University. She is also a Returned Peace Corps Volunteer, who served in Lesotho, Southern Africa (1997–1999) as an agricultural extension agent. She is currently the Vice President of the Central Arizona chapter of the Association for Women in Science, the newsletter coordinator for Friends of Lesotho, and a member of the National Alliance on Mental Illness.

for technical and lay audiences and stay busy with projects varied in both scope and content. Our office is a model for others on campus. The work is rewarding, fast-paced, and synergistic.

How did I get here?

I have two science degrees and no professional training as a writer. I do have years of experience in reading, writing, and editing for a variety of audiences. This experience has been from volunteering to write for special interest newsletters and magazines, as well as from my employment. I do not know if I could recreate my trajectory. I can offer some recommendations though.

I find that if I keep a few truths at the forefront of my vision, I tend to make better decisions. This also melds well with my rational and process-driven decision-making nature. One, how will this choice make me happier than I am now? This can manifest in a variety of ways: providing additional work during down times, challenging my understanding of a topic, or deepening my skill set. Two, is it a short-term investment with long-term rewards? Three, can I commit myself to this action without sacrificing my life, my free time, or events in which I enjoy participating? I must be able to satisfy this last question with a clear conscience and not give short shrift to my other obligations.

In addition, many of the positions I have interviewed for have had minimal requirements beyond the interview, but I have always taken the time to create an exceptional portfolio for each. Taking the time to create a polished product signals that you take the interviewer's time seriously and also take pride in your skills. My portfolio has changed over time. Initially, it contained my thesis, my teaching philosophy, and sample lesson plans. Then, it came to include examples of my writing and a successful grant application. A portfolio can contain anything from exceptionally elegant experiments to proposed work. Additionally, when you leave the portfolio with the interviewer (always including a means to have them send it back to you), it allows them to spend more time reviewing you than an interview would permit. By far, the $40 I spent on my leather binder for my portfolio was the largest and best investment I made in myself that last year of graduate school. Finally, I never assumed that I had the job "in the bag." I always approached each interview as if it were critically important.

> *"I find that if I keep a few truths at the forefront of my vision, I tend to make better decisions."*

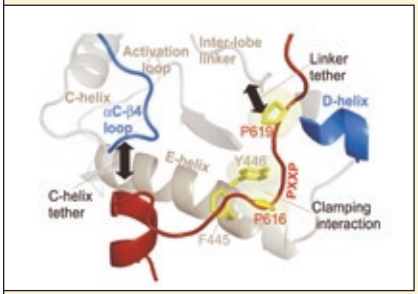
It is also important to keep your network alive. Each professional transition I have made has been facilitated by someone I was familiar with. This also means that your reputation needs to be a positive one. Be aware that a network is no good to someone who uses it incorrectly, not judiciously, or relies on it too much. To ensure that your network is alive, a certain amount of "pressing the flesh" is required. Invest time to reinforce connections through happy hours, professional networking events, online directories, and social connections (*e.g.* I participate in Phoenix area Returned Peace Corps Volunteer events). This allows others to know your interests, your work, and your potential.

I would also add one final recommendation—volunteer. In whatever small ways you are able to, volunteer to do something outside your everyday work routine. Examples include coordinating activities for a professional or social group or assisting with an activity at your workplace.

As one final example of how this works, I volunteered a few years ago to help edit the *Association for Women in Science Magazine*, where I met Nicole Kresge, the editor of this magazine.

A Tail for Two Chaperones

Protein kinases regulate key integrative processes such as cell growth, proliferation, and apoptosis. For many kinases, an important regulatory step is polypeptide maturation and processing, which usually requires input from a complex containing the chaperone proteins Hsp90 and Cdc37, which ensure that the kinase attains an appropriate conformation during synthesis, activation, and deactivation. Accordingly, understanding how Hsp90/Cdc37 interact with their client kinases is important. In this study, the authors identify a critical and conserved binding motif on the C-terminal tail of AGC kinases (a large protein family that includes protein kinases A, G, and C) necessary for the maturation of several protein kinase C (PKC) proteins. They show that this P*XX*P motif, coupled with additional sequence determinants within the PKC core domain, is essential for Hsp90/Cdc37 binding, an event that is required for subsequent processing of PKC via phosphorylation. Given the conservation of the P*XX*P motif in the AGC family and the importance of Hsp90/Cdc37 for the maturation of other protein kinase families (e.g. the Raf proteins), these findings reveal an important and potentially widespread mechanism controlling chaperone binding.



Structural representation of the key PKC residues involved in Hsp70/Cdc37 binding: the C-terminal P*XX*P motif (*dark red*) and determinants in the αE-helix of the catalytic domain (*yellow*).

