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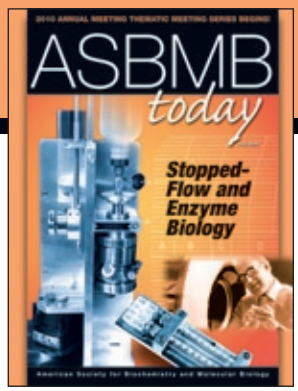

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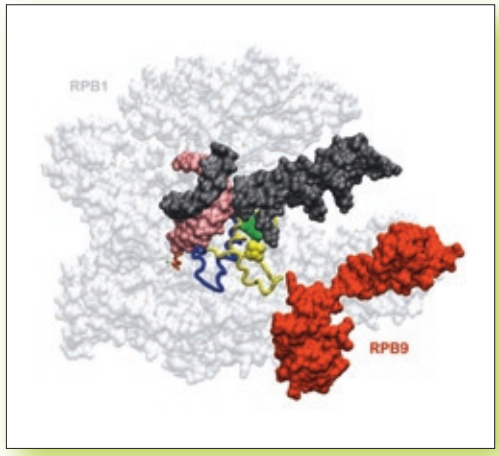

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ASBMB today

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2008 APEX AWARDS FOR PUBLICATION EXCELLENCE

letters to the editor

History Repeats Itself in Big Pharma

Dear Greg,

As always, I enjoyed your President's Message in the May 2009 issue of *ASBMB Today*. I agree with most of your points, although not all of them. I have been pointing out for almost a decade that what has been happening to big Pharma in the past decade seems to be similar to what happened to General Motors, Chrysler, and Ford about 40 years ago. The big three automakers went from making the best cars in the world to selling us whatever they could make. So it is with big Pharma. They have gone from inventing and developing the best drugs in the world to companies that sell you whatever they can make. Their business plan is to sell drugs. Look at their corporate statements, what they spend their money on, who is on their boards, and who their CEOs are. Compare this with the same information from 30 years ago. Are they too big to succeed now? I hope it will change as we try to address the serious problems in our healthcare system.

By the way, a similar phenomenon is happening in universities, especially public universities. (You are sheltered in a private university.) Education is a commodity; the presidents of our universities are primarily salesmen (hucksters, if you wish); tuition is rising in a similar manner to drug prices, at two to four times inflation; and university administrators' salaries are rising at about the same rate. Meanwhile, faculty raises are hardly keeping up with inflation, and tenured faculty to student ratios are increasing every year. Even in our local school districts, 15 percent of our teachers were given pink slips. ("It's the economy! We have no choice!") The "social model" you so decry in your message is everywhere. I don't see anyone, not even President Obama, who is going to change it, though I do hope he will try.

Maybe it's the U. S. A. that is too big to succeed. We will soon find out.

My best wishes,
Victor J. Hruby
University of Arizona, Tucson, AZ

Render unto Darwin*

BY GREG PETSKO

You probably haven't encountered a website for something called BioLogos. If you have, you will undoubtedly already have formed a strong opinion about it—it's that kind of site. If you haven't, you really ought to check it out (www.biologos.org). It's the website for something called the BioLogos Foundation. According to its mission statement, "The BioLogos Foundation promotes the search for truth in both the natural and spiritual realms, seeking harmony between these different perspectives." The foundation was established by Francis Collins with a grant from the John Templeton Foundation, a much older organization with a similar mission. And that, apart from its intrinsic interest, is why you should check it out and why I'm wagering you will have strong opinions when you do. Francis Collins is the scientist who headed the publicly funded Human Genome Sequencing Project in the 1990s. Until last August he was the head of the National Human Genome Institute at NIH, which continues that work and funds much of the genome biology in the United States. And he just might be the next director of NIH, the largest scientific research funding organization in the world.

> "...The BioLogos Foundation promotes the search for truth in both the natural and spiritual realms, seeking harmony between these different perspectives."

