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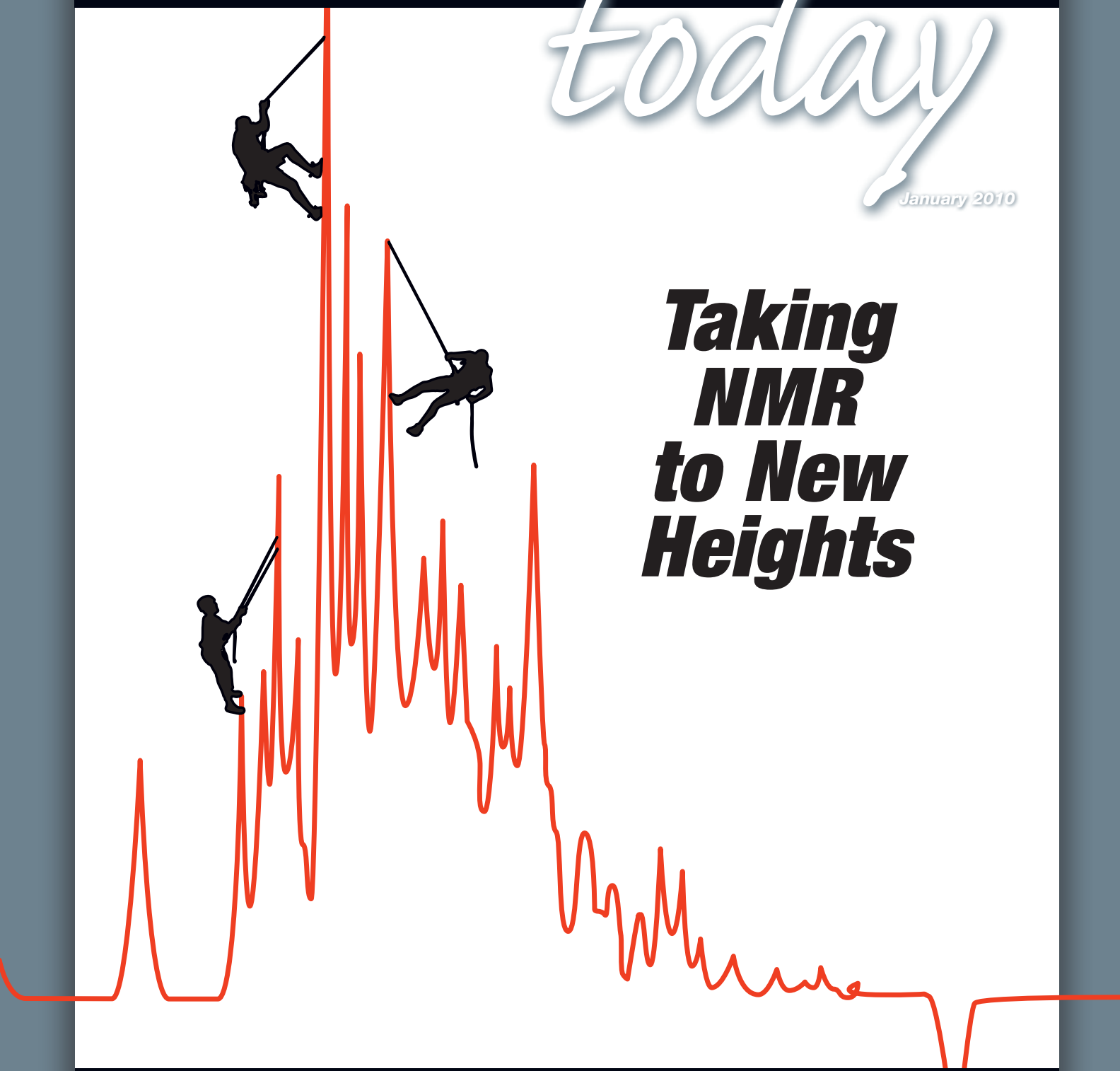

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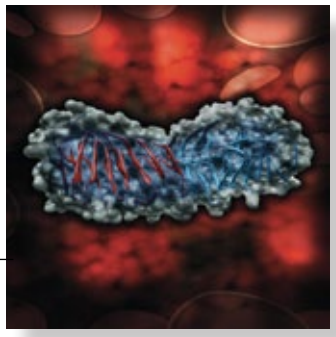

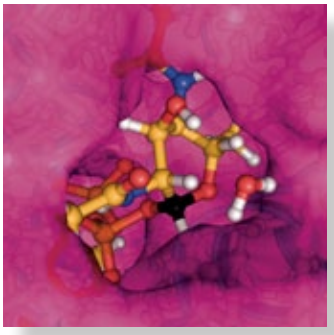

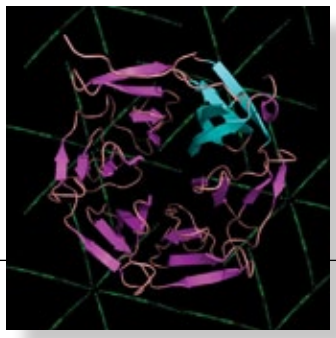

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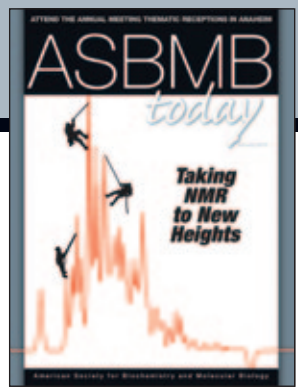

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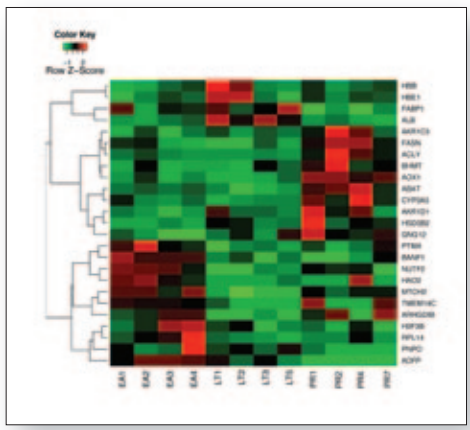

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podcast summary

Learn more about science comedian Brian Malow, featured in this month's issue, in our latest ASBMB podcast.

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

ASBMB today

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New Eye Lipids Thematic Review Series in JLR

BY MARY CHANG

In January 2010, the Journal of Lipid Research begins a thematic review series that gives a closer look at the lipids and lipid-soluble compounds in the cells and tissues of the vertebrate eye. The series, "Lipids and Lipid Metabolism in the Eye," will contain five articles published from January to May.

The series begins with an article by Raju V. S. Rajala of the University of Oklahoma Health Sciences Center. Rajala discusses phosphoinositide 3-kinase (PI3K) signaling in the vertebrate retina. He and his co-workers were the first to show that light in retinal rod receptors regulates the PI3K-dependent pathway in the retina. Improper regulation of PI3K has been implicated in diabetic retinopathy, a common blinding disorder, and, as such, research on the PI3K pathway may lead to therapeutic applications.

Bis-retinoids have been linked to cell death of the retinal pigment epithelium (RPE) and retinal degenerative diseases, including age-related macular degeneration (AMD), a major cause of visual impairment in older adults. In February, Janet Sparrow of Columbia University will publish a look at the formation, physical attributes and possible functions of bis-retinoids in the retina.

In her review for March, Christine A. Curcio of the University of Alabama at Birmingham will look at extracellular lipid deposits that are tell-tale signs of AMD. Evidence indicates that those deposits result from lipoprotein formation and

export by RPE cells, which is similar to the more intensively studied process of atherosclerotic lesion formation.

Norma Giusto at Universidad Nacional del Sur, Bahia Blanca, in Argentina, will examine retinal rod outer segments. The review will discuss the possible relationship between lipid-dependent signaling events, translocation of important molecules and association/disassociation of membrane proteins.

In the final review, Haydee E. P. Bazan and Sachidananda Kenchgowda of the Louisiana State University Health Sciences Center School of Medicine will look at the lipids involved in corneal injury and repair mechanisms and how that knowledge may lead to treatments for corneal wound healing.

Mary L. Chang (mchang@asbmb.org) is managing editor of the Journal of Lipid Research.

Ring in the New

BY GREGORY A. PETSKO

Here's to the new year: May it be a damn sight better than the old one.

It started out with such promise. We had a new president — one who promised to restore science to its rightful place in the councils of government (and, to our joy, he has). We had $10 billion in stimulus money for the National Institutes of Health to spend. Health-care reform looked imminent. The war in Iraq was winding down. I had only another one-and-a-half years as American Society for Biochemistry and Molecular Biology president. All was well.

But as 2009 winds down, that feeling of optimism has given way to one of anxiety — almost of impending doom. Delight over the stimulus has become frustration with the NIH Challenge Grants in Health and Science Research and the fear that the 2011 NIH budget will be disastrously small. Health-care reform is being held hostage by a small group of senators who either wish to use it as way of restricting abortion rights or, one is forced to conclude, who may be in the pockets of the insurance industry. As the war in Iraq winds down, the war in Afghanistan is growing larger. And I still have six months to go as ASBMB president.

I thought it might be a good time to take stock of the state of science in general, and the state of the ASBMB in particular, as we get ready to welcome in the first year of the second decade of the 21st century. I have to say that I think the state of science is good, though still threatened from the usual sources. And, I think the ASBMB is healthy but would be healthier if we had more young members.

Let me start with the ASBMB. Online is where it's at. Last fall, we launched a new Web site for the Journal of Biological Chemistry, and now the editorial side is making adjustments (see article on p. 10). Our two other journals, the Journal of Lipid Research and Molecular and Cellular Proteomics, also will be getting similar Web sites in the coming year. MCP is going online-only in 2010, and JBC and JLR will follow when the time is right for our users. Along with that, we soon will have a new Web site for ASBMB Today, replacing the old online pseudo-journal format. We think that

these represent real improvements in how we deliver content to our members over the World Wide Web. The sites are meant to be easier to navigate, easier to browse and packed with more opportunities to find more information. Our publications are intended to serve you, our members, first and foremost. So, write to us and let us know what you think of the new Web sites. And, if you have suggestions, please let us hear from you. We will listen.

As I said, I am still concerned with the demographics of our membership. I know this is also a major concern of my successor, Suzanne Pfeffer (and while I'm at it, let me offer her my condol— er, my congratulations on becoming president-elect) and that she already has a number of exciting ideas for getting more young people to join the society and for improving the ways in which we serve our younger members. But we still need your help. Please, urge your best postdoctoral fellows to take advantage of our free-for-the-first-year membership offer. We believe that once they experience the benefits of membership, they will want to continue. They're our lifeblood, and we are anemic at the moment.

Otherwise, the health of the society is good. Thanks to prudent fiscal management (which is to say I had no input into it whatsoever), our finances are in relatively good shape, and we have been able, despite the recession, to launch a few interesting new initiatives. One you will be reading more about in the coming months is a series of joint conferences in Latin America, sponsored by ASBMB and our sister society in Brazil. My counterpart in that society, Debora Foguel, and ASBMB past-President Bettie Sue Masters have taken the lead in getting this cooperation off the ground, for which I would like to convey my deepest thanks. The first meeting will take the form of an advanced school on the subject of biofuels, an area of biochemistry in which Brazil already is among the world's leaders. Watch ASBMB Today for more details.

Finally, our annual meeting, to be held in Anaheim, Calif., in April 2010, is looking to be very popular. Advance registration is running hot and heavy, so be sure to get yours in to secure your place at the Woodstock of biochemistry. (OK, I admit that Jimi Hendrix and Janis Joplin won't be there, but it will still be a great party.)

But, if the state of ASBMB is largely good, the same cannot be said of the state of science in general. As I write this, the U.S. Senate— the same Senate that seems to be using health-care reform as a football— has just passed an appropriations bill that calls for about a 2.3 percent increase in the NIH budget and about a 6.7 percent increase in the National Science Foundation budget. While the latter is on target with President Obama's stated intent to double the NSF budget, the former is below the expected level of scientific inflation. It would put the 2010 NIH budget at just under $31 billion. My Federation of American Societies for Experimental Biology counterparts and I have calculated that we need a 2011 appropriation for NIH of about $37 billion to avoid a catastrophic shrinkage of the NIH Research Project Grant Program (R01) pool when the stimulus winds down.

Of course, everything will depend on the state of the economy around this time next year, and, if you can

"...Italy's foremost science agency actually funded the publication of a creationist book authored by its own vice president."

predict that, you don't need me to tell you anything. My guess is that we will see the gross domestic product, which I regard as a nearly useless statistic, grow by around 3 percent next year, which means the recession will be "officially" over. But I am also guessing that this will be a jobless recovery, by which I mean that unemployment will still be between 8 and 10 percent by the end of next year. If I'm right, a big boost for NIH will be very difficult to obtain— though not impossible— as the multiplier for NIH funds (the return to the economy for every dollar invested) is about $2.20.

Speaking of NIH, kudos to Jeremy M. Berg, the head of the National Institute of General Medical Sciences, for managing to keep the payline at NIGMS for competing R01 applications at right around the 30th percentile, even when the stimulus money is not added in. I'm not going to ask him how he managed that particular feat of legerdemain when so many other NIH institute directors seemed to have had trouble doing so, but I suspect having fewer big science initiatives to fund didn't hurt.

Health-care reform is turning out to have more cliffhangers than the last Indiana Jones film. Without getting into the politics of it, let me simply say that it's going to be a very tough battle to get this passed. That's nothing new: Seven previous U.S. presidents have tried, and failed, to reform the health-care system in this country (beginning with Woodrow Wilson, who almost succeeded in 1916 but was interrupted by a little something

called World War I, and ending with Bill Clinton, whose failure still rankles), so, if Obama succeeds, it will be a monumental accomplishment no matter what the bill looks like. But, make no mistake about it, this present reform is not about controlling costs — it's about getting everybody covered. There is no possibility that health-care costs will go down, for the long term, unless we address the soaring cost of end-of-life care and shift our mindset more toward prevention rather than treatment. All of this makes biomedical research an essential part of any real effort to get costs under control, which is another reason why I wouldn't give up just yet on that $37 billion NIH budget for 2011.

Looking back on 2009, though, the most ominous sign I see that all is not right with the world of science is the continued efforts on the part of religious fundamentalists to inject religious doctrine into the teaching of science in our public schools. Their latest ploy masquerades as "critical thinking" or "freedom of expression" and takes the form of laws prohibiting someone from being dismissed from his or her job for teaching the alleged controversy about evolution, by which they mean that it's perfectly OK for a so-called science teacher to present creationism, intelligent design and other Bible-in-science-clothing religious doctrines as legitimate alternatives to evolution, even though anyone who does so ought to be fired for incompetence. Don't be fooled: Fundamentalists have no interest in critical thinking. They do not want debates about the truth. Their intention is to replace science with religious doctrine, and I don't mean a choice of religions either. This is all about a very narrow, fundamentalist Christian point of view, one that seeks to replace evidence-based thinking with a blind faith in authority. It is very dangerous, it is not going away and it has to be fought.