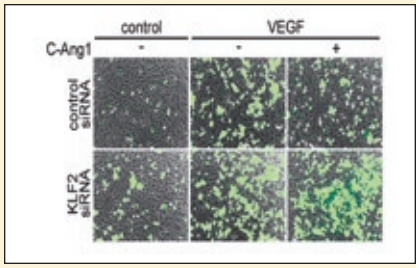
The Chaperones Hsp90 and Cdc37 Mediate the Maturation and Stabilization of Protein Kinase C through a Conserved P*XX*P Motif in the C-terminal Tail

Christine M. Gould, Natarajan Kannan, Susan S. Taylor, and Alexandra C. Newton

J. Biol. Chem. 2009 **284**, 4921-4935

KLF2 and Blood Vessel Quiescence

Angiopoietin-1 (Ang1) regulates either the quiescence or angiogenesis of blood vessels depending on the cellular context of its receptor Tie2; cell-contacted Tie2 promotes quiescence, whereas extracellular matrix (ECM)-associated Tie2 stimulates angiogenesis. The cell-contacted Ang1-Tie2 complex induces the expression of the transcription factor KLF2 (Krüppel-like factor 2); this process was investigated further in this study. The researchers found that mutating the myocyte enhancer factor 2 (MEF2) binding site on the KLF2 promoter could abolish Ang1-stimulated expression, as did cellular depletion of MEF2 with siRNA. On the other hand, MEF2-dependent transcriptional activity could be enhanced by phosphoinositide 3-kinase (PI3K) and AKT, indicating a role for this major pathway. Interestingly though, ERK5, an important mediator of blood vessel integrity, is not essential for KLF2 expression. The researchers also found that depletion of KLF2 increased vascular endothelial growth factor (VEGF)-mediated inflammatory responses like monocyte adhesion to endothelial cells, indicating that Ang1 may promote vascular quiescence by counteracting VEGF via PI3K/AKT and MEF2.



Ang1-induced expression of KLF2 inhibits VEGF-mediated adhesion of monocytes (*green*) to endothelial cells.

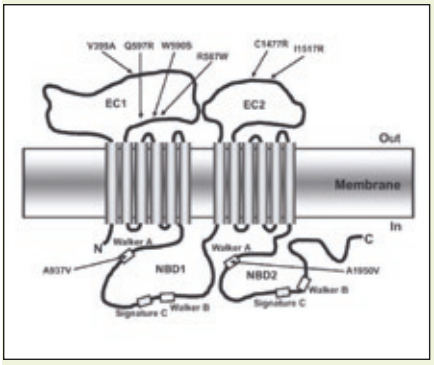
Angiopoietin-1 Induces Kruppel-like Factor 2 Expression through a Phosphoinositide 3-kinase/AKT-dependent Activation of Myocyte Enhancer Factor 2

Keisuke Sako, Shigetomo Fukuhara, Takashi Minami, Takao Hamakubo, Haihua Song, Tatsuhiko Kodama, Akiyoshi Fukamizu, J. Silvio Gutkind, Gou Young Koh, and Naoki Mochizuki

J. Biol. Chem. 2009 **284**, 5592-5601

The Interdependence of Lipid Export

The ABCA1 protein exports cholesterol and phospholipids from cells using a multistep pathway that involves forming cell surface lipid domains, solubilizing the lipids by apolipoproteins, binding the apolipoproteins to ABCA1, and activating signaling processes. In this study, the authors prepared one artificial and seven naturally occurring ABCA1 mutants with varying degrees of impairment to examine the relationship between ABCA1's different activities. They expressed the mutants on the surface of baby hamster kidney (BHK) cells and measured ABCA1-dependent lipid export, apolipoprotein A-I (apoA-I) binding, and signaling; the results showed that all of these functions are highly correlated. For example, lipid efflux and cellular apoA-I binding correlated significantly with the ability of ABCA1 to form cell surface lipid domains. Likewise, lipid export, cellular apoA-I binding, and formation of lipid domains also correlated with the amount of apoA-I that could be cross-linked to ABCA1. Moreover, each of these lipid activities correlated with the activation of Janus kinase 2 (JAK2). This interdependency suggests that ABCA1 forms a tightly interactive pathway to modulate lipid export from cells.



Topological model of ABCA1 showing approximate locations of the missense mutations used in this study.