In a public statement, Collins said that he established the BioLogos Foundation

> "to address the escalating culture war between science and faith in the United States. On one end of the spectrum, 'new atheists' argue that science removes the need for God. On the other end, religious fundamentalists argue that the *Bible* requires us to reject much of modern science. Many people—including scientists and believers in God—do not find these extreme options attractive. BioLogos represents the harmony of science and faith. It addresses the central themes of science and religion and emphasizes the compatibility of Christian faith with scientific discoveries about the origins of the universe and life. To communicate this message to the general public and add to the ongoing dialog, the BioLogos Foundation created BioLogos.org."

Let's dissect this statement, because if ever there was a statement that needed dissecting, this is one. I completely agree with Collins that there is a culture war between science and faith in the United States. But I do not agree that the war is due primarily to the clash between the extremists on both sides. Take the "new atheists," for example. There are many atheists in the United States, and some of them are scientists. But only a handful would take the extreme—and, to my mind, incorrect—position that science disproves the existence of God. The British scientist Richard Dawkins might, but he doesn't speak for the majority of scientists I know, and his eloquent but strident voice has only served to inflame the opposition by preaching to the converted. There are many more agnostics who simply believe that there is no compelling evidence to believe in any deity.

Now let's look at the opposition, the "religious fundamentalists" who argue that "the *Bible* requires us to reject much of modern science." There are a lot more of those, especially in the United States, but—and this is a crucial distinction, as we shall see—they are almost entirely evangelical Christians, not "religious fundamentalists" in general. Evangelical Christians often take the *Bible* literally, and a literal reading of the *Bible* is certainly incompatible with many of the findings of science.

One of the missions of the BioLogos website is to advance the idea of theistic evolution, a concept discussed in depth in Collins' book *The Language of God*, which is also promoted on BioLogos.org. Essentially, theistic evolution means that evolution is the way God created life. I was first clued into this website by Jonathan Eisen, an evolutionary biologist and open access publishing maven at the University of California, Davis. Eisen, whose blog, "The Tree of Life" (http://phylogenomics.blogspot.com) is a delightful and thoughtful commentary on the worlds

of both genomics and scientific publishing, wrote about BioLogos on May 5. Just so you know where he's coming from, here's his opening statement:

> "I am all for trying to have discussions about science and religion. But I do not think the two topics are really compatible in the sense of merging them together. Science (and medicine) should be about, well, science. And religion can be about whatever it wants to be. And when we can get religious and scientific leaders together to talk about the implications of each area on the other and on the world, fine too. But merging the two together into one hybrid such as Christian Science and Creation Science? Not for me."

He goes on to make a pointed criticism of the underlying logic—or lack thereof, in his view—behind BioLogos.

> "The details of Collins' attempt to merge science and religion into a version of theistic evolution are really unclean. Basically, he is trying to argue that on the one hand, science and religion are completely separate activities (I support this) but at the same time argues that God can intervene in the setting up of natural laws and in providing some guidance here and there in order to, for example, produce human beings in his image. The website repeats some things from Collins' book that are equally illogical—such as saying that altruism can be explained by science (and even specifically saying that science is the way to explain the natural world) but then turning around and saying that science cannot explain extreme forms of altruism (and therefore implying that actually, the natural world cannot be explained by science). Which is it? Is science for the natural world or not?"

> *"…Collins said that he established the BioLogos Foundation 'to address the escalating culture war between science and faith in the United States.'"*

Eisen is right that this, and some of BioLogos' other talking points, smack of setting up a straw man.

But in the end, BioLogos aims to show that the findings of science are not inconsistent with the existence of God. And not just any God. BioLogos is all about the Christian God. It even says so: "The creation story of BioLogos is compatible with many faith traditions, and there is no way to give a scientific proof for one monotheistic faith over another. Therefore, this response will simply show the compatibility of Christianity with BioLogos." And again, more forcefully, in their mission statement: "the website is a reliable source of scholarly thought on contemporary issues in science and faith that highlights the compatibility of modern science with traditional Christian beliefs."

Here's another example: "For believers, these [scientific] discoveries must ultimately be compatible with the truth that is revealed in the *Bible*, and it is the conviction of BioLogos that this compatibility is not only desirable but also possible. The limitation is that our access to all forms of truth, including scientific and religious, is at best partial." The statement that it is Biblical truth that science must be compatible with (and there are other comments that make it clear BioLogos means the Christian *Bible*, especially *The New Testament*) marks a clear attempt to link science with one brand of religion.