And, for those of you in more secular Europe congratulating yourselves on not having this problem, let me point out to you that the American Association for the Advancement of Science ScienceInsider reported on Dec. 9 that Italy's foremost science agency actually funded the publication of a creationist book authored by its own vice president (http://bit.ly/8NADZF). Entitled "Evolutionism: The Decline of an Hypothesis," the book was funded by the Italian National Research Council (CNR) and authored by Roberto de Mattei, a professor of the history of Christianity and Catholicism at the European University of Rome and, as I said, a vice president of the council. The book is based on the proceedings of a conference on the same topic that was, believe it or not, sponsored by the council in February. Among its creationist claims, the book asserts that fossil-dating methods are wrong and that dinosaurs have been extinct for only 40,000 years. Now, you might think, Italy being a Catholic country, that the Roman Catholic Church was behind this somehow, but you'd be wrong. The fascinating thing about this is that physicist Nicola Cabibbo, president of the Pontifical Academy of Sciences, the group of scientists who advise the Pope, has expressed strong disapproval of CNR funding such a book. "The Catholic Church has accepted the thesis of evolutionism," he points out. All of which suggests to me that we are shooting ourselves in the foot if we make the strident voices of the Richard Dawkinses of the world our spokespeople. We have more in common with sensible people of faith than we sometimes realize, and we need to build bridges to them so we can join against the forces of ignorance.

So, here's to the new year — may it be a damn sight better than the old one. And may we all be healthier, happier and living in a more peaceful, more rational world when it's over.

More Bang for the Buck

BY KYLE M. BROWN

Even as the president and Congress make overtures about the importance of greater investment in science, federal agencies are under increasing pressure to make the most efficient use of the funds they are given. Bruce Alberts, editor-in-chief of Science Magazine, and others say that traditional funding mechanisms have created a peer-review culture that funds conservative and incremental science (1). In response, federal agencies, nonprofits and private enterprises are developing new ways to fund creative, innovative and breakthrough-oriented science. But will they create more scientific "bang" for our buck?

Identifying Innovative Projects

Traditional science funding is project oriented. Proposals historically have required detailed descriptions of specific methods and preliminary data. Peer-review panels traditionally have chosen proposals that may be the best science but are also most likely to succeed. Many policymakers and scientists say that approach has created a culture adverse to the risk-taking necessary for innovative research.

In response, federal agencies recently have re-evaluated their grant-review procedures to make the process more innovation-friendly. For example, the National Institutes of Health recently changed its grant application form, reducing its length and requiring less preliminary data and fewer specific research methods (2). Further, the National Science Foundation has adopted the language of innovation into every grant review it facilitates. Since 2008, the NSF has used a definition of so-called "transformative" research to instruct reviewers in identifying research on the scientific cutting edge (3).

But, the NIH and the NSF have gone even further and created project-based funding mechanisms that attempt to specifically fund innovative research. For example, the NIH's Exceptional, Unconventional Research Enabling Knowledge Acceleration (EUREKA) Awards "target investigators who are testing novel, unconventional hypotheses or are pursuing major methodological and

technical challenges" (4). Demonstrating that it, too, will fund yet-untested ideas, the NSF has created the Early-concept Grants for Exploratory Research (EAGER) to support potentially transformative ideas or approaches in the absence of preliminary data (5).

Other agencies in the U.S. defense and energy departments are specifically tasked with funding innovative research projects. The Defense Advanced Research Projects Agency is famous for supporting efforts that led to the development of the stealth fighter and the Internet (6). The Department of Energy's Advanced Research Projects Agency-Energy, ARPA-E, is modeled after DARPA and aims to fund "nimble, creative inventive approaches to transform the global energy landscape" (7).

"People, Not Projects"

While federal agencies rely on project-based grants to fund the vast majority of research, some private foundations have developed different philosophies. By funding "people, not projects," Howard Hughes Medical Institute believes that scientists will be able to "capitalize on a flash of insight that occurs at three in the morning," Gerald M. Rubin, vice president of the institute, said in recent testimony before the U.S. House of Representatives' Committee on Science and Technology (8). The institute's investigator program provides multiyear funding to individuals who will creatively push the boundaries of science, working at the frontiers of their chosen fields. With funding that is not tied to any specific project or proposal, the institute hopes to give investigators the "ability to move quickly to take advantage of unforeseen targets of opportunity," Rubin said.

Following that model, the Pew Scholars Program in the Biomedical Sciences provides funding for early-stage investigators. Each year, between 15 and 20 early-career faculty members are chosen to receive the four-year awards. While freed from the constraints of presenting extensive amounts of preliminary data, investigators must demonstrate creative, innovative, risky approaches and ideas (9).

Even the NIH is experimenting with this approach. In 2010, it awarded seven Pioneer Awards to investigators who proposed pioneering and transformative approaches that could have an unusually high impact on a broad range of biomedicine (10). Additionally, the NIH Director's New Innovator Award is tasked with "stimulating highly innovative research and supporting promising

House and Senate Negotiators Agree on 2010 Science Budgets

U.S. House and Senate negotiators have agreed on the 2010 budgets for several large scientific agencies, including the National Institutes of Health and the National Science Foundation. While traditionally passed in separate appropriations bills, the NIH and NSF budgets will become part of a large omnibus bill, combining six appropriations bills into one piece of legislation.

While Congress and the president previously had passed five of the 12 bills that traditionally fund the federal government for 2010, the budgets for the NIH and the NSF and 85 percent of federally funded life science research had yet to be finalized. With the publication of the conference committee's report, the House and Senate have paved to way for final passage by both houses of Congress.

According the report, the NIH will be funded at $30.72 billion for 2010. Adding an additional $692 million to the NIH budget, this 2.3 percent funding increase from the previous year is a compromise between the 3.14 percent and 1.47 percent proposed by the House and Senate, respectively.

The NSF will receive a larger relative boost. Negotiators have agreed to increase the NSF budget by 6.7 percent to more than $6.9 billion. The bill's summary also supports the president's initiative to double the funding for basic research at "key agencies," such as the NSF, in 10 years.

Perhaps the most dramatic increase was given to the U.S. Department of Veterans Affairs Medical and Prosthetics Research program. This program's budget will grow by 13 percent in 2010 to a total of $581 million.

UPDATE: The House and Senate have passed the Consolidated Appropriations Act of 2010, the large omnibus spending bill that includes budgets for the NIH, NSF and U.S. Department of Veterans Affairs Medical and Prosthetics Research program. The final budgets reflect the agreements reached by House and Senate negotiators in early December. The House passed the appropriations act on Dec. 10 and the Senate passed the bill on Dec. 13. President Obama signed the science funding bills in mid-December.

new investigators" by funding early-career faculty who may lack preliminary data (11).

Innovation Prizes

Popular in the private sector, innovation prizes soon may fund federal science research. These competitions award large cash prizes to teams that successfully complete predefined tasks. Previously, awards have inspired scientists and engineers to measure a ship's latitude accurately, fly across the Atlantic Ocean and even develop better algorithms for predicting how much someone is going to enjoy a movie based on their Netflix movie preferences (12, 13). Now, the U.S. House of Representatives is encouraging the NSF to explore innovation prizes as a possible catalyst for scientific innovation (14).

Impact Uncertain

With so many new mechanisms for funding innovative research, it is difficult to determine which will prove the best. More time and more research will be needed to assess whether these novel mechanisms are fostering high rates of breakthrough science. But, by carefully comparing them and other programs, we should soon know the outcome of our nation's innovation experiment.

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

FOOTNOTES

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Highlights from the Policy Blotter

The American Society for Biochemistry and Molecular Biology Policy Blotter blog posts regular news and commentary about current science policy issues. Below are some recent highlights. You can read them and other posts at http://asbmbpolicy.asbmb.org.

- **A Lesson From Nobel Laureates: Basic Science Requires Federal Dollars**
  (http://wp.me/pFLHF-27)
  President Obama's recent visit with the 11 American 2009 Nobel Prize laureates underscores the importance of federal funding for basic science.
- **An Ongoing Conversation: Women In Science**
  (http://wp.me/pFLHF-2c)
  Several nonprofits, blogs and federal agencies recently have released publications about women in science, and some have surprising takes on the issue.
- **NIH, Collins Announce Approval of Stem-Cell Lines**
  (http://wp.me/pFLHF-23)
  The National Institutes of Health has approved the use of 13 lines of stem cells under a new policy that will expand dramatically the resources available for regenerative biomedical research.
- **"Growing Pains" for Evolution**
  (http://wp.me/pFLHF-1W)
  Actor Kirk Cameron has teamed up with a creationist group to promote a version of Darwin's "Origin of the Species" with a creationist introduction.

FASEB Opposes Great Ape Protection Act

BY CARRIE D. WOLINETZ

The Federation of American Societies for Experimental Biology is leading opposition to the Great Ape Protection Act (H.R. 1326), a bill that would end all invasive research on great apes, including chimpanzees, gorillas, bonobos, orangutans and gibbons. (Note: Gibbons are not technically great apes, but they are defined as such in the legislation.)

In a letter sent to all members of the U.S. House of Representatives, FASEB, along with other scientific organizations, patient-advocacy groups and research institutions, expressed concern that the bill would "harm medical research that helps both humans and great apes." The legislation was reintroduced in the 111th Congress after failing to gain support in the previous Congress and has rapidly gained more than 100 co-sponsors. Passage of the legislation is considered a high priority by a number of animal-rights groups, including the Humane Society of the United States and the Physicians Committee for Responsible Medicine.

The joint letter of opposition emphasizes "that the research community is strongly committed to ensuring that the highest quality of humane care is maintained for all animals used in research, that animals are housed and maintained under conditions appropriate to their species and that research involves only the minimum number of animals required to obtain valid results."

Unfortunately, if the Great Ape Protection Act is passed, it could halt a number of ongoing biomedical research studies, particularly on hepatitis C, for which chimpanzees are currently the only existing animal model. "Chimpanzees are a unique and invaluable resource for ethically conducted biomedical research, particularly translational research through which scientific discoveries are advanced into treatments and cures," the letter continues. Chimpanzees serve as models in studies investigating malaria, human cytomegalovirus, rotavirus, norovirus, respiratory syncytial virus, prion diseases and monoclonal antibody development, among others. Under the existing research system, chimpanzees no longer used in research are not euthanized; rather, they are humanely maintained in retirement facilities until their natural deaths.

The Great Ape Protection Act has a broad definition of "invasive research," including "any research that may cause death, bodily injury, pain, distress, fear, injury or trauma." This includes testing of any drug or other substances, research that would involve restraining, tranquilizing or anesthetizing the animal, removal of the animal from its social group or taking tissue samples, including blood, outside of necessary veterinary care. FASEB is concerned that this broad definition could not only have a negative impact on biomedical research on human diseases but also research that is designed to benefit the great apes themselves, such as the development of an Ebola virus vaccine for wild chimps or the treatment of heart disease in captive gorillas. This also could limit relatively noninvasive work, such as genomic or cell culture studies, which require tissue collection.

In addition to the joint letter, FASEB has been working with its member societies and scientists to educate policymakers about the potential consequences for research under the bill, as well as raising awareness about the multiple legal and regulatory protections that exist for animals used in research, particularly nonhuman primates. The Great Ape Protection Act has been referred to the House Energy and Commerce Committee, which has not held hearings on the subject and is currently quite busy dealing with health-care reform legislation. A companion bill has not yet been introduced in the Senate.

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

For more information:

- FASEB's joint letter to the House of Representatives concerning the Great Ape Protection Act can be found at http://bit.ly/6aPRSc.
- If you would like more information on this legislation and its status, contact Carrie D. Wolinetz at cwolinetz@faseb.org or 301-634-7650.

JBC: A Call for Papers and a Modest Course Adjustment

BY ROBERT D. SIMONI

The Journal of Biological Chemistry was founded in 1905 with the principle that the journal would publish work on the "chemical side" of any biomedical discipline. While the fields have evolved over the past 100 years, this guiding principle applies as well today as it did when the journal was founded.

The co-founders of the JBC, the first editor, John Abel, and chief financial supporter Christian Herter, wrote to many prominent "biochemists" announcing the purpose of the new journal: "We are willing to publish anything of a chemical nature in the whole field of biology whether this touches the plant or animal kingdom." This broad statement of purpose has evolved into the recently recast JBC mission statement: "The Journal of Biological Chemistry publishes papers based on original research that make novel and important contributions to understanding the molecular and cellular basis of biological processes."

The JBC has defined "anything of a chemical nature" as work that provides clear "mechanistic insight" into any biological process. In this age of expanding interdisciplinary research, a great number of exciting molecular and cellular biology studies are being carried out in neuroscience, developmental biology, cell biology, medical science, biophysics, immunology, microbiology, physiology, etc. We wish to emphasize that we consider "mechanism" to mean "the molecular process through which biological processes are carried out" and that much of the research in these areas would be very welcome in the JBC.

Upon submission to the JBC, an author's work receives broad, fair consideration with timely and constructive reviews. JBC has one of the fastest turnaround times from submission to first decision: 22 days. And, if the work is judged to be novel, important, of broad interest and technically sound, it will be accepted and published in the JBC, an icon among scientific journals. The time from acceptance to publication is one day!

In our ongoing effort to improve our service to the research community, changes recently have been made with respect to how papers are submitted, reviewed and published:

- The Table of Contents headings now reflect all areas of biology that can be studied at molecular and cellular levels to emphasize that we welcome submissions from the entire range of modern biological research.
- Articles now may be listed under more than one Table of Contents heading, in keeping with the increasingly interdisciplinary nature of biological research.
- The submission fee for articles has been discontinued to hold down costs to authors and simplify the submission process.
- The JBC Web site, www.jbc.org, has been updated with many new features to better serve readers and authors.

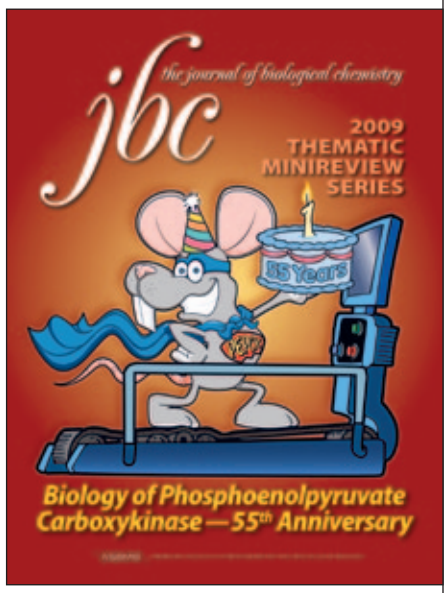
We thank you for making the Journal of Biological Chemistry one of the most highly cited journals in the world. With your support, JBC will continue to publish original research articles that make "novel and important contributions to understanding the molecular and cellular basis of biological processes" for the next 100 years. This is our mission of service.

Robert D. Simoni is a professor at the department of biology at Stanford University. He is also deputy editor of the Journal of Biological Chemistry. He can be reached atrsimoni@asbmb.org.