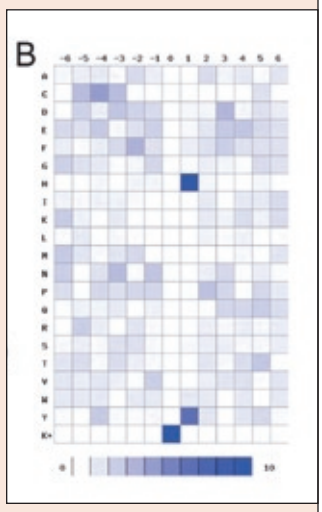
ABCA1 Mutants Reveal an Interdependency between Lipid Export Function, ApoA-I Binding Activity, and Janus Kinase 2 Activation

Ashley M. Vaughan, Chongren Tang, and John F. Oram

J. Lipid Res. 2009 **50**, 285-292

Uncovering Bacterial Acetylation

While lysine acetylation is known to play a pivotal role in mammalian cellular physiology, the importance and extent of this post-translational modification in prokaryotic cells remains largely unexplored. To help overcome this hurdle, the researchers in this study report the first global screening of lysine acetylation in *E. coli*, which identified 138 acetylation sites in 91 proteins—none of which had been previously associated with this modification. Interestingly, more than 70 percent of the acetylated proteins were metabolic enzymes (53 percent) and regulators of translation (22 percent), suggesting an intimate link between this specific modification and energy metabolism. The researchers provided some more evidence for this by showing that the lysine acetylation profile was altered in response to stress stimuli. This data set suggests that lysine acetylation could likely be more abundant in prokaryotes than appreciated and that the chromatin-independent role of lysine acetylation is evolutionarily conserved from bacteria to mammals.



Density map of lysine acetylated peptides, highlighting the frequency of occurrence of amino acid residues surrounding lysine acetylation sites relative to the residue frequency within the entire *E. coli* genome.

Lysine Acetylation Is a Highly Abundant and Evolutionarily Conserved Modification in *Escherichia coli*

Junmei Zhang, Robert Sprung, Jimin Pei, Xiaohong Tan, Sungchan Kim, Heng Zhu, Chuan-Fa Liu, Nick V. Grishin, and Yingming Zhao

Mol. Cell. Proteomics 2009 **8**, 215-225

Communicating Science in an Online World

BY ALLEN DODSON

Social networking, Facebook, and blogs have become an increasing part of our culture, and their impact is beginning to be felt within the scientific community.

A group of bloggers, journalists, publishers, and educators met in North Carolina this January for the Science Online '09 conference, where they examined some of the benefits and issues surrounding online communication and research.

Promoting and Facilitating Science

Social networking has tremendous potential to help communicate—and even perform—science. For example, scientists at NASA used Twitter (twitter.com) to post short updates about the Mars Phoenix mission, written from the perspective of the robotic vehicle on the surface of Mars. These notes attracted over 41,000 site users to follow the mission, greatly increasing the public profile of the research.

In another creative use of social networking, biologists on a site called Friendfeed (friendfeed.com) created a "room" called "The Life Scientists," which has attracted over 500 members. Scientists can post questions about experimental protocols or reagents in the room, and other members can forward the request to their contacts with a single mouse-click.

Another successful site, Nature Network (network.nature.com), has been working to promote scientific community around major scientific hubs in Boston, London, and New York. The network hosts local events, such as (offline) pub nights that help introduce local scientists to their peers, in addition to providing an online forum for discussion of science news and events.

Impact and Issues in Science Blogging

Many scientists feel that blogging about their trials and tribulations at the bench is a tremendous source of emotional support. In particular, female scientists at *Science Online* (www.sciencemag.org) praised the online community for helping them persevere through the challenges of balancing families and careers while occasionally being faced with overt sexism from their offline peers.

Though blogging can be greatly beneficial to the blog writer, some advisors and employers are concerned about having any bloggers in their groups, even if the blog is not work-related and does not contain ranting or offensive content. Some writers prefer anonymity to avoid such conflicts, or to separate their online and offline lives. However, it is not always possible to remain anonymous on the internet, so many bloggers suggest "sleeping on" controversial posts and not publishing anything that the writer would not say in person.

For other authors, blogging under their own names has been an asset. Several professors remarked that their departments viewed their blogs as valuable efforts at outreach to the public and the academic community. Some bloggers were even offered jobs due in part to their online activities. Even authors who never found such prominence agreed that penning a blog on a regular basis has helped them improve their writing skills.

Starting a Blog

Budding science bloggers have a number of free options available to them, including Blogger (blogger.com) and Wordpress (wordpress.org). Members of the Nature Network can also apply for a blog on the site. Other commercial networks, such as the popular Scienceblogs.com, actively recruit prominent writers of existing blogs from the community.

Regardless of where the blog is hosted, experienced bloggers agreed that it is important to update the blog regularly and to participate in the community by linking to, and commenting on, other blogs (whose authors may return the favor).