The creators of BioLogos have every right to make the foundation and website about whatever they want. And I suppose you could argue that, as I see it, because it is evangelical Christians who are the chief opponents of modern science, especially evolution, it is sensible for scientists to promote the compatibility of science with Christian beliefs. But I don't agree. I think it's a huge mistake.

G. K. Chesterton, a devout Roman Catholic, has his priest-detective Father Brown say, in the superb short story "The Sign of the Broken Sword," "When will people understand that it is useless for a man to read his *Bible* unless he also reads everybody else's *Bible*? A printer reads the *Bible* for misprints. A Mormon reads his *Bible* and finds polygamy; a Christian scientist reads his and finds we have no arms and legs." I've always liked this quotation and not just because I agree that one huge problem with putting your faith in the literal reading of a book is that you can find justification in that book for almost any form of behavior, from altruism to genocide to slavery. I like it for a reason that Chesterton probably never intended: it reminds me that there are many more religions than Christianity, and many more people of faith than monotheists. I think if you are going to understand people of faith and try to see how we as scientists can find common ground with them, it is discriminatory—and possibly something worse—to focus on Christians or even monotheists (which, in the modern world, pretty much consists of Muslims, Christians, and Jews—Zoroastrians being in short supply nowadays—and I'm pretty sure that the BioLogos folks would not include Islam in their mission, given that faith's denial of the divinity of Christ). If you are going to read the Christian *Bible* you should also read the Jewish *Bible*. And *The Book of Mormon*. And the *Koran*. And the *Bhagavad Gita*. If you

really care about making contact with people of faith, you should not exclude most of them just because they worship different gods from yours.

In some temples in India, during services the priest will read from the Hebrew or Christian *Bible*, and the Muslim *Koran*, as well as the Hindu *Gita*, moving from one to the other as though it did not matter what precise words were being spoken, as long as there was something greater than the individual self that was being worshipped. How can we as scientists find common ground with people of faith unless we recognize the commonalities they share with each other? At its best, all religion is about a love for the natural world, a desire to help other people, and a sense that life is well lived only when it is not lived selfishly and pettily—values that typically underlie most scientific research. At its worst, religion is about unquestionable certainty, authoritarianism, exclusion, and discrimination—things that have no place in science either. Scientists can make common cause with people of faith through the values we share but must reject the extremist, intolerant views that poison both spheres.

And in the end, that's my big problem with BioLogos—at its heart, it strikes me as implicitly exclusionary (plus I agree with Eisen that its logic is shaky). I would have much preferred a clear-cut effort to emphasize the nonconnectedness of science and faith: that science is about evidence and testable hypotheses, whereas religion is about believing in things for which there is no evidence whatsoever and cannot be. That would place them in separate realms, but with common ground as I defined it above. The moment you start trying to say that data from science is compatible with the Christian religion in particular, you imply that, for example, polytheistic religions are wrong, and maybe not just as a matter of faith, but as a matter of science.

Nothing is more dangerous than such absolutism. It sets one type of religion as being true and therefore can be used to support the branding of all the others as false. However well intentioned, BioLogos isn't likely to bring peace to the war between science and religion if it is oriented so strongly towards one religion. I would have loved to see the resources that the Templeton and BioLogos Foundations spent on BioLogos.org—both financial and in terms of human effort—devoted to clarifying and promoting the distinctions between science and religion and to a search for a common ground that does not exclude anyone of faith. That's something I could support (and, I bet, something that Jonathan Eisen and possibly Charles Darwin could support, too). But the idea that science provides information that cannot be explained by science alone—and therefore that science "needs" the Christian God for a complete description of the universe—strikes me as the wrong thing to do. Render unto Darwin the things that are Darwin's and unto God the things that are God's. But for God's sake (or should that be Darwin's?), don't mix them together.

* This article originally appeared in *Genome Biology* (2009) 10, 106 and was reprinted with permission from BioMed Central.