JBC Wishes PEPCK a Happy Anniversary!

Thematic collection honors 55 years of PEPCK research

BY NICK ZAGORSKI



Over the past 55 years, many important studies on the enzymology, genetics and metabolic role of phosphoenolpyruvate carboxykinase (GTP) (also known as PEPCK) have graced the pages of the Journal of Biological Chemistry. Whether it's the original trilogy of articles from 1954 by Merton F. Utter describing the purification and preliminary characterization of the mitochondrial form of PEPCK (then referred to as oxalacetic carboxylase) or Richard W. Hanson's widely read 2007 article detailing the metabolic effects of overexpressing the cytosolic form of PEPCK in mouse skeletal muscle, JBC always has published cutting-edge research on the important enzyme.

Perhaps fittingly, then, the journal has decided to mark the 55th anniversary of the publication of Utter's articles with a special PEPCK compendium that combines both research and review articles.

On the research side, the collection features the seminal article by Utter and Kiyoshi Kurahashi describing the purified enzyme, along with 10 other articles that have appeared in the JBC in the past decade.

The recent articles cover a variety of biological areas, including the regulation of PEPCK transcription by factors such as glucocorticoids, functional insights gained from recent structural analysis and the evolving story of the enzyme's metabolic role in vertebrates.

The compendium also contains three minireview articles published in the JBC in October. The first, by Gerald M. Carlson and Todd Holyoak, provides insight into the reaction mechanism of PEPCK. Despite the efforts of many dedicated researchers, the mechanism of PEPCK has remained elusive over the years, but recent high-resolution structures of the enzyme from a variety of organisms have revealed details about the reaction's reversibility and nucleotide specificity.

That new information has clarified the metabolic role of PEPCK, a topic covered in the second minireview by Jianqi Yang, Satish C. Kalhan and Hanson. Rather than being involved exclusively in gluconeogenesis as originally thought, PEPCK plays a broader role in cataplerosis, the process of removing anions from the citric acid cycle. Thus, PEPCK has a role in four metabolic pathways: gluconeogenesis, glyceroneogenesis, serine synthesis and the conversion of amino acid carbon skeletons to pyruvate for subsequent oxidation in the citric acid cycle.

The third minireview, by Jianqi Yang, Lea Reshef, Hanoch Cassuto, Gabriela Aleman and Hanson, discusses transcription control of the gene for the cytosolic form of PEPCK. The authors note the emerging importance of histone modification as a key regulator of tissue-specific PEPCK-C transcription and also highlight the insights that may be gained from a critical analysis of the PEPCK-C gene promoter across an evolutionary range of species.

Hanson, who in addition to contributing to the minireview series helped coordinate the JBC compendium, notes that, despite 55 years of research on the mechanisms, metabolism and molecular biology of PEPCK, many gaps in our knowledge still remain. However, he said he is confident that research on the fascinating enzyme shows no signs of slowing down, and he's looking forward to celebrating many more PEPCK anniversaries in the future.

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

For more information:

The PEPCK 55th anniversary collection can be found at www.jbc.org/site/thematics/pepck, where it is also available for print purchase.

Retrospective: Mildred Cohn (1913–2009)

Mildred Cohn, the first female president of the American Society for Biochemistry and Molecular Biology and the first woman appointed to the Journal of Biological Chemistry editorial board, passed away on Oct. 12 at age 96. Information on Cohn's life and pioneering work in nuclear magnetic resonance can be found in an article, titled "Mildred Cohn: Isotopic and Spectroscopic Trailblazer," in the September 2009 issue of ASBMB Today. Below are reflections by her friends and colleagues.

Mildred Cohn was one of the great figures of 20th century biochemistry/biophysics. She influenced several generations of scientists with her brilliant use of physical methods to probe the structures and functions of proteins. She was also one of my scientific heroes. She wasn't very tall, but if, as Robert Browning said, the best way to measure someone is by the length of the shadow that his or her mind casts, then Mildred Cohn was a giant.

Gregory A. Petsko
Gyula and Katica Tauber professor
of biochemistry and chemistry
Brandeis University

Mildred didn't have very many graduate students, and I was her last. It was 1976. Mildred distinctly told me that I could do a rotation but that she was no longer taking students. A fellowship allowed me to persist, and, one or two papers later, she officially accepted me as her student. At first, I was intimidated and couldn't bring myself to call her "Mildred" like everyone else did. She was only slightly younger than my grandmother, and it just didn't seem right to call someone of her generation by his or her first name!

When Mildred was elected the first female president of the American Society of Biological Chemists (now ASBMB), I don't recall there being any great fuss about that honor in the lab. She did, however, include me in the presidential festivities at the annual meeting. While I was a student, Mildred also was honored in a fete thrown by members of the chemistry department at Penn. But it is not the honors that stand out. Mostly, I recall the extreme pleasure of spending hours in her long, narrow and windowless office bouncing around ideas about methods and mechanisms. Mildred's questions were piercing, and it was quite an education to learn to expect them. She was a fabulous mentor. By example, she taught both scientific integrity and generosity. Mildred also insisted that I earn first authorship on our papers by writing them myself.

Later, in my role as a student, I also got the pleasure of house-sitting for Mildred and Henry in Penn Valley. There, I came to appreciate that in her professional life she was Mildred Cohn, but in her personal life was Mildred Primakoff. In fact, when editing our papers, she would sometimes call my writing girlish, meaning not succinct, and sign her comments "MCP." It was an era when "male chauvinist pig" was a common phrase, and Mrs. Primakoff enjoyed the irony of her initials!

When I was no longer a student, Mildred became a friend. After Henry's death, I remember helping her hang pictures after she moved into her apartment overlooking Rittenhouse Square. Before Henry got sick, Mildred used to occasionally talk about what they would do together in their retirement. In recent years, Mildred became a theater buddy. We enjoyed countless hours in the theater, and the meals before or after were always filled with rich conversation — sometimes science, often personal.

I will miss Mildred. I will miss seeing the family photographs grow in size. I will miss hearing about the accomplishments of children and grandchildren and the arrival of great-grandchildren. I was fortunate to have become Mildred's student when I was young and to have had her as part of my life for so many decades. I knew Mildred as a great woman, a great scientist, a great mentor and as a great friend.

Eileen K. Jaffe
Professor
Fox Chase Cancer Center

As Mildred Cohn's first postdoctoral fellow, I was deeply saddened by her death. Mildred was a perfect mentor, inspiring by example, and was understanding and supportive of my ventures into mechanistic chemistry, tolerant of my idiosyncrasies and corrective of my errors. As an independent investigator, I long continued to rely on Mildred for sound scientific and administrative advice.

I am consoled by the fact that Mildred led a long, productive and mostly healthy life, reaching 96 years. I take great pride in my association with Mildred and by the fact that, as a medical doctor, I continued to annoy her about her smoking until she stopped at age 50, which may well have contributed to her long life.

Albert S. Mildvan
Professor emeritus of biological chemistry and chemistry
Johns Hopkins University School of Medicine

It is a pleasure to remember Mildred Cohn as a friend and scientist. Her pioneering use of oxygen-18 for probing enzymatic reactions of phosphate compounds served as a basis for my later investigations. She cordially shared her knowledge of methodology and readily participated in discussions of mutual interest. Much of what I and my colleagues were able to accomplish was made possible by her contributions.

Paul D. Boyer
Emeritus professor of chemistry
University of California, Los Angeles

Mildred Cohn was a brilliant, nationally and internationally respected scientist who was a wonderful role model for her fellow scientists, especially for women. In her quiet way, she broke glass ceilings and was an innovative leader in her field. She was one of a handful of scientists who attended the ASBMB 50th anniversary celebration in 1956 and the 100th anniversary celebration in 2006. At the centennial celebration, at the age of 93, she gave a priceless presentation, highlighting her career at the female scientists' reception. The presentation captured her resilience and clarity.

Judith S. Bond
Professor and chair biochemistry and molecular biology
The Pennsylvania State University

I first met Mildred Cohn at the International Society of Magnetic Resonance meeting in Israel in 1971. I was an associate professor of physics at the Indian Institute of Technology in Kanpur. My expertise was in nuclear spin relaxation in liquids. I was fascinated by the possibility of applying this technique to investigate some biological problems. At one of the conference lunches, I serendipitously ended up sitting next to Mildred and her husband, Henry Primakoff. During the lunch, I sought Mildred's advice about my desire to apply NMR expertise to biological problems, considering my unfamiliarity with biology. She said that it is possible to overcome the barrier with some effort and stressed the importance of collaborating with biochemists who can identify significant questions to answer. She mentioned that she knew of physicists who used sophisticated methods to study trivial biological problems. This discussion was at the back of my mind when I wrote to her in 1972 about coming to her lab to explore my goal. She arranged a visiting scientist position for me, and, thus, a pivotal turn in my professional career occurred.

I started working in her group in December 1973. During the first six months, I was clueless as to how I could carve a niche for myself in this new field. Fortunately, Mildred knew how to communicate with and utilize the strengths of a physicist, and before long some significant results emerged.

I developed a warm personal relationship with Mildred. Her rich experience in science, and her marriage to Henry, an illustrious physicist, made Mildred a source of fascinating and entertaining anecdotes about science and scientists. She also had an excellent memory and was a most interesting raconteur. I enjoyed listening to, and being inspired by, many stories during my stay at Penn. I had the distinct pleasure of visiting Mildred at her home in Philadelphia this past August. We spent an hour and a half chatting about many matters of mutual interest. She was in fine fettle, and it was a joy to see every bit of the raconteur I admired and loved so much. Her passing away leaves an irreplaceable void for me.

B. D. Nageswara Rao
Professor of physics
Indiana University-Purdue University Indianapolis

In Memory of Mildred

Mildred Cohn's children have set up a Gmail account where friends and colleagues can post their memories for Mildred's family to collect. To contribute, send your recollections to memoriesofmildred@gmail.com.

Donations can be made to the Mildred Cohn Fund at The American Committee for The Weizmann Institute of Science, 633 Third Avenue, New York, NY 10017.

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Retrospective: Richard I. Gumport (1937–2009)

BY ROBERT L. SWITZER

The international biochemical community has lost a valued colleague with the death of Richard I. (Dick) Gumport in Chicago on Oct. 13. Gumport devoted his research career to the study of enzymes that act on nucleic acid substrates and to the characterization of biologically important protein-nucleic acid interactions. Moreover, he contributed generously to his profession through his service as a journal editor, as an educator and administrator and through his commitment to the promotion of international scientific cooperation.

Born in Pocatello, Idaho, on June 23, 1937, Dick Gumport worked his way through the University of Chicago with a variety of jobs and received a Bachelor of Science in general biology in 1960. His lifelong commitment to nucleic acids and the enzymes that catalyze their reactions can be traced to his doctoral studies on RNA polymerase, completed in 1968 at the University of Chicago with Samuel B. Weiss. The commitment was strengthened and broadened by Dick's subsequent research as a National Institutes of Health postdoctoral fellow with I. Robert Lehman at Stanford University from 1968 to 1971. With Lehman, he identified a covalent intermediate in the DNA ligase reaction, namely an adenylyl moiety derived from the NAD^+ (or ATP, depending on the source of the enzyme) substrate linked to an active site lysine residue as a phosphoramide. Dick often cited his experiences in the Stanford biochemistry department as inspiration for his ideal of an academic department as a close-knit community of collaborating scholars.

Dick joined the faculty of the biochemistry department at the University of Illinois at Urbana-Champaign in 1971 and spent his entire career there. He was the first full-time faculty member in the fledging Urbana campus of the University of Illinois College of Medicine, and he devoted much energy to the biochemical education of medical students and to administrative service to the medical school. At Illinois, Dick's research initially centered on phage T4 RNA ligase. In collaboration with Olke C. Uhlenbeck, he demonstrated that RNA ligase could be used to join oligoribonucleotides, and he developed this method as a valuable tool for synthesis of RNA oligomers of defined sequence. Subsequently, Dick extended the use of RNA ligase to the joining of oligodeoxyribonucleotides, which was widely adopted in DNA synthetic chemistry. Recognizing the extraordinary value of DNA oligomers of known sequence as research tools, Dick became one of the pioneers in adapting newly developing methods of chemical synthesis of DNA oligomers, which could then be joined to form larger oligomers using RNA ligase. DNA oligomers prepared in Dick's lab were used in pioneering studies with techniques that are now universally used: site-directed mutagenesis, primers for sequencing, templates for in vitro synthesis of RNA and mapping the specificity of protein-nucleic acid interactions. Often, Dick gave his oligomers to other researchers with no expectation of co-authorship.

Dick and Jeffrey Gardner, his colleague in Illinois' microbiology department, conducted a productive collaboration for more than 20 years. They investigated the mechanism of site-specific recombination in bacteriophage lambda via characterization of integrase, integration host factor (IHF) and Xis and FIS interactions with DNA and the roles of these interactions in the regulation of the directionality of recombination and in forming nucleoprotein complexes. They also collaborated on research on the mechanism of transcription attenuation in regulation of the Escherichia coli threonine biosynthetic operon.

Dick's interest in DNA synthesis led him to develop methods for the incorporation of base analogues into syn-

thetic oligomers for use in detailed characterization of DNA recognition by proteins, both in collaboration with others and in his own laboratory. He conducted an extensive program of research into DNA recognition by the EcoRI and RsrI restriction endonucleases and methyltransferases, a group of four proteins chosen because they all bind to the same DNA sequence but catalyze different reactions and have little amino acid sequence homology. His studies provided valuable insight into the details of DNA recognition by these enzymes.

As is clear from this description, Dick Gumport believed strongly in research collaboration rather than competition. He was devoted to the highest standards of research integrity and effective education, and he gave abundantly of his time in support of those ideals. He served as associate head of the department of biochemistry at Illinois for 12 years and as acting head for one year, and he was associate dean of the University of Illinois College of Medicine, Urbana campus, from 2002 to 2007. Dick generously devoted his efforts to the work of several American Society for Biochemistry and Molecular Biology committees and served for 10 years on the Journal of Biological Chemistry editorial board. An avid traveler, Dick enthusiastically supported international cooperation in biochemistry. He was among the American biochemists who traveled to China after the end of the Cultural Revolution as part of the China-United States Biochemistry and Molecular Biology Examination Administration (CUSBEA) program in 1984 and in many subsequent years. He formed scientific collaborations with biochemists in Russia, Finland and Turkey. Dick was honored by the award of a Guggenheim Fellowship in1979 and election as a fellow of the American Academy of Arts and Sciences in 2001.

No retrospective of Dick Gumport's life and career would be complete without remembering his wonderful sense of humor. It provided a sense of perspective and made him a delightful colleague. "Academic politics are so vicious," he'd say, "because the stakes are so small." His e-mail messages closed with a quote from Mark Twain: "There is something fascinating about science. One gets such wholesale returns of conjecture out of such trifling investments of fact."

Below are reflections from his friends and colleagues.