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

ASBMB Online:

- **Friendfeed rooms for the ASBMB annual meeting public affairs symposia:**
  friendfeed.com/rooms/nihinfrastructure09
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- ***MCP* Blog: mcpblog.mcponline.org**
- **ASBMB Lipid Group blog:** *Coming soon!*

James Imlay: the Chemistry behind Oxidative Damage

BY NICK ZAGORSKI

Physiologically, oxygen embodies both the yin and the yang; as a ready and willing electron acceptor, oxygen is a necessity for the efficient respiration needed to support complex life, yet this same property makes it one of the most dangerous elements present inside cells. As James Imlay, Professor of Microbiology and Romano Scholar at the University of Illinois at Urbana-Champaign, notes, "for Earth's first two billion years, life thrived in an anaerobic world; oxygen would have been quite lethal to these early microbes. And as all basic metabolism evolved from these anaerobes, humans and other organisms have had to cope with the residual threat of oxygen toxicity ever since."

The main agents in oxygen toxicity are a pair of molecules containing reduced and highly reactive oxygen: superoxide (O_2^-) and hydrogen peroxide (H_2O_2). To highlight just how deadly these molecules can be, Imlay points out that in the world of microbial warfare, oxygen is the weapon of choice. Plants secrete antibiotics that generate reactive oxygen species to ward off invading bacteria or fungi (or even other plants), while macrophages in our own immune system spray invading pathogens with a wave of superoxide and peroxide to kill them.

Yet despite its claim as nature's oldest pesticide, reactive oxygen remains a big mystery; our understanding of basic questions, from how it's made to how it's regulated, are still incomplete. But for more than 20 years now, Imlay has been diligently pondering these questions and has been at the forefront in providing answers to both the mechanisms of oxidative damage and the enzymes that defend cells against oxidants.

Imlay has been unique in the field of oxidation biology in that the near entirety of his work utilizes *E. coli* as a model system, compared to the vast majority of researchers working in mammalian systems. "Due to its genetic malleability, *E. coli* is tremendously useful because it allows us to monitor specific pathways very closely; we can easily knock-out a target gene to make strains that can't scavenge oxygen radicals and see what happens," he says. And because *E. coli* metabolism is fairly well understood, defects are easily analyzed. "It's harder to figure out what goes wrong in a cell when you don't understand a pathway in the first place."

"Plus, *E. coli* can survive in an anaerobic environment," he adds. "So you can completely knock-out their oxygen tolerance, grow them anaerobically, and then transfer them to an oxygenated environment and see what happens. You can't do that with a mouse."

A Well-placed Book

Unlike other scientists who caught the biology bug early, Imlay had minimal interaction with the life sciences growing up and in college at Duke University, where he majored in chemistry and English. His brief exposure to biology occurred during his senior year, as the chemistry lab where he was conducting undergraduate research did carry out one project involving histones.

Though learning about histones provided some of the initial interest, Imlay really became hooked—albeit unexpectedly—after graduating from Duke in 1981 and taking an industry job at a high-tech chemical company outside of Chicago. "One day, I just happened across a copy of Lehninger's *Principles of Biochemistry* at my local library, and I started reading the section on cell membranes," he says. Imlay was fascinated by how the book explained a fairly complex biological structure using chemical principles he

understood well and decided to give biochemistry a try.

He ended up at Berkeley and joined the lab of Stuart Linn, who was studying the enzymology of DNA repair. "Coming in with my chemistry background, I didn't understand what most of the researchers were doing," Imlay admits, which made choosing his lab rotations somewhat challenging. "In the end, after talking with Stu, he seemed very affable and his work on DNA repair seemed medically relevant, so based on those two things, I picked that lab."

Imlay began a project examining the rate at which *E. coli* cells die or survive (by kicking in their repair machinery) in response to hydrogen peroxide. That would end up being his introduction into the arena of oxidative damage. "I certainly approached it from a funny angle," he says. "It turned out the phenomenon I observed, that hydrogen peroxide could induce two separate modes of killing, had more to do with the nature of cell damage than how the cells were repairing it," he says. "So it brought back my training because my work evolved into more of a chemistry problem than a biology problem."

Ever since, Imlay has been elucidating the molecular mechanisms by which oxidants damage cells. His first stop was a return trip to Duke, where he carried out a postdoc with Irwin Fridovich, one of the noted leaders in oxygen metabolism research. "Irwin gave a seminar at Berkeley as I was wrapping up my doctoral studies," Imlay recalls, "and (much like the Lehninger textbook) his work involved a strong chemical sensibility that really drew me in." Imlay got Linn to write a letter on his behalf to Fridovich, and Fridovich took him in.