Improving the Scientific Research Climate

BY CARRIE D. WOLINETZ*

In addition to our advocacy activities supporting sustainable research funding, FASEB's Office of Public Affairs (OPA) focuses on improving the research climate for scientists by developing proactive policy positions, advising on regulatory affairs, and responding to calls for comments from federal agencies on issues that affect biomedical research. FASEB's Science Policy Committee (SPC), which comprises representatives from FASEB member societies, works with OPA staff and issue-specific working groups of FASEB society scientists to ensure that the voice of biomedical research science is heard by policymakers. Recently, FASEB released statements on a number of biomedical research policy issues.

Draft Embryonic Stem Cell Guidelines

In April, NIH released draft guidelines for federal funding of human embryonic stem cell (hESC) research and issued a call for public comments. FASEB responded with a number of concerns. The draft guidelines would be applied retroactively, and their strict compliance requirements for informed consent could exclude some hESC lines that were allowed under the previous policy. FASEB urged NIH to consider a system that would allow grandfathering of existing lines. In addition, the draft guidelines would only allow federal funding for lines created from surplus fertility clinic embryos, rather than embryos created specifically for research, through IVF or other technologies.

U.S. Working Group on Biosecurity

The Working Group on Strengthening Biosecurity in the United States, which was formed by executive order to examine the current system of regulations governing select agents and high-containment labs, held its first and only public meeting on May 13. In conjunction with the meeting, the Working Group issued a series of questions and called for stakeholder feedback. FASEB and the Association of American Medical Colleges (AAMC) issued a joint statement, providing input on a number of issues being addressed by the Working Group. In particular, FASEB-AAMC endorsed a recent report by the National Science Advisory Board on Biosecurity (NSABB), which stated that the current security screenings used for the select agent program were adequate, and there was no need for additional personnel reliability measures. In addition, FASEB-AAMC called for a stratification of the select agent list based on risk, advocated for performance-based standards, and recommended modification of the requirements for inspection and inventory. Finally, the letter suggested that more data need to be made available about the current status of biosecurity in our nation's labs and cautioned the Working Group to differentiate between the related-but-distinct terms of biosafety and biosecurity.

Institutional Review Board Accountability

FASEB has also issued comments on the Office for Human Research Protection's (OHRP's) advance notice of proposed rulemaking regarding holding institutional review boards (IRBs) and the institutions or organizations operating them (IORGs) directly accountable for meeting regulations for the protection of human subjects. In its letter to OHRP, FASEB stated that shifting the locus of responsibility from institutions engaged in human subjects research to IRBs or IORGs would diminish research institutions' concerns about regulatory liability, facilitate collaborative review arrangements, and reduce barriers to conducting multi-center human research projects. Where it is appropriate for either IRBs or institutions to meet certain regulatory requirements, FASEB recommended that both parties be required to designate in their IRB authorization agreements which responsibilities they will each assume. FASEB noted that the IRB process could be further improved by eliminating the requirement that institutions designate specific IRBs on their Federal-wide assurances and replacing it with a commitment by institutions to rely only on registered IRBs. FASEB hopes these regulatory changes will increase the efficiency of the IRB process and the pace of clinical research without compromising the effectiveness of the review system or the safety of research participants.

The above FASEB documents can be found at: opa.faseb.org.

Carrie D. Wolinetz is director of Scientific Affairs and Public Relations for the Office of Public Affairs at FASEB. She can be reached at cwolinetz@faseb.org.

Jennifer Hobin of the FASEB Office of Public Affairs contributed to this article.

Hill Roundup: Sebelius Cautioned, Hill Visits, Appropriations Markups

BY PETER FARNHAM*

June 2 marked the first appearance of Health and Human Services Secretary Kathleen Sebelius before the House Appropriations Subcommittee on Labor, Health, and Human Services. Although the hearing focused primarily on health care issues, a couple of important NIH-related matters came up during the question period following her testimony.

Subcommittee Chairman David Obey (D-WI) expressed strong disapproval of the President's 2010 budget request for disease-specific research allocations targeting cancer and autism. Obey cited the committee's strong, lengthy, and bipartisan history of allowing scientific priorities to be set by scientists and NIH, not by Congress or the political process. Obey then flatly told Sebelius that the committee would not support the administration's request in this regard and asked her to so inform the White House. She said she would do so but restated the President's belief that cancer can be cured in his lifetime with proper funding.