Dick embodied the ideals of the true intellectual university professor. He was a citizen of the world with an insatiable curiosity, rock-solid integrity and a clear eye for reality filtered by a sense of humor that would have made Mark Twain envious. He was a mentor to many and showed us all how to live according to strong and honest values. He leaves an incredible void, and we miss him profoundly.

Bradford Schwartz
Dean of the Urbana campus
University of Illinois College of Medicine

Knowing Dick for more than 30 years both as a colleague in the restriction enzyme field and as an executive editor of Nucleic Acids Research, I grew to respect and admire him greatly. He combined the professionalism of a journal editor and scientist with the fun-loving exuberance of a committed researcher. I cannot remember a dull moment when Dick and his wife, Bobbie, were around. Laughter and friendship (plus a little alcohol) were the order of the day. He was very much a scientist's scientist, who set a marvelous example of how to live and love life both in and out of the laboratory. I miss him greatly.

Richard J. Roberts
New England Biolabs

Dick and I arrived as rookie assistant professors from West Coast postdocs in the fall of 1971. Since we shared long hair, an abhorrence of neckties and an interest in nucleic acids, it was perhaps inevitable that we became firm friends and collaborators. Dick first suggested that the newly discovered T4 RNA ligase could solve my difficulties in making RNAs of defined sequence and then took the lead in making T4 infected cells, purifying and assaying the enzyme. By the summer of 1973, we had successfully shown that the enzyme could join two RNA fragments, and the resulting paper got us tenure and launched our careers. Dick was a joy to collaborate with — optimistic, careful, funny, hard working and thoughtful. Above all, you could trust Dick. Looking back, Dick not only taught me how to work with enzymes, but he provided an environment that made doing science fun.

Olke C. Uhlenbeck
Professor and chairman
Department of biochemistry, molecular biology and cell biology
Northwestern University

Dick and I had a wonderful scientific collaboration that lasted 25 years. I was trained as a geneticist, but Dick's knowledge and background in nucleic acid-binding proteins gave me an appreciation for the power of biochemical approaches to problems.

Two of Dick's most prominent characteristics were his wit and wonderful sense of humor. I remember a particularly long group meeting, where it seemed that no progress had been made in one of our projects. Dick took

out the fountain pen he always carried and wrote me a note. I thought he was going to suggest that we end the meeting. When I read the note it said: "This is why the university pays us these fantastic salaries."

Jeffrey F. Gardner
Professor of microbiology
University of Illinois at
Urbana-Champaign

Dick had a wonderful, quirky sense of humor, and he peppered the lab with absurd pictures and sayings. Over the sink was a drawing of a snail, titled "The Pace of Research." As a graduate student in his lab, I thought that it was just a funny cartoon. However, I came to understand that it represented what made Dick such an outstanding scientist and effective mentor. He taught us that, to do science right, you must be careful and methodical — in technique, of course, but especially in your reading of the literature and design of the experiment. However, what made Dick so special was that this rigor was coupled with an unusually kind and generous spirit. He considered every scientist, from undergraduate student to seasoned primary investigator, to be a colleague. I feel exceptionally privileged to have had him as my thesis mentor.

Deborah Hinton
Chief, gene expression
and regulation section
Laboratory of molecular
and cellular biology
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health

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Mildred Cohn Retrospective

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My interactions with Mildred date back to the 1970s when I became a postdoc in the laboratory of Ernie Rose at Fox Chase Cancer Center. She was very cordial, intellectually stimulating and already a legend, making her a bit intimidating for me at the beginning of my career. Our interactions became much more personal when I found myself on the verge of divorcing and becoming a single parent. Mildred stepped in, had me to dinner at her home, and more or less took me under her wing. This friendship/mentorship was to endure for many decades, through Mildred's sabbatical to Berkeley and the decades that followed.

Our interests in stable isotopes and their use in reaction mechanisms and enzymology were one thing that drew us together. A second was the never-easily-answered question of how to raise a family and be active in science. Mildred will always be my heroine in this regard. Lastly, there was the bond of two women who became friends and cared about each other. I have one particularly fond memory of introducing Mildred, who was visiting her family in California, to my mother who had moved to California. My mother insisted that we make cookies together, and I don't think Mildred liked being ordered around by my mother in the kitchen at all. Both Mildred and my mom are now gone, and I can only smile broadly when I think about this moment.

I am deeply saddened by the loss of Mildred. She was truly a grand lady — in every way.

Judith Klinman
Professor of molecular and cell biology
University of California, Berkeley

In 1960, when Mildred Cohn and Henry Primakoff were contemplating moving to the University of Pennsylvania because Henry had been offered a great professorship in physics, Mildred approached Lucile Smith and I (we were the only two female faculty members in what was then the Johnson Foundation for Medical Physics) to ask how we felt women were treated at Penn. Lucile had moved to Dartmouth Medical School and had not been happy with her experiences at Penn. However, I responded that, although the director, Britton Chance, was a tough taskmaster, he was equally fair to both women and men. When the chairman of the department of biochemistry (Samuel Gurin) indicated he did not want a female faculty member in his department, Brit was delighted to welcome Mildred to his faculty.

Helen C. Davies
Professor of microbiology
University of Pennsylvania
School of Medicine

Russell Wins the Avanti Award in Lipids

BY ANGELA HOPP AND NICK ZAGORSKI

The 2010 Avanti Award in Lipids, which recognizes outstanding research contributions in the area of lipid research, has been awarded to David W. Russell, the Eugene McDermott distinguished chair of molecular genetics at the University of Texas Southwestern Medical Center at Dallas.

Russell will present an award lecture, titled "Oxysterols: Cholesterol Metabolites of Diverse Function in Mice and Men," at 2:15 p.m. Sunday, April 25, at the 2010 annual meeting in Anaheim, Calif.

Russell received his bachelor's degree in biology from the University of Texas at Austin in 1975 and a doctorate in chemistry from the University of North Carolina in 1980, where he studied in the laboratory of Linda Spremulli. He then moved on to the University of British Columbia as a Damon Runyon Cancer Research Foundation postdoctoral fellow, working with Nobel laureate Michael Smith before joining the faculty at UT-Southwestern in 1982.

Shortly after arriving at UT-Southwestern, Russell began a collaborative effort with another pair of Nobel laureates, Michael S. Brown and Joseph L. Goldstein. Together, the trio successfully cloned the gene for the recently-purified low-density lipoprotein receptor and characterized the receptor's functional domains, which helped them elucidate the molecular basis of familial hypercholesterolemia, one of the most common human genetic disorders.

After that, Russell decided to move away from the cholesterol receptor and focus more on the cholesterol itself. Over the next several years, Russell emerged as a scientific leader in elucidating the enzymatic pathways responsible for the metabolic breakdown of cholesterol into other components, such as sterol hormones, vitamins and bile acids. Through a combination of basic biochemical studies and genetic analyses knocking out individual genes involved in cholesterol metabolism, Russell's laboratory has determined the precise role of each enzyme in the cholesterol degradation pathway.

Russell also has revealed important aspects of the regulation of this cholesterol breakdown and identified the genes responsible for several diseases characterized by abnormal cholesterol and lipid metabolism. And, he identified 24-hydroxylase as the enzyme responsible for most cholesterol turnover in the brain and recently demonstrated that 24-hydroxylase deficiency is linked to defects in memory and learning. The biochemical underpinnings of this connection are currently a strong focus of his lab's efforts.

"David has an uncanny insight into biochemical processes and seems always able to come up with a critical experiment to test a novel finding," says colleague Edward A. Dennis, distinguished professor of chemistry, biochemistry and pharmacology at the University of California, San Diego. "His current work on the metabolic role of oxysterols will clearly lead to new science."

"In addition, as part of the LIPID MAPS Consortium, I have had an opportunity to work closely with David and watch firsthand as he developed a complex lipidomics analysis of the sterol category of lipids," Dennis adds. "From carefully designed systems biology approaches, he made insightful conclusions and knew exactly how to follow up with imaginative experiments to probe the depths of what underlie his observations."

The 2010 Avanti Award in Lipids will add to a long and impressive list of honors Russell has received for his studies on lipid metabolism and cholesterol breakdown. He has been awarded the American Heart Association Louis N. Katz Award, the Texas Instruments Kirby Science Place Award, the Endocrine Society Ernst Oppenheimer Award and the Falk Foundation Adolph Windaus Prize, among others. He also was elected to the National Academy of Sciences in 2006.

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Wells Receives ASBMB-Merck Award

BY ANGELA HOPP AND NICK ZAGORSKI

James A. Wells, professor and chairman of the department of pharmaceutical chemistry at the University of California, San Francisco, and director of UCSF's small molecule discovery center, has been named the winner of the 2010 American Society for Biochemistry and Molecular Biology-Merck Award for his pioneering studies in the field of protein engineering.

Wells, who also serves on the ASBMB Council, will present an award lecture, titled "Probing and Controlling Cellular Remodeling Enzymes," at 2:15 p.m. Monday, April 26, at the 2010 annual meeting in Anaheim, Calif.

Wells integrates multiple disciplines, including biophysics, cell biology, chemical biology, molecular biology, enzymology and proteomics, to design small molecules and proteins that can selectively activate or inhibit cellular processes, such as differentiation and apoptosis. Through those efforts, Wells hopes to better understand how signaling events drive responses, such as cell growth and death, and perhaps discover new drugs to treat diseases like cancer.

Along the way, Wells has developed numerous innovative methodologies to improve protein engineering, molecular screening and pharmaceutical chemistry, including a disulfide-based protein-trapping technology, substrate-assisted catalysis and N-terminomics.

"[Wells] is an exciting and highly creative scientist," noted Ian A. Wilson, professor of structural biology at The Scripps Research Institute, "and these methods that he has pioneered have been invaluable to countless researchers in a multitude of fields."

"His unbridled enthusiasm is infectious and ensures his lab is fully regaled with a plethora of ideas," Wilson continued, "so they can unleash their individual talents to further progress drug discovery, biochemical mechanisms, protein function and understanding of key cellular events that impact human health."

Wells' impressive expertise in protein engineering stems from a long and renowned career in the pharmaceutical industry. Before joining UCSF, Wells spent nearly two decades at Genentech Inc., where he was a founding scientist of its protein engineering department. During his time there, Wells produced several key scientific breakthroughs. For example, his group's work with the protease subtilisin was one of the first instances of scientifically improving upon evolution and nature, as they designed a subtilisin enzyme that was more stable to oxidation, heat and alkali (paving the way for its industrial use in laundry detergents and other household products).

Later, in 1998, Wells founded and served as president and chief scientific officer of Sunesis Pharmaceuticals and helped invent a novel drug-discovery platform called Tethering, which efficiently screens molecules to identify the most potent compounds that block specific protein action.

Prior to that, Wells received his bachelor's degree in biochemistry from the University of California, Berkeley, in 1973 and his doctorate in biochemistry from Washington State University in 1979 (working with Ralph Yount). He also took on postdoctoral fellowships at both Washington State University and the Stanford University School of Medicine before joining Genentech in 1982.

"Over his career, Wells has made enormous contributions to our understanding of enzyme mechanisms, allostery, protein plasticity, protein-protein interfaces, small molecule discovery, hormone receptor signaling, molecular recognition, protease signaling and apoptosis," said Molecular and Cellular Proteomics co-editor Alma Burlingame, who is also a professor of chemistry and pharmaceutical chemistry at UCSF. "Not only has his science led to fundamental discoveries, it also produced new products in both the industrial enzyme and pharmaceutical sectors."

The ASBMB-Merck Award, presented annually, recognizes outstanding research contributions in the fields of biochemistry and molecular biology.

See the December 2008 issue of ASBMB Today to read an ASBMB Roundtable discussion with Wells on improving the global health system.

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Keller Garners Avanti Young Investigator Award

BY ANGELA HOPP AND NICK ZAGORSKI

Sarah L. Keller, a professor of chemistry and adjunct professor of physics at the University of Washington, has been named the winner of the 2010 Avanti Young Investigator Award in Lipid Research for her innovative and cutting-edge studies on membrane lipids.

As part of this award, established by American Society for Biochemistry and Molecular Biology's Lipid Research Division, Keller will present a lecture, titled "Dynamic Domains in Lipid Membranes near a Miscibility Critical Point," at 11:45 a.m. Monday, April 26, at the 2010 annual meeting in Anaheim, Calif.

Keller's interdisciplinary research has been instrumental in revealing how lipid composition affects the physical parameters of cell membranes and how that can lead to changes in membrane protein activity and aggregation. Some of her early studies directly inspired models of protein aggregation within membranes and provided an experimental basis for the theory of membrane lateral pressure.

Keller's interest in this field began with her graduate education at Princeton University, where she studied the interactions between ion channels and lipid membranes. Working with Sol M. Gruner, Keller showed that the conductance state of alamethicin channels changes dramatically when the channels are present in dioleoylphosphatidylethanolamine compared with dioleoylphosphatidylcholine membranes. Those results had far-reaching implications, for at that time there was little evidence for the idea that lipid composition could affect membrane protein activity in the absence of charged lipids, a large change in membrane thickness, a transition to the gel state or direct binding between lipids and proteins.

Since arriving at the University of Washington in 2000, after postdoctoral positions at the University of California, Santa Barbara, and Stanford University, Keller has combined her in-depth knowledge of chemistry and physics to tackle even more daring and ambitious projects related to membrane lipids.

In just a few years, Keller already has provided numerous insights into the formation and diffusion of lipid domains and how lipid composition can alter the activities of lipid domains and membrane proteins in both an intra- and inter-leaflet manner.

"Sarah is fearless in her choice of projects — the tougher the better," noted Keller's postdoctoral adviser, Joseph Zasadzinski, a professor in the department of chemical engineering and engineering materials at UCSB. "She instills a magic sense of confidence in her graduate students that it will all work out in the end. She lets them take credit for the successes, and she will take the blame for the failures. And she does it calmly and with grace."

She presented the first results demonstrating how micron-scale domain formation in membranes varied with cholesterol content and temperature. Later, she showed that lipid domains can be induced from one membrane leaflet to another — a study that counteracted the prevailing hypothesis — and that alterations in the composition of one leaflet could annihilate all domains in the membrane, even when one leaflet would have made domains on its own. Given the fact that the molecular details of how lipids in one leaflet of a membrane could affect lipids in the opposing leaflet were unknown, those exciting findings have opened a brand new area of study.

Many of her colleagues have noted that Keller's thorough analyses and phase diagrams of lipid domains with respect to the surrounding membrane have become the gold standard in the field of membrane research.

They also point out that Keller's excellence extends beyond the laboratory. "Her student evaluations are off the charts, and she has won every teaching award on offer at UW," noted Michael H. Gelb, Harry and Catherine Jaynne Boand endowed professor of chemistry at the University of Washington. "I am confident that, as a result of her inspiring teaching, many of these students will pursue advanced and creative research in the future."

He added, "I have already told her that I want to sit in on her course and see how she does it."