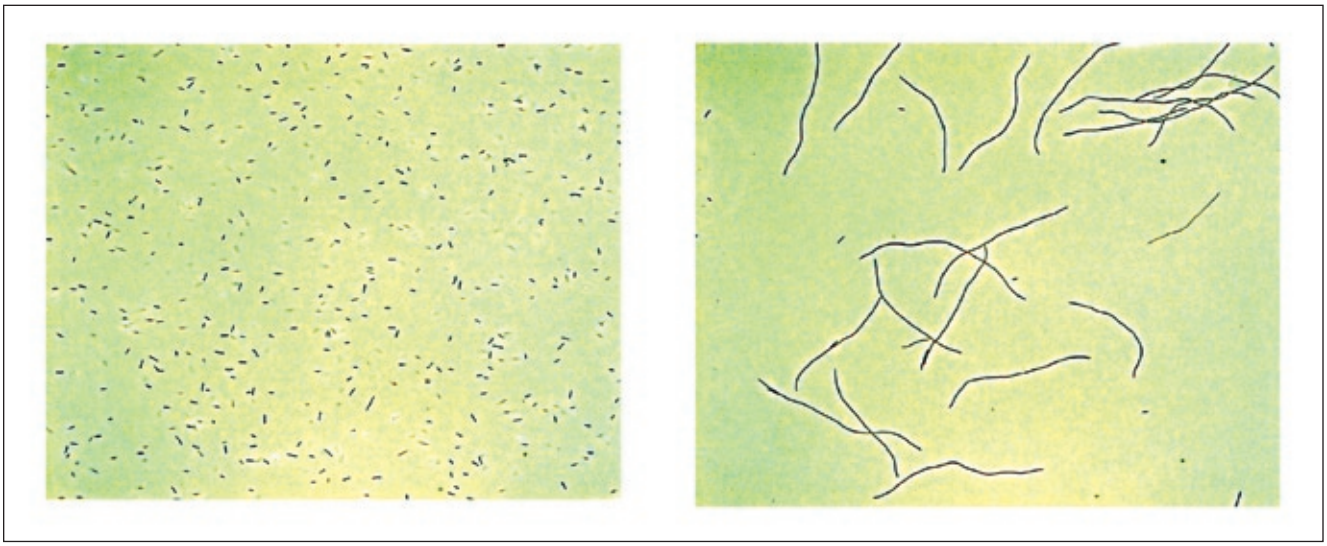
During his postdoc, Imlay became more acquainted with the other half of the reactive oxygen duo, superoxide, as well as superoxide dismutase, the protective enzyme that scavenges superoxide molecules. After leaving Duke in 1992, he set up his own lab at the University of Illinois, continuing his work in this exciting area.

"It has ended up being a good fit for my personality," he says. "I'm the kind of person who likes to pick up a problem, dig down, and stick with it." That attitude was actually a major motivation for his decision to leave industry behind, as projects at the chemical company he worked for had a failure rate of 97 percent. "People could spend their whole career there, and nothing would ever come out of their work," he says. "And it wasn't even necessarily because their project didn't work; many of them were simply shut down after years because of market changes or other external factors."