Several other members on the subcommittee (both Democrat and Republican) publicly agreed with Obey's position during their question periods, stating that prioritizing diseases would not be good for research in the long run.

During a Senate hearing in May, much the same point was made, so it appears unlikely that this portion of the president's medical research agenda will pass muster with Congress.

Another NIH-related issue came up during a question from Rep. Jerry Lewis (R-CA), ranking Republican member of the full Appropriations Committee. Lewis expressed concern about the so-called "cliff" effect, caused by the fact that the $10 billion in stimulus money NIH received under the American Reinvestment and Recovery Act (ARRA) is supposed to be spent by the end of fiscal year 2010. The President has only asked for a 1.3 percent budget increase for NIH in 2010. Sebelius acknowledged the problem and said that a multiyear plan is needed to address the issue.

Hill Visits

ASBMB staff, along with two members of the FASEB Science Policy Committee, including ASBMB member Margaret Offermann, vice president of the American Cancer Society, attended the Sebelius hearing and then spent the day on the Hill discussing NIH research funding. NIH continues to enjoy broad support on Capitol Hill, although it was clear in several offices that we should not expect NIH to receive much beyond the President's request this year, given the stimulus money it received earlier in the year. Every staffer visited, however, was aware of the "cliff" issue. This is good news because it is more likely that something will be done to avoid the dislocation caused by the sudden 25 percent decrease in NIH's budget.

If you are going to visit Washington, feel free to contact the ASBMB public affairs office to arrange a Hill visit for yourself.

Markups Begin

On June 4, the 2010 Commerce, Justice, Science, & Related Agencies Appropriations Bill was marked up. The NSF, funded under this bill, received a total of $6.94 billion, $446 million over

continued on page 29

The Challenges of Challenge Grants

BY ALLEN DODSON

On March 4, 2009, shortly after passage of the $787 billion American Recovery and Reinvestment Act (ARRA), NIH issued the largest Request For Applications (RFA) in its history. The Challenge Grant program announcement, which was 220 pages long, invited applications from scientists to address hundreds of scientific challenges in areas like bioethics, translational science, and genomics. Researchers met that call in spectacular numbers, preparing and submitting over 20,000 applications to the program in the two months between its announcement and the April 2009 deadline. This created a major challenge for NIH's Center for Scientific Review (CSR), which evaluates a total of 48,000 applications in a typical year.

The Logistics of Doubling Grant Review

To review the challenge grants within the limited time available—decisions are expected by August 2009—CSR has had to think outside the box. The 20,000 applications will be distributed to approximately 15,000 reviewers for preliminary mail reviews. These reviews will be passed along to one of thirty "editorial board" study sections for a second phase of evaluation. Overall, the challenge grants nearly double the 16,000 applications and 8,000 reviewers involved in a typical review cycle.

Even if the review can be completed by August, the story of the Challenge Grants will not be over. NIH issued a memo in mid-May clarifying the policy on resubmission of responses to an RFA. They anticipate that many unsuccessful Challenge Grant applications will be resubmitted for funding via other mechanisms, such as R01 grants. The regulations require a decision on the initial application before resubmission. Due to the expected August response date and the deadline for grant submissions in the second cycle of 2009, resubmitted challenge grants cannot be considered until the third review cycle of 2009. Beyond that initial delay, however, investigators will be free to resubmit their proposals as new applications.

The challenge grant announcement originally stated that NIH would commit $200 million—enough for only 200 of the $1 million, two-year awards—to the program. In testimony before the Senate Appropriations Committee in May, Acting NIH Director Raynard Kington stated that he expected the funding number to double. Kington also observed that institutes and centers would have the flexibility and discretion to make additional challenge grant awards if desired. Still, in comparison to the 20,000 total applications, it does not appear likely that even 5 percent of the challenge grant applications will ultimately be funded. The potential for 19,000 challenge grant resubmissions looms as a potential problem for future review cycles.

Challenging Grant Crunches Ahead?

In his Senate Testimony, Kington described the response to the challenge grants as proof of an untapped supply of great ideas for biomedical advances. Members of the ASBMB Public Affairs Advisory Committee took the same message to Capitol Hill in May. The PAAC made the case that there is a tremendous capacity for progress but that researchers will require sustainable increases in funding to support the breakthroughs of the future. However, it is unclear whether that funding will be available in the post-stimulus era, when the focus in Washington is likely to shift to reducing the federal deficit.