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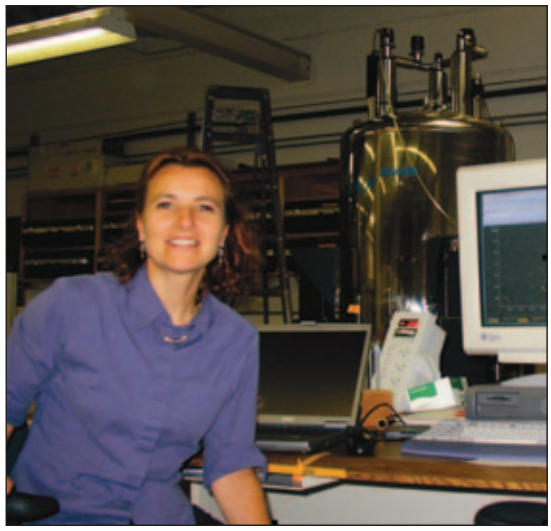
Anne-Frances Miller: Spinning Toward Success

BY NICK ZAGORSKI

Anne-Frances Miller believes enzymes are catalysts extraordinaire. Consider the following: The industrial process used to make the vast quantities of fertilizer necessary to support agriculture worldwide involves exposing nitrogen gas (N_2) to temperatures in excess of 400 degrees Celsius at 200 atmospheres of pressure. This illustrates the difficulty of breaking the triple bond in dinitrogen (second in strength only to that of carbon monoxide). Meanwhile, in the roots of leguminous plants, bacterial enzymes are carrying out the same chemical conversion at room temperature under standard pressure.



Anne-Frances Miller in front of one of her NMR machines.

This is the reason that Miller will never cease to be fascinated by enzymes. "Their ability to speed up chemical reactions by factors of millions, billions or more gives biology access to chemistry that would be useless at uncatalyzed rates," she says.

However, Miller, an associate professor of chemistry at the University of Kentucky and director of the university's nuclear magnetic resonance spectroscopy facility, is quick to point out that proteins should not get all of the glory. "Many of the most marvelous enzymes subcontract out the dirty work," she says. "The most difficult chemistry is actually being executed by metal ions or organic cofactors. What the protein does is help select the proper substrate, focus the reactivity on the desired reaction and coordinate the reaction with other aspects of metabolism."

That partnership between the protein and its cofactor forms the basis of Miller's research interests. Using spectroscopic tools like NMR and electron paramagnetic resonance, which can reveal the details of the molecular interactions occurring at the interface of the protein and cofactor, Miller seeks to understand the mechanistic basis behind enzyme catalysis, particularly oxidation-reduction reactions.

And, by answering questions about, for example, how proteins guide the specificity of broadly reactive cofactors like metal ions or how a flavin's chemical properties change when it becomes associated with a protein, Miller hopes to figure out one of the most enduring mysteries in enzymology: how proteins can both activate and control such powerful chemical reactions.

"Take dioxygen, for example," Miller says. "Molecular oxygen is an extremely reactive molecule thermodynamically, but it also has a large kinetic barrier for activation. This is why it has accumulated to about 20 percent of our atmosphere. Because of that barrier, dioxygen holds a huge reservoir of potential energy."

"Then, look at proteins," she adds. "As reagents, they're pretty mild-mannered — we even eat them for breakfast. How can proteins catalyze reactions with oxygen and not get burned up?"

Across the Border

Such a sense of wonder about the natural world has been a staple of Miller's mindset since her youth in Toronto. She recalls that her scientific awakening occurred around the time she was 13 years old, when her family took her and a friend for a weekend naturalist program on Ontario's Bruce Peninsula. During their hikes, Miller was fascinated by how much information the guides knew about every moss, plant and liverwort they passed, including tidbits such as the plant's habitat range, what chemicals were inside it and how the indigenous people used it.

"I remember one foggy morning walk in particular," she says. "We had heard a squawk in the distance above us, and

one of our guides immediately told us that was a goshawk. That weekend revealed for me just how much information surrounds us, but we don't notice, and so it passes us by. And I keep thinking how much richer our whole experience could be if we paid attention more."

That weekend getaway eventually led to a vigorous pursuit of science projects, both for science fairs and personal curiosity; Miller even dabbled in some plant breeding, which led her to pursue a degree in molecular genetics at the University of Guelph in Ontario, Canada.

Along the way, Miller also began taking physics courses, because she found that most of the biology courses were too descriptive and she was eager to understand science at a deeper level; in fact, by the time she graduated in 1982, Miller was just one course short of a physics major.

At Guelph, Miller also got her first taste of NMR and EPR spectroscopy. "The notion that we could observe signals from single atoms or electrons was just amazing," she says, "and it was a technology I wanted to learn more about."

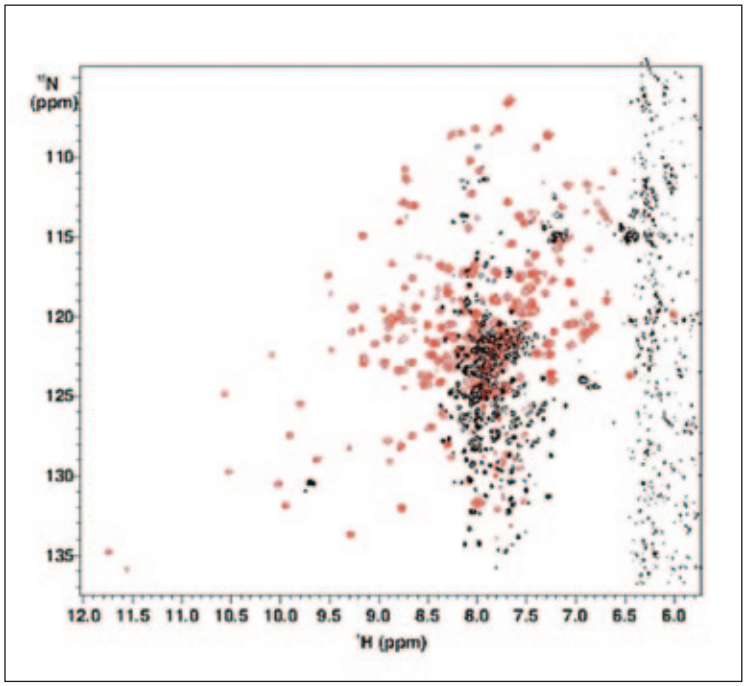
To do that, Miller crossed the border into the United States, following a career trajectory that included graduate studies at Yale University with Gary Brudvig, analyzing the assembly and mechanism of photosystem II, a postdoctoral position with William Orme-Johnson at the Massachusetts Institute of Technology and a second postdoctoral fellowship with Al Redfield at Brandeis University, conducting NMR studies on the conformation changes in the p21-Ras protein that contribute to tumor development. Her first independent appointment was at the Johns Hopkins University in 1992.

Her professional journey was far from a series of seamless transitions. For example, Miller considers her time in graduate school to have been quite rewarding but not entirely successful. "I had two projects that either didn't prove interesting to anyone other than me, or, by the time they worked, someone else had published the result," she admits, adding that she learned valuable lessons about what constitutes good science, and that helped her career immensely later on. "I am enormously grateful to Gary Brudvig for giving me independence so I could learn these important lessons before it was my career on the line. This was especially courageous of him considering that, at the time, his was."

Other events were unforeseen, however, such as Miller having to leave her first postdoctoral position at MIT because her lab ran out of funding, forcing her to scramble to find a new lab to work in. This situation was made more difficult by the facts that her husband had just gotten a job in the Boston area and that Miller wasn't a U.S. citizen and would have to leave the country if she didn't find a U.S. Immigration and Naturalization Service-acceptable position very quickly.

And, while Miller did secure a position at Brandeis, two years later the "two-body problem" became an issue again. After many unsuccessful attempts at finding a suitable destination with her husband, Miller eventually received a job offer she simply could not refuse: assistant professor in the Johns Hopkins University chemistry department.

Although her long-distance "e-marriage" was trying, Miller had a fantastic time at Hopkins. "I had a chance to launch some very exciting studies and to work with fabulous colleagues; I would have loved to have been able to stay permanently." Despite the best efforts by her colleagues, the university couldn't find a way to open up a spot in the physics department for her husband. "After eight years, our family had reached a point where our first child was ready to start school, and we just had to be in the same city."



Overlay of heteronuclear single-quantum coherence spectra of uniformly 15N-labeled nitroreductase, collected at 37 C (red) and 4 C (black) showing a striking loss of dispersion attributable to conformational averaging.

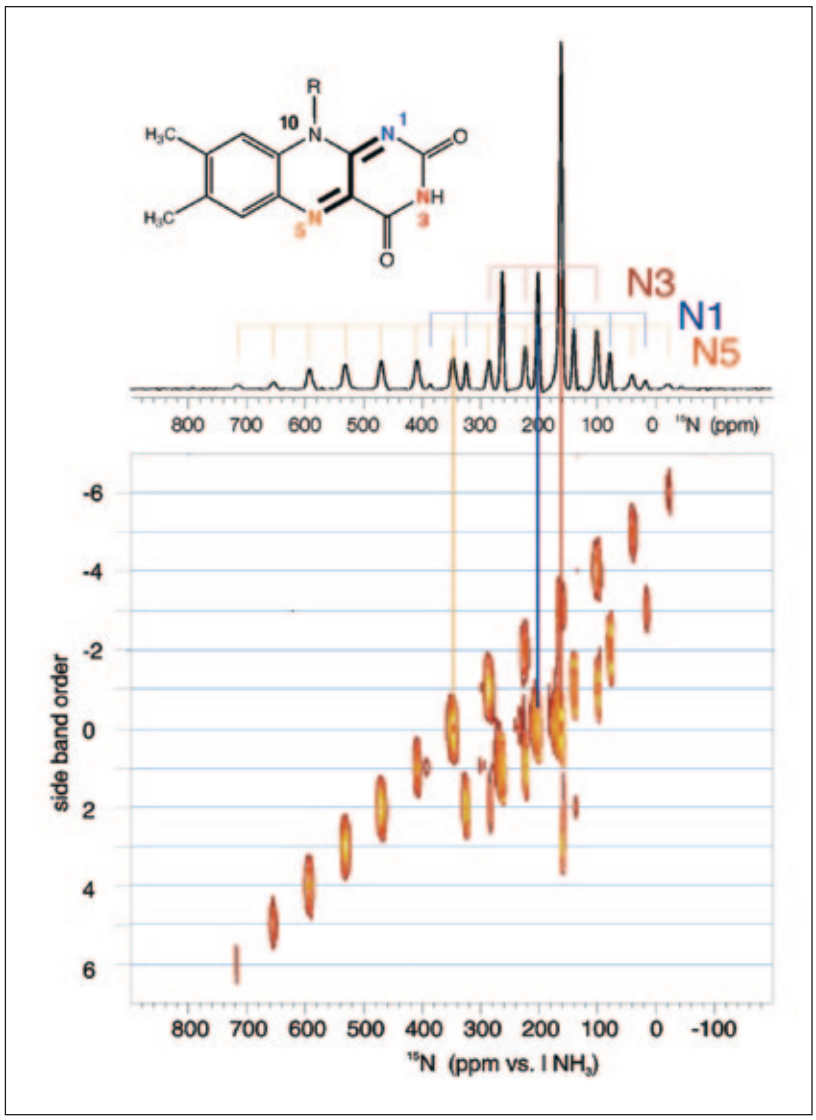
That led Miller to a difficult professional decision — relocating her lab to the University of Kentucky in 1999 so her family could be together.

Heading into Orbit

While the nature of the projects in Miller's group at the University of Kentucky varies to exploit the composition and interests of her lab members, she maintains an overall theme of combining principles of biophysics and spectroscopy to examine protein control over cofactor reactivity.

The lab focuses on two enzyme types: superoxide dismutases and enzymes that use flavins as cofactors. Superoxide dismutases, which metabolize toxic superoxide ions (O_2-), regulate the reactivity of potentially reactive chemical species and are fairly well studied, providing a firm foundation for detailed studies of fundamental questions.

"That is not to say superoxide dismutase has no more new stories to tell, because it certainly has," Miller says, noting some exciting work in which her lab provided the first mechanistic explanation as to why iron- or manganese-containing superoxide dismutases become inactive if their cofactor is exchanged with the opposing ion, even though the three-dimensional structures of the two enzyme types are basically superimposable.



2D PASS solid-state 15-NMR spectrum (bottom) and cross-polarization magic angle spinning 15N solid-state NMR spectrum of tetracetyl riboflavin labeled with 15N at positions N1, N3 and N5. For details, see Koder et al. 2006.

Other recent spectroscopic analysis has revealed insights into how superoxide dismutase controls the movement of the electrons between the active site metal ion and substrate. "Proteins do not have good means of controlling electrons directly," Miller says. "But we found that the big bridge by which superoxide dismutases regulate the sources and destinations of the transferred electrons is the protein's exceptional control over protons, because the protons have a very big influence over where the electrons go."

Miller chose enzymes that use flavins as cofactors as her second interest, because these cofactors, which resemble nucleotides, hearken back to the ancient RNA world and are likely the remnants of the evolutionary ancestors to enzymes. And, as organic molecules, not inorganic metal ions, they have different spectroscopic properties that enable Miller to ask a different set of questions.

Solid-state NMR, which, as implied by the name, examines samples that are solids or frozen solutions, can prevent the molecules under study from moving or reorienting. This allows orientation-dependent properties to be observed in the spectra, and, in Miller's case, allows the three orientationally distinct components of the chemical shift to be resolved.

Miller has looked at the carbon and nitrogen atoms of the flavin ring system to complement solution NMR studies of the surrounding amino acids of the protein. Most importantly, the solid-state NMR results often can distinguish between effects on different orbitals of the flavin, resulting from different interactions between the flavin and the protein. With that information, she hopes to understand how different protein environments cause the bound flavin

to emphasize different reactivities out of its inherently broad repertoire. Meanwhile, solution NMR studies of the surrounding protein address issues such as how some flavoenzymes like nitroreductase have such a broad substrate specificity range.

Beyond these studies, though, Miller is also busy trying to improve on the existing NMR and EPR technologies, so as to give them a broader and more cost-effective appeal.

In discussing her drive to do this, Miller reflects back on when she first came to the U.S. for graduate school. "At the time I left Guelph, there were very few positions available in Canada, as funding for universities was very tight," she says. "My professors not only repaired laboratory equipment themselves, because they couldn't afford to get it serviced, they built the equipment themselves as well."

Considering the perilous nature of today's economy, such memories resurface. "In a time of tightening budgets, there will be questions about the need to continue to run expensive NMR facilities," she says, adding that the cost not only reflects the machines but the cryogens and reagents (like heavy isotopes of carbon and nitrogen) required to produce NMR-quality samples. While NMR holds many advantages as a tool for structure determination, it is weak when it comes to sensitivity because the magnetic moments of nuclei are quite small, thus, requiring large amounts of pure protein in each sample.

Some research groups have begun trying to alleviate the sensitivity problem by combining elements of NMR and EPR technology in a new application known as dynamic nuclear polarization. Rather than directly polarizing (or exciting) nuclear magnetic moments, DNP polarizes electrons first, as they have magnetic moments about 660 times that of the ^{1}H magnetic moment. DNP then transfers that polarization to nearby nuclei. "So in theory," says Miller, "you could have an NMR signal that's 660 times more powerful than usual, which is mind-boggling."