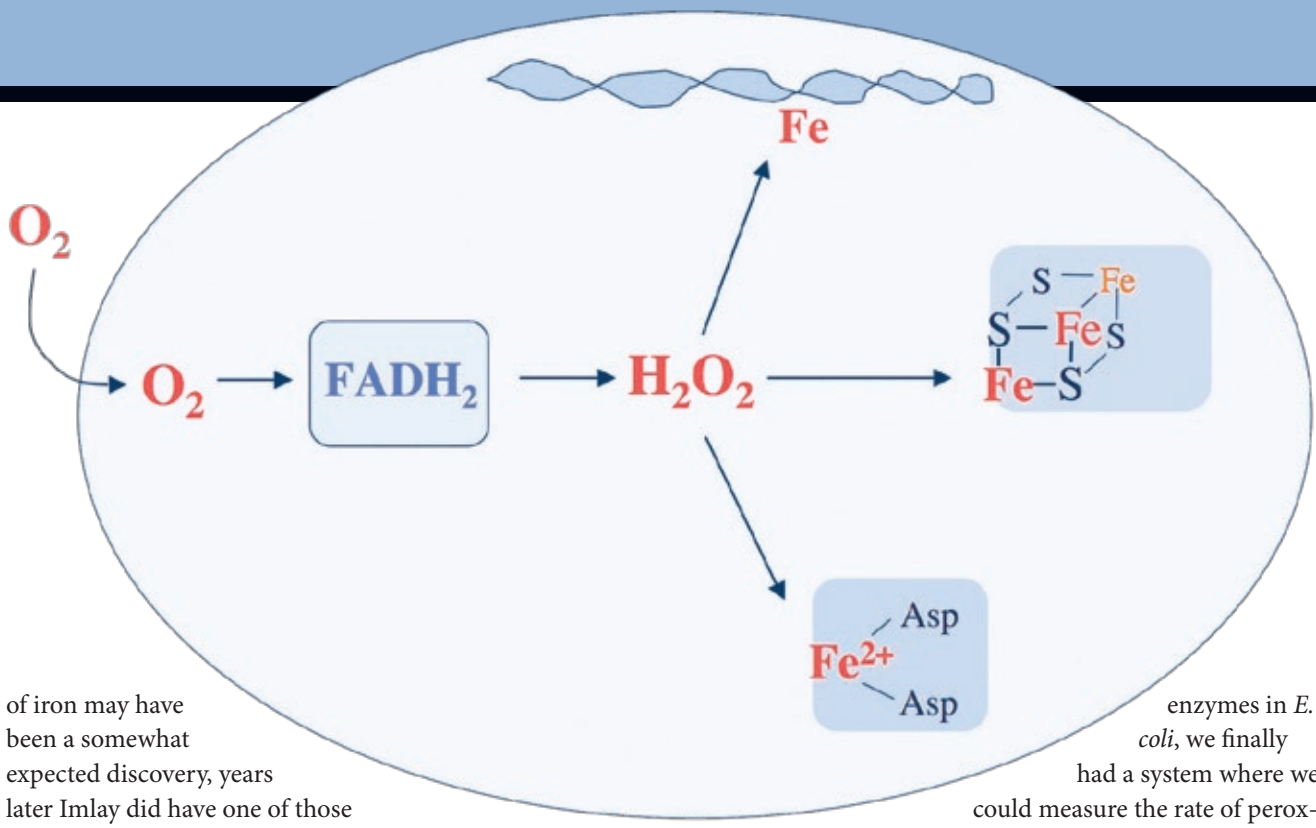
Less Can Be More

During his graduate school years, Imlay came through with his first big discovery, uncovering the critical role that iron plays in damaging DNA in bacterial cells. "The initial product formed by the peroxide was not a hydroxyl radical, but rather a ferryl iron intermediate (generated through a process called a Fenton reaction)," he says.

He does add that the findings, which appeared in the journal *Science*, were really more a confirmation that the peroxide chemistry observed *in vitro* also occurred in living cells than a true groundbreaking result. "There were plenty of indications from other studies that this Fenton reaction was a true event," Imlay says, "so some of that work was due to my ignorance of the literature." While the importance



"Filamentation" occurs when cells cannot replicate H_2O_2-damaged DNA. Because they cannot produce two daughter chromosomes, the cells postpone septation, even as their growth continues. *Left:* Catalase/peroxidase mutants in anaerobic medium. *Right:* Catalase/peroxidase mutants in aerobic medium.



The mechanisms of hydrogen peroxide damage. Molecular oxygen generates H_2O_2 by oxidizing reduced flavoenzymes; the H_2O_2 in turn can oxidize solvent-exposed iron. When the iron binds to DNA, it produces hydroxyl radicals that can severely damage DNA.

of iron may have been a somewhat expected discovery, years later Imlay did have one of those "out of left field" experiences that ended up being quite significant to the whole oxidation community.

A big riddle in the 1990s involved the scavenging enzyme catalase, a major cellular defense mechanism against hydrogen peroxide—or so most experts in the oxidation field believed. As hydrogen peroxide is naturally produced at low, but still potentially harmful, levels in cells from aerobic metabolism, scientists naturally believed this enzyme was indispensible; thus, it was quite shocking that *E. coli* mutants devoid of all catalase activity had absolutely no problems growing and thriving in an aerobic environment (in contrast, superoxide dismutase mutations could completely incapacitate a cell).

Now, high levels of exogenous hydrogen peroxide were still toxic to these catalase mutants, but one day, Imlay happened to be conducting some studies with the mutants and decided as a control to expose one batch to a very low peroxide concentration (micromolar instead of the typical millimolar amounts). "As it happened, the mutant cells could scavenge micromolar peroxide as well as regular *E. coli*," he says. "That meant they had some secondary mechanism to handle naturally occurring peroxide."

Imlay scanned through a series of candidate genes and identified the culprit: alkyl hydroperoxide reductase (Ahp), an NADH-dependent peroxidase enzyme that acted on various organic molecules. "Ahp is extremely efficient at scavenging peroxide, even more so than catalase, though it saturates at lower concentrations," Imlay notes. What this meant was that *E. coli* had an efficient two-pronged approach to handle peroxide toxicity; at physiological levels, the Ahp peroxidase takes care of business, while in times of high peroxide stress, the catalase activates and cleans up the excess.

"In a sense, everything opened up, scientifically, once we had identified the existence of this peroxidase," Imlay says. "Once we got rid of both enzymes in *E. coli*, we finally had a system where we could measure the rate of peroxide synthesis inside a cell and monitor its toxic activity at natural levels."