Thanks to a sabbatical she took, Miller, in collaboration with Thorsten Maly and Robert G. Griffin at MIT's magnet lab, has tried to take DNP one step further. "Currently, DNP relies on added free radicals as bearers of the unpaired electrons," she says, "but I realized that biology provides built-in radicals whose unpaired electrons can be used as sources of polarization. Many flavoproteins can be prepared with the flavin in a radical state, and the flavin molecule is bound in exactly the same way in each molecule. So we know where the polarization starts in every instance, in contrast with the random and uncontrolled locations of exogenous radicals." Moreover, the flavin radical is often located in the enzyme's active site.

"So, instead of having to analyze an entire protein, you can take a shortcut and focus your measurements just on the active site," she continues. This "smart" DNP, as Miller refers to it, should make the technique more applicable than ever, as a researcher won't need large quantities of protein or even a pure sample. Only protein molecules containing the flavin would be evident in a DNP-NMR spectrum.

Out of Focus: Language Barrier

While you won't catch more than a hint of a Canadian accent in speaking with Miller these days, she admits to having had occasional communication "challenges" when she first moved from Guelph to New Haven, Conn. This led to one of her more bizarre graduate school experiences. One day, while returning from school, she was approached and accosted by a pair of youths who demanded her bicycle. "Their accent was so strong and foreign to me that I could barely understand them," she says. Add in the fact that she came from a small, quiet college town, and she was not prepared for such a situation. "So rather than run away immediately (and lose my bike), I responded with a polite, if scared, refusal. Then they had trouble comprehending me. After several back-and-forth exchanges in which I can remember thinking I was completely crazy to be insisting on retaining my bicycle and repeating 'I beg your pardon' (because I still could not understand their English), instead of fleeing back up the street, one of them cracked a smile." She says, "This whole conversation was probably the last thing they expected and in retrospect, it really was humorous. Once it had become a joke, they waved me on and I rode off. I would, nonetheless, not recommend this as a general strategy."

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Brian Malow: A Stand-Up Man for Science

BY NICK ZAGORSKI

Fairly or unfairly, the public's perception of science seems to include a series of less-than-flattering words that begin with "S": stodgy, stuffy and serious. But it doesn't have to be that way; science also can be silly.

Brian Malow would wholeheartedly agree with that assessment; in fact, he believes in science's humor potential so much that he's made an unusual career out of it, performing across the country as a "science comedian" for the past decade.

Whether he's giving quick one-liners like "I just started reading 'The Origin of Species;' don't tell me how it ends!" or longer musings about how the constant weight fluctuations between his parents — whenever his mom lost weight, his dad gained weight — was a prime example of the first law of thermodynamics, Malow seamlessly intersperses scientific terminology into jokes about everyday topics, like parents and relationships, that are the staples of comedic routines.

And that little extra science kick, which has given Malow the kind of distinctive niche that every comedian seeks, might be a valuable tool in making the average person more knowledgeable about science.

"After listening to some of my new material, a friend once told me, 'Your jokes contain more information than other comedian's jokes,'" Malow says. This inspired him to begin adding more educational content to his routines – wrapping education in a bit of laughter is a great way to teach people without them knowing it.

At the very least, Malow hopes to inspire more enthusiasm about science during his routines, which have run the gamut from intimate shows at places like Washington, D.C.'s Marian Koshland Science Museum of the National Academies to a nationally televised appearance on the "Late Late Show" with Craig Ferguson.

Although Malow has no professional scientific background, he embraced science early on. Growing up, he loved reading both science fiction and nonfiction, and he was especially influenced by authors like Isaac Asimov and

PHOTO: JOHN GILBEY

Arthur C. Clarke, who could write both types of material with equal skill.

Today, he continues to immerse himself in the latest print and online scientific stories daily, turning his brain into a giant scientific database. Physics and astronomy remain his favorite subjects, but he touches on all types of science in his comedy.

Malow's foray into stand-up was not premeditated. "It's certainly not a career I planned," he says. "My friends thought I was pretty funny, but I was never labeled the class clown in school or anything like that."

While living in Austin, Texas, he was encouraged to participate in a "funniest person in Austin" contest. Although he didn't win, the positive feedback he received convinced him to try comedy.

Over the years, as Malow progressed from working the local comedy-club circuit to becoming a nationally known comedian, he began incorporating more science into his routine. "It proceeded through a natural evolution," he says. "I had all this scientific information in my head, and, as I worked out some comedic material, some weird little fact would pop out that would fit in so well with the joke."

Even so, Malow never really considered himself a "science comedian" until recently, after he started doing more

shows for scientifically savvy audiences. While he tries to keep most of his science content at a level anyone can understand, he found occasional jokes based on obscure scientific references just didn't work for a general audience. However, those same jokes would get big laughs from scientists, giving him a new outlet for his less traditional material.

A nice example is his one-liner: "I'm so spontaneous, I have a negative delta G." Malow notes that joke would pass over the head of most people, but it's a riot among chemists.

Malow really enjoys performing in front of scientific audiences, whether at universities, museums or companies like Apple or Dell. "Nothing is more fun than making scientists laugh. I feel that, if I can bring some levity into their science world, using their science terms, then I've done a great job."

"Now, it does add a layer of difficulty," he notes, "since, unlike other comics, I have to not only be funny but also scientifically accurate. We've probably all heard jokes that make no sense, but, among scientists, if your joke is based on a false premise, then it may fall flat, no matter how funny the punch line is."

So, beyond laughter, Malow likes to scan his scientific audiences to see if anyone is nodding along in with the joke, signaling that the scientific reasoning behind it is sound.

On the plus side, Malow reads about new scientific discoveries every day, so he holds a distinct advantage over other stand-up comedians who talk about their foibles, annoying parents and spouses or other types of observational humor: He never runs out of material.

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

For more information:

- Go to www.asbmb.org/audio.aspx to learn more about Brian Malow in a podcast in which he further discusses what it's like telling jokes to scientists and details some of his recent efforts to improve science awareness and engender enthusiasm.
- You can visit Malow's Web site at http://www.sciencecomedian.com

University of Oregon's Institute of Molecular Biology Celebrates 50 Years

BY CHRIS TACHIBANA

In 1959, the University of Oregon began a daring experiment. Just six years after James Watson and Francis Crick published their paper on the structure of DNA, the university founded its Institute of Molecular Biology, bringing scientists from chemistry, biology and physics together in a common space to work in a new field that combined all three areas.

Fifty years later, the risk-takers who founded and nurtured the enterprise have a lot to be proud of, including generations of scientists who were shaped at and inspired by IMB.

The Early Years under Aaron Novick

At an anniversary celebration this fall, institute Director Bruce Bowerman recalled how chemist Terrell L. Hill conceived the institute in 1957 and recruited its first director, biophysicist Aaron Novick.

Hill met Novick when they were both working on the Manhattan Project, and Novick's time there influenced his career and the institute. Carol Gross, a professor at the University of California, San Francisco, and keynote speaker at the 50th anniversary symposium, was a graduate student with Novick. She said that, because of Novick, "the institute was very political. Having worked on the atom bomb and knowing its aftermath, Aaron was very antinuclear and antiwar." She added that Novick's open, egalitarian attitude set the tone of the institute: "He always ate lunch in the lunchroom so he could participate in discussions [on topics] like: Given rate of protein synthesis, could a spider make silk de novo or did it have to be premade?"

Novick created the nucleus of the IMB by hiring its first members with the help of biochemists John and Charlotte Schellman, who were known for advancing the study of protein structure, folding and stability through techniques such as circular dichroism spectroscopy. Their first hire was Frank W. Stahl, who had just shown, with Matthew Meselson, that DNA is replicated by a semiconservative mechanism. Stahl, now emeritus, continues to focus on the mechanisms of meiotic recombination. In a recent biology department newsletter, he said the institute was founded on three principles: No one would be called "professor" or "doctor," facilities would be shared and new hires would recruit new members.

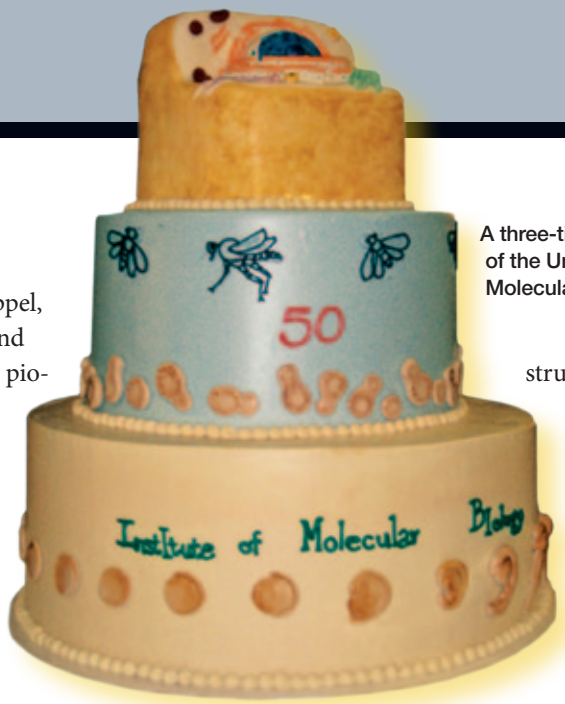
Oregon Makes a Splash with Zebrafish

In keeping with the last principle, in 1960, Stahl recruited phage biologist George Streisinger, whose work illustrates the collaborative, multidisciplinary philosophy of the IMB: Streisinger generated a series of T4 lysozyme mutants that were used by protein biochemists like the Schellmans and Rick Dahlquist and biophysicists like Brian W. Matthews, S. James Remington and Joan Wozniak for studies on protein structure and thermostability.

In the 1970s, Streisinger used his knowledge of aquarium fish to develop the zebrafish as a research model. Zebrafish are small, hardy and easily bred, developing from transparent egg to fish in 24 hours. Streisinger realized that zebrafish could be used as a vertebrate model for studies on development and behavior that had previously used fruit flies. So, he developed techniques for breeding, mutagenizing and screening zebrafish, including generating haploid fish for easy phenotypic analysis. The University of Oregon continues to be internationally recognized for zebrafish research.

Gross pointed out that this project illustrates the value placed on maximizing every individual at the IMB. She described the long process Streisinger went through to find and develop a new model organism and said "He finally hit on zebrafish, and what stuck with me was the time he was given to really think through this transition. All the while, he had the support of everyone around him."

Another major discovery that came from the institute was the first three-dimensional structure of a DNA-binding protein, published in 1982 by Matthews. Steve Kowalczykowski, now a professor at the University of California, Davis, was a postdoctoral fellow with Peter von Hippel. He still remembers the day he saw preliminary data for the Cro repressor structure: "One of Brian Matthews' postdocs showed me how its spacing was perfect to fit into the major groove of the DNA. It was stunning."



A three-tiered cake marks the 50th anniversary of the University of Oregon's Institute of Molecular Biology. CREDIT: JACK LIU.

Von Hippel Reinvents the Institute

In 1967, the institute hired von Hippel, who Bowerman called "the heart and soul of the institute." Von Hippel, a pioneer in the biophysical analysis of DNA transcription and replication complexes, was institute director from 1969 to 1980. Gross did a postdoctoral fellowship with him and said, "[Novick] invented the institute, but Pete reinvented it, bringing a big-science energy and perspective, with more graduate students and bigger labs. He kept all the great things but brought the institute into the next phase."

At the anniversary symposium, Bowerman announced the creation of the Peter von Hippel graduate student endowment, seeded with donations from faculty and alumni (see sidebar). In his spontaneous response, von Hippel praised the IMB for its ability to "evolve with the times and grow," saying, "I'm impressed to look around and see people who have done extremely well, spread out all over the world and are having an impact."

An Interdisciplinary Institute

A primary goal of the IMB is fostering collaboration between scientists with different expertise, and interaction is encouraged in many ways. Kowalczykowski recalls, "We didn't really separate the social and the scientific. Everyone was so accessible. It was such an easygoing place, but that belied the scientific intensity." He remembers having easy access to people like Streisinger, Sidney Bernhard, Stahl, Dahlquist, and the Schellmans. "When the institute was formed," he says, "everyone was all on the same floor and complimented each other fantastically. Decades later, [institutes] were trying to implement programs that were already in place at the IMB. That was the genius of the founders, to fuse biology, chemistry and physics to solve long-standing problems. It's a place that was way ahead of its time."

The institute's multidisciplinary approach inspired Rhett Kovall of the University of Cincinnati, who recalls the openness and community and said that playing on softball teams and interacting with other graduate students definitely influenced his career. Although he was solving protein structures in the Matthews lab, his roommate was studying Caenorhabditis elegans genetics in the Bowerman lab. Now the head of his own research group, Kovall says, "We don't just solve structures, we do a lot of biology, and I think that goes all the way back to my graduate training."

Today, the institute has 23 active faculty members, housed in contiguous facilities in the university's science complex. Everyone has access to proteomics, genomics, DNA sequencing and histology laboratories; electron and confocal microscopes; facilities for biophysical studies, including x-ray crystallography and nuclear magnetic resonance and on-site production of monoclonal antibodies and transgenic mice.

Looking ahead to the next 50 years, and perhaps trend-spotting for molecular biology in general, Matthews, an institute faculty member since 1969 and a former director, said, "At the time that I joined the institute, a major emphasis was on the 'molecular' part of 'molecular biology,' i.e. on the basic structure and function of biomolecules. To some degree, the physics drove the biology. Now the emphasis is more on the 'biology' aspect. I expect this trend to continue. In the future, it will be the biology that will drive the identification of important questions, but techniques from physics will still be a key in solving many of these problems."

Chris Tachibana (chris.tachibana@gmail.com) is a science writer based in Seattle and Copenhagen. She acknowledges Bruce Bowerman and Sarah Cheesman for assistance with the article.

A Tribute to Peter von Hippel

Unveiled at the 50th anniversary celebration for the Institute of Molecular Biology, the Peter von Hippel graduate student endowment fund is "a tribute to von Hippel's generosity and magnanimity, and his many and longstanding contributions to the university and the institute." The endowment will support one graduate student a year, contributing to his or her stipend and tuition expenses beginning in 2010.

If you are interested in making a tax-deductible contribution to the endowment, contact Sarah Cheesman at sec@uoregon.edu or 541-346-0044.

Promoting Diversity in Research

Championing an Inclusive Scientific Work Force

BY SHAWN R. DREW

What is diversity? In the sciences, it's the variety of interdisciplinary fields that we often combine to solve complex biomedical problems; it's the mathematician, biologist, neurologist and physicist working together. Diversity is also an array of human characteristics that differ among us and shape our experiences.

The Problem

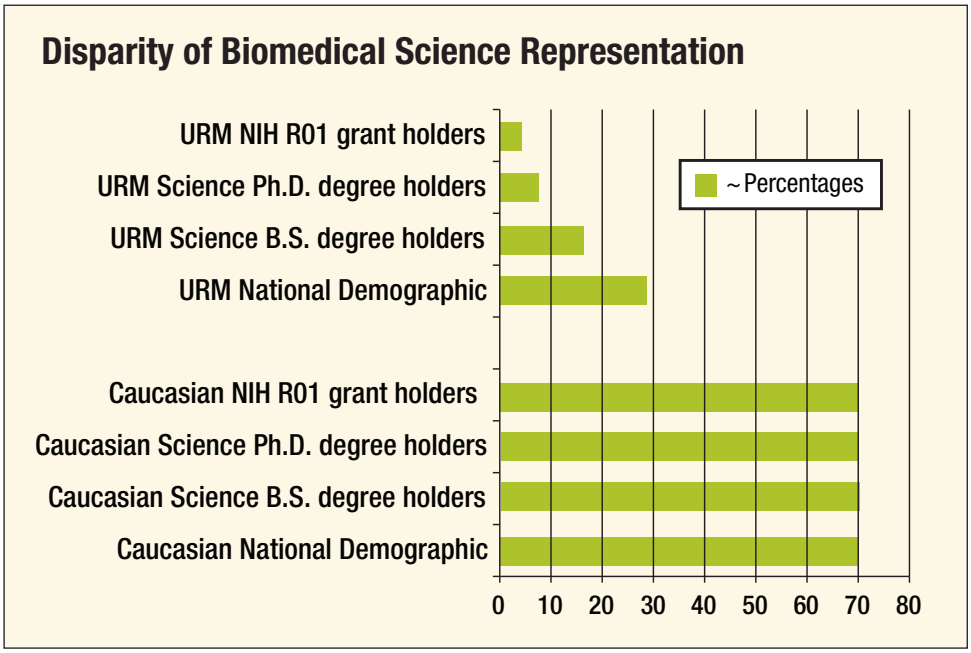
A current problem in today's biomedical work force is the underrepresentation of certain groups — namely minorities (such as African-Americans, American Indians, Alaska Natives, Hispanic/Latino Americans and U.S. Pacific Islanders) and individuals with disabilities.

Figure 1 shows that there is a disparity in the proportion of underrepresented minorities (URMs) versus Caucasians in the sciences. While URMs represent approximately 29 percent of the U.S. demographic, they represent only approximately 4 percent of the National Institutes of Health R01 biomedical research grant holders. This same downward trajectory is not seen with Caucasians, whose representation is at or greater than parity at the noted levels. The underrepresentation in the sciences we see for URMs also holds true for individuals with disabilities: They represent 11 percent of the Bachelor of Science holders but only 1 percent of the population with scientific doctoral degrees.

You might wonder whether it really matters who is doing science as long as good science is being done. It does matter; research shows that diverse teams are better at solving complex problems (1). On homogeneous teams, unquestioned assumptions remain unquestioned, and everyone gets stuck in the same place. If we only listen to people who agree with us, we cease to grow. In the words of writer Walter Lippmann, "Where all men think alike, no one thinks very much."

Representation does not mean mere numbers or even a quota. It means having qualified individuals from various backgrounds, perspectives and influences to strengthen our ability to solve complex scientific problems. In doing this, diversity is not just a feel-good issue or simply the right thing to do; it benefits everyone through improved outcomes.

Additionally, scientific researchers are better able to relate to the general public when the scientific work force



Sources: *U.S. Census Bureau; NIH Office of the Director; National Science Foundation "Women, Minorities and Persons with Disabilities in Science and Engineering Report."*

Note: *Underrepresented minorities (URMs) in the biomedical sciences are African Americans, American Indians and Alaska Natives, Hispanic/Latino Americans and U.S. Pacific Islanders.*

Note: *While Asian Americans make up 4 percent of the U.S. population, they account for close to 14 percent of the scientific work force and are not considered underrepresented in the biomedical sciences in the U.S.*

has adequate minority representation. Remember the Tuskegee syphilis experiment and the 40 years of unethical treatment of African-American men that left a lasting legacy of distrust of the medical/research community? It's that distrust that is an underlying reason why many African-Americans are not organ donors and do not participate in clinical trials. Furthermore, for the majority of this country, the autonomy of the individual in agreeing or disagreeing to participate as a research subject is paramount. But for some communities, especially some American Indian tribes, autonomy of the group outweighs that of an individual. When scientists do not reflect various communities they intend to study, there can be rampant mistrust and/or an underappreciation of certain cultural value systems.

What the NIH Is Doing

To increase the diversity of the scientific work force, the NIH requires all applicants for its predoctoral and postdoctoral institutional research training (T32) grants to submit a plan to recruit and retain individuals from underrepresented groups. At the National Institute of General Medical Sciences, we take a very serious look at these plans and their outcomes. The plans to enhance diversity are first considered by the initial review group, then by the National Advisory General Medical Sciences Council and finally by an administrative staff committee. Applications with unacceptable diversity plans are barred from funding until an updated plan is acceptable, regardless of the priority score.

NIH also provides research supplements to promote diversity in health-related research. Those "diversity supplements" provide funds to an existing NIH research grant to support an underrepresented student or postdoctoral fellow to work in a grantee's lab. Each NIH institute or center, much like academic departments, has different policies or practices for program implementation. At NIGMS, we allow more than one student or postdoctoral fellow per NIGMS grantee for this program. This encourages principal investigators to bring multiple underrepresented participants into their labs. Also unique to NIGMS is that, beyond the college level, we expect PIs to indicate how they will foster the transition of their underrepresented graduate student or postdoctoral fellow over to traditional funds. We think of the diversity supplement program as a hand up, not a handout or entitlement, and we expect our mentors to aid in transitioning their trainees to mainstream training mechanisms.

Online Resources

Information on NIH/NIGMS diversity programs:

- NIH T32 training program: http://bit.ly/4GxEUQ
- Frequently asked questions about NIH T32 required recruitment and retention plan to enhance diversity: http://bit.ly/7AF80m
- NIGMS Research Supplements to Promote Diversity in Health-Related Research: http://bit.ly/6PGZCe
- NIGMS Minority Opportunities in Research Division programs: www.nigms.nih.gov/Minority

Minority-oriented science student conferences:

- Annual Biomedical Research Conference for Minority Students: www.abrcms.org
- Society for the Advancement of Chicanos and Native Americans in Science: www.sacnas.org

Academic institutions with a high concentration of underrepresented students:

- Department of Education: For details on historically black colleges and universities, Hispanic-serving institutions and tribal colleges: www.ed.gov/index.jhtml
- Appalachian College Association: www.acaweb.org
- Gallaudet University (for deaf and hearing impaired undergraduates): www.gallaudet.edu

10 Things You Can Do

There are several ways you can help increase diversity in the biomedical sciences:

1. Take on a leadership role in the diversity debate. You can "lead from below" until the "tone at the top" of your institution is as committed as you are to increasing diversity in the sciences. Organize campuswide discussions on diversity issues.
2. Participate in the NIH diversity supplement program and other underrepresented-student development programs supported by the NIGMS Minority Opportunities in Research Division.
3. Attend national minority-oriented science student conferences, such as the Annual Biomedical Research Conference for Minority Students and the Society for the Advancement of Chicanos and Native Americans in Science meeting, to recruit underrepresented students. More than 2,000 URM students attend each conference

annually to present scientific research. A good way to interact with students is as a judge.

4. Establish partnerships with academic institutions that have high concentrations of underrepresented students. The partnerships can be used to both recruit students to your program and better prepare students for your programs. For example, talk to students and faculty at minority-serving institutions about what it takes to be competitive enough to enter your graduate program.
5. Establish partnerships with local organizations that hold health and science fairs where underrepresented groups are prevalent. These efforts go a long way to help establish trust of the medical research community.
6. Contact the office of disability services on your campus or at your company and ask officials for advice on how to make science more accessible.
7. Google "recruit student disabilities," and tons of useful information will come up to help you reach out to these individuals.
8. Ensure that your Web sites, brochures and other marketing materials have welcoming and inclusive language. Do you include images of people from diverse backgrounds? Instead of saying "Persons with disabilities are welcome to apply," try "People with disabilities are valued members of our institution." In order to reach out to others, look inward and ask questions like: What is our message? Is our program/institution welcoming and accommodating? What is our track record? Who is delivering our message?
9. Update your business cards to include Braille; this is a great way to showcase an inclusionary spirit.
10. Publish your findings on diversity issues. Describe your approaches and conclusions regarding issues of diversity. Web sites like Diverse Issues in Higher Education (http://diverseeducation.com/home.html) or Inside Higher Ed (www.insidehighered.com) are useful sources to accomplish this.

Shawn R. Drew (DrewL@mail.nih.gov) is the Minority Access to Research Careers program director of the Division of Minority Opportunities in Research, program director of the biostatistics training grant program and chairwoman of the Committee to Maximize Representation at NIGMS.

REFERENCE

1. Scott E. Page (2007) *The Difference: How the Power of Diversity Creates Better Groups, Firms, Schools and Societies.* Princeton, NJ and Oxford: Princeton University Press, , pp. 448.

An Opportunity to Make a Difference

BY J. ELLIS BELL

In a recent speech to the National Academy of Sciences, President Obama said, "So I want to persuade you to spend time in the classroom, talking — and showing — young people what it is that your work can mean and what it means to you. Encourage your university to participate in programs to allow students to get a degree in scientific fields and a teaching certificate at the same time. Think about new and creative ways to engage young people in science and engineering, like science festivals, robotics competitions and fairs that encourage young people to create, build and invent — to be makers of things."

The USA Science and Engineering Festival

The USA Science and Engineering Festival offers scientists a great opportunity to answer this clarion call. According to the organizers, "the festival promises to be the ultimate multicultural, multigenerational and multidisciplinary celebration of science in the United States." It will take place between Oct. 10 and Oct. 24, culminating in a two-day expo on the National Mall in Washington, D.C.. The expo will give more than 500 science and engineering organizations from all over the United States the opportunity to present hands-on, fun science activities to inspire the next generation of scientists and engineers.

Festival founder Larry Bock is encouraging the participation of universities, colleges, professional organizations and industry, and, as discussed in the November issue of ASBMB Today, the American Society for Biochemistry and Molecular Biology is committed to participating.

The festival organizers also are inviting scientists and engineers around the nation to host satellite events that can be tied in to the festival's themes. In a time when the scientific community is increasingly being asked to justify the nation's investment in research, and when there is much talk of the U.S. falling behind the world in science education, it behooves each of us to think creatively about how we can effectively educate the general public about science and its benefits and also encourage a diverse section of our K-12 population to get interested in science.

Take the "Science on the Mall Challenge"

ASBMB is also urging everyone to get involved with the festival through the "ASBMB Science on the Mall Challenge." We are asking anyone interested in science, science education or science outreach to design a fun, interactive biochemistry- and/or molecular biology-themed activity to take to the festival.

Entries will be accepted through June 30 and can be submitted by posting them to the ASBMB Facebook fan page (http://bit.ly/4ynmfn) or e-mailing them to uancommittee@asbmb.org or wzhao@asbmb.org.

The submissions will be judged by the ASBMB Undergraduate Affiliate Network Committee, and the best entries will be taken to the USA Science and Engineering Festival. Top finalists who are undergraduates or high school students will receive travel stipends to come to Washington, D.C., to attend the expo.

Get Involved in Outreach

If each ASBMB member agreed to spend just two hours a month in meaningful outreach activities, we could have a major impact on science literacy and the pipeline of future scientists.

So, the challenge to all ASBMB members is this: Find two hours a month and get involved in outreach activities. Over the next six to eight months, we will track member outreach activities and post updates on our Web site. Send an e-mail to wzhao@asbmb.org to tell us about your outreach activities.

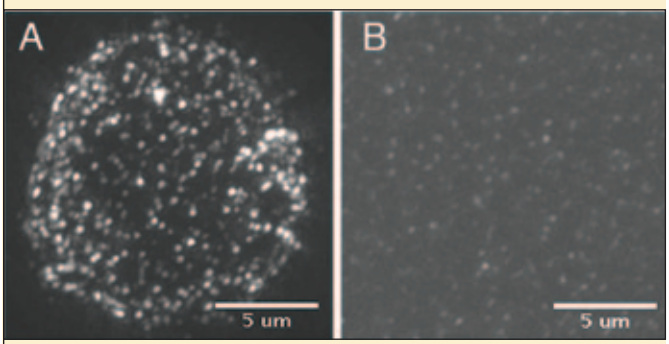
J. Ellis Bell (jbell2@richmond.edu) is professor of chemistry and chair of the biochemistry and molecular biology program at the University of Richmond. He is also chairman of the ASBMB Education and Professional Development Committee.

For more information:

- To learn more about the USA Science & Engineering Festival, go to http://usasciencefestival.org.
- For more information on the ASBMB Science on the Mall Challenge, go to http://bit.ly/5RD7Jg.

For Talin, It's Avidity Not Affinity

The protein talin can bind to the cytoplasmic tail regions of β3 integrins and regulate the activity of αIIbβ3 integrins. Talin itself is autoregulated – its integrin-binding globular head region can be inhibited by binding to the talin C-terminal tail. Interestingly, while overexpression of the talin head domain increases integrin activity in mammalian cells, such effects are not seen in Drosophila, suggesting talin-integrin interactions may be different in those organisms. However, in this paper, the author shows that the discrepancies are due to differences in methodologies. Using a Drosophila-based assay that employs only monovalent ligands (where one ligand binds to one integrin receptor), the author found that talin had no effect on the affinity of αIIbβ3 integrins for ligand in Chinese hamster ovary (CHO) cells or human platelets. Talin did increase the ability of integrins to bind to multivalent ligands that can interact with more than one receptor, but this was due to increased integrin clustering and not affinity. This study helps reconcile the experimental differences and also suggests a new model by which talin regulates integrin activity.



PAC-1 IgM binding to CHO cells is clustered.

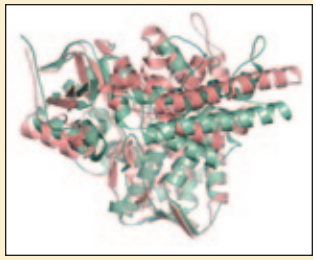
Integrin αIIbβ3 Activation in CHO Cells and Platelets Increases Clustering Not Affinity

Thomas A. Bunch

J. Biol. Chem., published online Nov. 16, 2009

jbc

Don't Sleep on This Structure



Ligand-free trypanosomal 14α-demethylase (salmon) superposed with the related mycobacterial CYP51 (green).

Current treatments for trypanosome diseases like sleeping sickness often lack specificity and have severe side effects. Thus, newer, better drug targets are needed. Trypanosomal sterol 14α-demethylase (14DM), an essential enzyme in the production of membrane sterols, is a highly promising lead, as its fungal counterpart is a major drug target for treating fungal infections in humans. In this study, the authors solved 1.9 Å resolution crystal structures of 14DM from Trypanosoma brucei in both a native state and in a complex with the inhibitor VN1. Together, they provide the first structural insights into a eukaryotic microsomal 14DM. The structures show that the organization of the active site cavity and the location of the substrate access channel differ profoundly in 14DM compared with water-soluble members of the CYP51 family. VN1 binding does not cause large-scale conformational rearrangements, but it does induce local changes in the active site, including the formation of a hydrogen bond network connecting VN1 and two distant and functionally essential protein segments. The structural details of VN1 binding provides a possible explanation for both its selectivity toward trypanosomal 14DM and its potency, and it should provide an excellent template for designing novel parasite-specific drugs.