From there, Imlay and his group were able to really get at some of the fundamental questions surrounding reactive oxygen; how peroxide and superoxide are produced inside a cell (auto-oxidation by flavin-containing enzymes is a major factor), in what amounts (*E. coli* typically produce 10 μM/s peroxide, though peroxidase scavenging keeps intracellular levels below 0.1 μM), and what molecules are targets of the reactive oxygen (notably the iron-sulfur clusters of certain enzymes).

Ironing out the Problems

When asked about his past as an English major in college, Imlay admits that he certainly had a fondness for English literature growing up (he even spent the summer before his senior year studying at Oxford), but by the time he graduated, most of the things that seemed fresh and new when he started had started to feel a bit familiar and stale. "That's been one real nice feature of scientific research," he says. "There are always new things coming along the road."

"For one, we are still trying to

identify all the biomolecules that can be damaged by physiological levels of peroxide or superoxide—as opposed to the damage caused by dumping massive amounts of peroxide on the cells." In the case of peroxide, all the targets identified so far involve iron in some way, whether it's free intracellular iron atoms or the iron cofactors of enzymes. Imlay notes that this is a product of another fateful evolutionary choice, "The absence of oxygen in the early atmosphere ensured that dissolved iron was abundant," he says, "so it was naturally selected as a cofactor for multiple enzymes."

But, that also leads him to wonder, "Are there non-iron targets?" In *E. coli*, at least, Imlay and graduate student Lee Macomber found that copper does not contribute to oxidative DNA damage, so maybe iron has some unique properties.

In his efforts at finding new peroxide targets, Imlay has begun riding the coattails of microarray studies, such as work by Gisela Storz at the National Institutes of Health and Mike Maguire at Case Western Reserve University which has identified which genes are overexpressed during times of oxidative stress. "Normally, we don't begin with a specific hypothesized target," Imlay says. "We first identify oxidative vulnerabilities through growth defects; using a variety of media, we can identify the particular metabolic pathway that has failed and then dig deeper to identify and analyze the protein that has been damaged. The microarray data has given us fresh leads on potential genes."

One over-expressed protein of note was not even an enzyme, but rather an ion channel that takes up manganese; sure enough, when Imlay's group knocked it out in *E. coli*, the cells failed to tolerate peroxide. Imlay thinks he has deduced why manganese import would be critical, and it does again tie in with iron. "Many enzymes require divalent iron, which is leached out by peroxide thus rendering the enzymes inert," he says. "In this event, the cells are actually quite smart and pump in extra manganese to fill in these empty active sites as a substitute." He notes that it's similar to working with enzymes *in vitro*; ferrous iron isn't stable in solution and iron enzymes are activated by buffer ions such as cobalt or manganese instead.

So, at least for now, the search continues.

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

Out of Focus: I Can't Breathe

Though *E. coli* is the staple, Imlay's group has tackled questions on why obligate anaerobic bacteria can't tolerate oxygen. For a while, the consensus seemed to point to a complete inability to handle reactive oxygen, as oxygen sensitive microbes generally lack catalase and superoxide dismutase (SOD). However, these bacteria were later found to have a mechanistically different enzyme called superoxide reductase which negated that idea (a parallel realization was that they use peroxidase instead of catalase). By examining specific metabolic pathways like his ***E. coli*** studies, Imlay and postdoc Ning Pan found that molecular oxygen itself (O_2) was the culprit, as many anaerobic enzymes have structures that made them highly susceptible to oxygen attack (though these anaerobes have also devised many ways to minimize the damage). "These enzymes like pyruvate:formate lyase streamline anaerobic metabolism; you cannot be a competitive anaerobe without them," Imlay notes. "At the same time, all organisms are at least transiently exposed to oxygen in today's world; so it's interesting that evolution hasn't yet forced anaerobes to change these enzymes." As to why some bacteria choose superoxide reduction over dismutation is another intriguing and related question. The logical consensus seems to be that dismutation, carried out by SOD and catalase, creates molecular oxygen as a product, but Imlay also has other thoughts on that. "I think it might be a matter of kinetics; in a situation where you need high enzyme turnover, like brief exposure to oxygen-rich air, a reduction may be far more efficient at recycling the enzyme than dismutation."