Crystal Structures of Trypanosoma brucei Sterol 14 alpha-demethylase and Implications for Selective Treatment of Human Infections

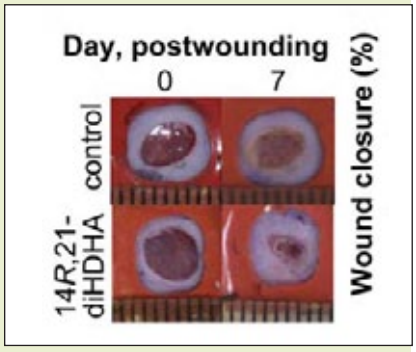
Galina I. Lepesheva, Hee-Won Park, Tatiana Y. Hargrove, Benoit Vanhollebeke, Zdzislaw Wawrzak, Joel M. Harp, Munirathinam Sundaramoorthy, W. David Nes, Etienne Pays, Minu Chaudhuri, Fernando Villalta and Michael R. Waterman

J. Biol. Chem., published online Nov. 18, 2009

jbc

Enhancing Wound Healing

Successful wound healing involves the coordination of multiple physiological processes, such as inflammation, cell migration, angiogenesis, formation of granulation tissue and tissue remodeling. A better understanding of the molecular mechanisms behind these processes may provide insight into developing improved wound healing therapies. In this study, the researchers found that cutaneous wounds induced the formation of novel endogenous dihydroxy-docosahexaenoic acid species (14S,21S-diHDHA,14R,21R-diHDHA, 14S,21R-diHDHA and/or 14R,21S-diHDHA). Using mass-spectrometry analysis, they detailed the structures of those novel compounds and the pathways of their formation from DHA by 12-lipoxygenase and cytochrome P450, enzymes found in both the skin and macrophages. Importantly, administration of 14S,21-diHDHA and 14R,21-diHDHA to induced wounds in mice enhanced wound closure, growth of granulation tissue growth and vascular formation. These newly identified 14,21-diHDHA stereoisomers may represent the molecular basis for the healing properties of macrophages and, given their abundance in the skin, may provide an ideal target for developing novel wound-healing therapeutic modalities.



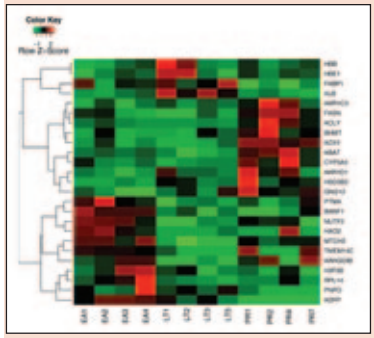
Representative photographs highlighting how 14,21-diHDHA treatment can accelerate wound closure.

Novel 14,21-dihydroxy-docosahexaenoic Acids: Structures, Formation Pathways, and Enhancement of Wound Healing

Yan Lu, Haibin Tian and Song Hong

J. Lipid Res., published online Nov. 5, 2009

Hibernation Is Quite Active



Heat map of the 25 most differentially expressed proteins during the hibernation cycle; EA, early arousal; LT, late torpor; PR, post-reproduction.

Mammalian hibernation is a complex process involving large-scale reorganization of metabolic and other pathways. In this study, the researchers constructed a database of more than 3,000 liver proteins from arctic ground squirrels (Urocitellus parryii) and then used label-free shotgun proteomics to analyze changes in protein expression throughout the torpor/arousal hibernation cycle. Consistent with previous studies measuring mRNA changes, proteins involved in glycolysis and fatty-acid synthesis were significantly underexpressed in both late-torpid and early-aroused squirrels compared with nonhibernating animals, while proteins involved in fatty acid catabolism were significantly overexpressed. However, in other cases, the protein and mRNA data did not entirely mesh; for example, proteins involved in translation, protein degradation, mRNA processing and oxidative phosphorylation were overexpressed in early-aroused animals compared with late-torpid animals, whereas no significant changes in mRNA levels between those stages had been observed. The discrepancies suggest substantial post-transcriptional regulation of proteins occurs during hibernation.

Shotgun Proteomic Analysis of Hibernating Arctic Ground Squirrels

Chunxuan Shao, Yuting Liu, Hongqiang Ruan, Ying Li, Haifang Wang, Franziska Kohl, Anna V. Goropashnaya, Vadim B. Fedorov, Rong Zeng, Brian M. Barnes and Jun Yan

Mol. Cell. Proteomics, published online Nov. 20, 2009

Taking the Path Less Traveled

BY CLIFFORD MINTZ

I always have liked science, and, by the age of 10, I decided that I wanted to be a veterinarian. However, after seeing the film "Ben Hur" — in which two characters who have leprosy are miraculously cured – at age 11, I fantasized about what it would be like to discover cures for infectious diseases. As corny as it may sound, the movie convinced me that my true calling in life wasn't veterinary medicine but microbiology. Nonetheless, I enrolled at Cornell University as a preveterinary medicine undergraduate with a dual major in animal science and microbiology. During my senior year at Cornell, Brooks Naylor, my food microbiology professor, invited me to do a senior research project in his laboratory. After several weeks in the laboratory, I was hooked, and I knew that graduate school, not veterinary school, was in my future.

I entered graduate school in 1974 and did my thesis research in Robert Deibel's laboratory in the department of bacteriology at the University of Wisconsin-Madison. I studied the pathogenesis of Salmonella gastroenteritis. Because Deibel was chairman of the department and a food microbiology consultant, he wasn't around much. This forced me to become a self-reliant independent investigator very early in my scientific career. When I started graduate school, my goal was to earn a doctoral degree and teach microbiology at a small liberal arts college. However, after three years at Wisconsin, I decided to eschew a career as a science educator in favor of becoming a tenure-track faculty member at a prestigious research institution.

I received my doctoral degree in 1981and chose to do a postdoctoral fellowship with Stephen Morse in the department of microbiology at Oregon Health and Science University. There, I investigated the pathogenesis of Neisseria gonorrhoeae. After two years in Morse's lab, I realized that the field of molecular biology finally had taken off and that I would need to develop molecular biological skills to compete for my coveted tenure-track faculty position. With this in mind, I joined Howard Shuman's laboratory in 1984 as a postdoctoral fellow in the department of microbiology at the College of Physicians and Surgeons at Columbia University. My work in Shuman's laboratory looked at the molecular pathogenesis of Legionella pneumophila, the causative agent of Legionnaires' disease.

In 1987, my newly acquired molecular biology training and respectable publication record helped me to land a tenure-track faculty position in the department of microbiology at the Leonard M. Miller School of Medicine at the University of Miami. I spent the next seven years feverishly doing laboratory research, teaching medical and graduate students, publishing papers and writing grants to establish an independent research program on the role of lipopolysaccharide in the molecular pathogenesis of L. pneumophila. While I was a productive researcher who regularly published work and was recognized on several occasions for teaching excellence, I failed to consistently win grant support to run my labora-

Clifford S. Mintz has held a variety of positions, including stints as a medical school professor, professional recruiter, management consultant and medical/science writer. He is the founder of BioInsights (www.bioinsights.com), a biopharmaceutical education and training organization, co-founder of BioCrowd (www.biocrowd.com), a social networking and career development Web site for bioprofessionals, and the author of BioJobBlog (www.biojobblog.com). He teaches product development and regulatory affairs in several biotechnology training programs and is an adjunct professor in the department of biochemistry and molecular biology at the Georgetown University School of Medicine.

tory. Consequently, in 1994, I was denied tenure and forced to leave academia — an emotionally devastating event that that ended a lifelong dream of becoming a world-class research scientist.

Luckily, at that time, the U.S. biotechnology industry finally had hit its stride, and I landed a job as a scientist at a New Jersey-based biotechnology company managing an antibacterial drug-discovery program. My two years in industry provided me with a firm understanding of the business side of science and, perhaps more importantly, convinced me that industrial research wasn't for me. This, coupled with a desire to teach again, prompted me to successfully apply for a job as chairman of biology at a local community college. It was a good idea at the time, but I quickly realized that, while I still loved to teach, administration wasn't my strong suit. I left the community college job after a year.

Unfortunately, by 1998 I effectively had exhausted most traditional career options for scientists with doctoral degrees, and I desperately needed a job — mainly because I had a wife and three young children to support. Fortunately, while working at the community college, I helped several professional recruiters place new hires into jobs at biotechnology and pharmaceutical companies; this prompted me to seriously consider professional recruiting as a career option. In early 1999, I landed a job as a recruiter at a local recruiting firm. As a new hire, I had to attend recruiter school for six weeks. Surprisingly, this training played a pivotal role in subsequent decisions that helped shape my career.

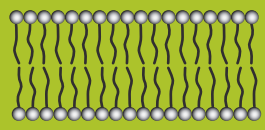
After three years as a successful professional recruiter, an Australian biotechnology company hired me as a science and business consultant to help guide its antibacterial drug-discovery program. The new job led to an almost four-year stint as an independent management consultant advising private and publicly traded biotechnology companies on business, scientific and financial matters. Also around this time, I decided to indulge my own entrepreneurial fantasies: In 2001, I founded a bioscience education and training company called BioInsights Inc. Two years later, Abraham Abuchowski and I founded Prolong Pharmaceuticals — a drug-delivery company with two drugs in early stage clinical development. Unfortunately, the rigorous demands of running BioInsights and starting Prolong ultimately led to the demise of my consulting practice, and, by 2004 I was forced to consider another career move.

"I was denied tenure and forced to leave academia — an emotionally devastating event that ended a lifelong dream of becoming a world-class research scientist."

Luckily, a few years earlier, I had started writing for several biotechnology industry trade publications. Although I wasn't getting paid to write, the job enabled me to hone and polish my writing skills. In late 2004, a medical communications expert whom I knew suggested that I take a stab at medical writing. At the time, I didn't know much about medical writing, but I quickly learned that it pays well and that medical writers are always in demand. I took her advice and landed my first medical writing job in 2005. Since then, I have worked at a variety of medical communications agencies and pharmaceutical companies preparing manuscripts, posters, slide presentations and other documents. Currently, I am a freelance science and medical writer, a blogger at biojobblog.com and a social media enthusiast who, along with Vincent Racaniello, started an online social network site for bio-scientists called BioCrowd (www.biocrowd.com).

Unlike many scientists, my career path has taken several unexpected twists and turns. I never intended it to be as eclectic or convoluted as it has been. Nevertheless, I believe that my unusual career trajectory has made me a better-rounded scientist than I would have been if I had been able to pursue my intended academic career. In retrospect, I attribute my career successes to solid problem-solving skills, an unrelenting desire to continue to learn and an unwavering ability to take risks.

Finally, and perhaps most importantly, I learned that there is no right or wrong career path in the life sciences — only the path that you choose for yourself!



Enzyme Aliases and Acronyms: What's in a Name?*

BY GEORGE M. CARMAN AND DANIEL M. RABEN

It's not unusual to be listening to a seminar or reading or reviewing a paper or grant and feeling overwhelmed and confused by the aliases and acronyms used for enzymes. These enzyme identifiers seem to be increasing almost as rapidly as the number of papers published each year. Confusion often results from the fact that these names frequently bear no relationship to the actual activity or function of their enzyme. For example, how many people know the names of the enzymes represented by the aliases autotaxin, desnutrin, lipin, neuropathy target esterase, PatA/VipD, PTEN, SHIP2 and wunen? It's pretty common to find a lipid scientist who doesn't know that the common enzyme names for these aliases are lysophospholipase D, triacylglycerol lipase, phosphatidic acid phosphatase, phospholipase B, lysophospholipase A, phosphatidylinositol-3-phosphate phosphatase, phosphatidylinositol-3,4,5-trisphosphate phosphatase and lipid phosphate phosphatase, respectively. If lipid scientists don't know what these aliases refer to, then how do we expect the general reader who is not a lipid aficionado to know?

There are a number of reasons why this practice got started. In many cases, the molecular function of a protein is unknown when it is discovered, and an alias is given based on a mutant phenotype or disease. In other cases, an investigator chooses a name, often with the admirable goal of making it easy to remember. No matter what the cause, rectifying this would go a long way to enhancing our ability to stimulate the enthusiasm and imagination of our colleagues.

Perhaps it would reduce confusion and increase clarity in the field at large if we changed the names of these enzymes to ones that reflect their activities. This, however, may not be straightforward. The names of most enzymes are derived from their substrates, products and the reactions they catalyze. Thus, many enzymes have a variety of names. For example, phosphatidate phosphatase 2, diacylglycerol pyrophosphate phosphatase and lipid phosphate phosphatase all refer to the same enzyme. Another problem is when an enzyme is more promiscuous than its name implies. For example, stearoyl-CoA desaturase implies the enzyme desaturates stearoyl (C18)-CoA. However, actually, the enzyme desaturates all acyl-CoA substrates from C14 to C20.

So how can we effectively and efficiently resolve this issue? Simply retaining the initial names of enzymes after their catalytic function is identified only perpetuates confusion in the literature. On the other hand, it is difficult to rename enzymes without upsetting the people who coined the aliases and acronyms, especially when those identifiers were established before the enzymatic functions of the proteins were known. For aliases, one solution is to refer to the enzyme activity followed by the alias in parenthesis or vice versa. The enzyme activity could be named according to standards set by the International Union of Biochemistry with emphasis on the thermodynamically favored reaction catalyzed. Similarly, acronyms should always be defined, especially when they are used in titles and abstracts. Whatever the solution, this may help to make lipid research more easily read and digested. In doing so, we will go a long way in conveying the excitement of lipid research.

> **"If lipid scientists don't know what these aliases refer to, then how do we expect the general reader who is not a lipid aficionado to know?"**

George M. Carman (carman@aesop.rutgers.edu) is a professor in the department of food science at Rutgers University. Daniel M. Raben (draben@jhmi.edu) is a professor of biological chemistry at the Johns Hopkins University School of Medicine.

FOOTNOTE

* This article was written in response to a discussion in the forum on the Web site for the American Society for Biochemistry and Molecular Biology's Lipid Research Division (www.asbmb.org/lipidcorner).

2010 ASBMB Annual Meeting

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How to Publish in the JBC Workshop
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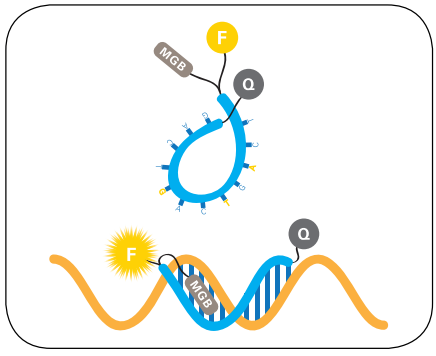

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