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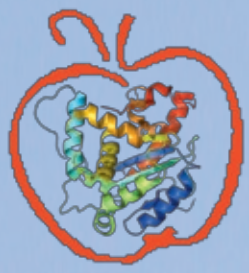

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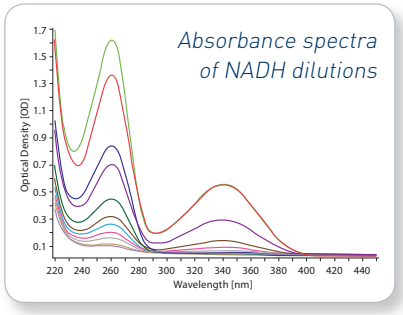

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JUNE 8–12, 2009
DUBLIN, IRELAND
www.selectbiosciencies.com/conferences/files/Agendas2009/CP2009_Agenda.pdf

Systems Biology: Integrative, Comparative, and Multi-scale Modeling
JUNE 11–14, 2009
AMES, IA
www.bb.iastate.edu/~gfst/phomepg.html

3rd EuPA Meeting—Clinical Proteomics
JUNE 14–17, 2009
STOCKHOLM, SWEDEN
www.lakemedelsakademin.se/templates/LMAstandard.aspx?id=2529

VII European Symposium of the Protein Society
JUNE 14–18, 2009
ZURICH, SWITZERLAND
www.proteinsociety.org

XV International Symposium on Atherosclerosis
JUNE 14–18, 2009
BOSTON, MA
www.isa2009.org

International Conference on Cytochrome P450
JUNE 21–25, 2009
OKINAWA, JAPAN
www.p450meetings.com

Gordon Research Conference: Atherosclerosis
JUNE 21–26, 2009
TILTON, NH
www.grc.org/programs.aspx?year=2009&program=athero

SEB at Glasgow 2009
JUNE 28–JULY 1, 2009
GLASGOW, SCOTLAND
www.sebiology.org/meetings/Glasgow/glasgow.html

Gordon Research Conference: Stress Proteins in Growth, Development, & Disease
JUNE 28–JULY 3, 2009
ANDOVER, NH
www.grc.org/programs.aspx?year=2009&program=stressprot

JULY 2009

Gordon Research Conference: Molecular & Cellular Biology of Lipids
JULY 19–24, 2009
WATERVILLE VALLEY, NH
www.grc.org/programs.aspx?year=2009&program=lipids

SWLA 4th Annual Scientific Forum
JULY 24–26, 2009
OKLAHOMA CITY, OK
www.lipid.org

23rd Annual Symposium of the Protein Society
JULY 25–29, 2009
BOSTON, MA
www.proteinsociety.org

Protein Lipidation, Signaling, and Membrane Domains
JULY 26–31, 2009
SAXTONS RIVER, VT
src.faseb.org

AUGUST 2009

Student-Centered Education in the Molecular Life Sciences: Essentials for Educating Biochemistry and Molecular Biology Undergraduates
AUGUST 5-8, 2009
COLORADO SPRINGS, CO
www.asbmb.org/meetings

ACS Fall 2009 National Meeting & Exposition
AUGUST 16–20, 2009
WASHINGTON, D.C.
www.acs.org/meetings

Kern Aspen Lipid Conference
AUGUST 22–25, 2009
ASPEN, CO
www.uchsc.edu/kernconference

18th International Mass Spectrometry Conference
AUGUST 30–SEPTEMBER 4, 2009
BREMEN, GERMANY
www.imsc-bremen-2009.de

SEPTEMBER 2009

50th International Conference on the Bioscience of Lipids
SEPTEMBER 1–5, 2009
REGENSBURG, GERMANY
www.icbl2009.de

Systems Biology for Biochemists
OCTOBER 22-25, 2009
TAHOE CITY, CA
Organizer: Arcady Mushegian, Stowers Institute for Medical Research
www.asbmb.org/meetings

World Congress on Oils and Fats and 28th ISF Congress
SEPTEMBER 27–30, 2009
SYDNEY, AUSTRALIA
www.isfsydney2009.com

6th International Congress on Heme Oxygenases in Biology and Medicine
SEPTEMBER 30-OCTOBER 4, 2009
MIAMI BEACH, FL
www.hemeoxygenases.org

OCTOBER 2009

3rd ESF Functional Genomics Conference
OCTOBER 1–4, 2009
INNSBRUCK, AUSTRIA
www.esffg2008.org

Bioactive Lipids in Cancer, Inflammation, and Related Diseases (11th International Conference)
OCTOBER 25–28, 2009
CANCUN, MEXICO
www.bioactivelipidsconf.wayne.edu

NOVEMBER 2009

4th Barossa Meeting: Cell Signaling in Cancer and Development
NOVEMBER 18-21, 2009
BAROSSA VALLEY, SOUTH AUSTRALIA
sapmea.asn.au/conventions/signalling09/index.html

20th International Symposium on Glycoconjugates
NOVEMBER 29–DECEMBER 4, 2009
SAN JUAN, PR
www.glyco20.org

FEBRUARY 2010

Biophysical Society 53rd Annual Meeting
FEBRUARY 28-MARCH 4, 2009
BOSTON, MA
www.biophysics.org/Default.aspx?alias=www.biophysics.org/2009meeting

APRIL 2010

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

JUNE 2010

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

AUGUST 2010

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