Beyond the short-term challenges of reviewing the applications and the medium-term issues with highly competitive application cycles as stimulus-funded two-year grants expire in 2011 and 2012, the challenge grants also raise some long term questions. If NIH cannot make the jump from President Obama's $31 billion budget request for 2010 to the approximately $36 billion needed in 2011 to continue stimulus-level support for research, what will happen to research capacity? Does the potential $400 million in support for challenge areas—primarily focused on translational research—come at the expense of the investigator-initiated basic biomedical research that lays the groundwork for future clinical breakthroughs? How will historically low success rates for the Challenge Grant program, and in the coming grant cycles, affect research?

The challenges of the challenge grants have only begun.

ASBMB is maintaining a web page at www.asbmb.org/recovery with details about the most recent developments in stimulus funding.

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

ASBMB Comments on New Stem Cell Policy

In a May 26, 2009 letter to National Institutes of Health Acting Director Raynard Kington, ASBMB President Gregory Petsko stated the Society's general support for the new stem cell guidelines, published in the Federal Register on April 23. However, a couple of problems caught the attention of the Society. First, the guidelines inadvertently appear to be more restrictive than the Bush Administration's policy that the new policy sought to overturn. ASBMB also noted that it hoped as time went on, the limitations on what sources of stem cells were allowable would be liberalized.

The full letter appears below.

If you have comments, we would appreciate hearing from you. You can send your thoughts to Peter Farnham, director of Public Affairs, at pfarnham@asbmb.org.

Dear Dr. Kington:

Thank you for the opportunity to comment on the "Draft NIH Guidelines for Human Stem Cell Research," published in the Federal Register on April 23, 2009.

The Guidelines are summarized as follows in the notice:

"These draft Guidelines would allow funding for research using human embryonic stem cells that were derived from embryos created by *in vitro* fertilization (IVF) for reproductive purposes and were no longer needed for that purpose. Funding will continue to be allowed for human stem cell research using adult stem cells and induced pluripotent stem cells. Specifically, these Guidelines describe the conditions and informed consent procedures that would have been required during the derivation of human embryonic stem cells for research using these cells to be funded by NIH. NIH funding for research using human embryonic stem cells derived from other sources, including somatic cell nuclear transfer, parthenogenesis, and/or IVF embryos created for research purposes, is not allowed under these Guidelines."

In general, we support the intent of these Guidelines. Our main concern, however, is that the Guidelines are inadvertently more restrictive than the previous administration's policy in some ways. This is a critical problem that must be addressed before the Guidelines are finalized.

This problem was discussed extensively in an article in the *Washington Post* on Monday, May 25. The Guidelines inadvertently make it harder to do some types of stem cell research than was allowed under the previous administration's policy. We are certain that this was not the intention of the Obama administration. The retroactive application of the requirements in these Guidelines would render unusable some existing hESC lines because of how they were derived. Since many of these lines were developed in the private sector and are in common use now, it would be a waste of resources to have to go back and recreate them under the current requirements.

ASBMB thus strongly supports some sort of "grandfathering" mechanism that would allow these lines to continue to be used. One of the major benefits of grandfathering existing lines is the resulting many new cell lines representing far greater genetic diversity than the original few dozen lines permitted under the previous policy. This same reasoning would apply to those cell lines that have been extensively studied, regardless of source. However, regardless of the mechanism NIH chooses to allow existing lines to be used, allowing the use of all extant lines must be addressed.

In addition, we also hope that as time goes on the Guidelines will be revisited with an eye to loosening up some of the restrictions on what stem cells can be used. We are confident that when embryonic stem cell research begins to pay off, the public climate will change to the point that a more liberal approach to what stem cell sources are allowed will be possible, provided that the research is conducted in keeping with appropriate regulations concerning informed consent and human subject protections.

The American Society for Biochemistry and Molecular Biology is a nonprofit scientific and educational organization with a membership of approximately 12,000 biochemists and molecular biologists that teach and conduct research at colleges and universities, in the private sector, and in the federal government. ASBMB publishes the *Journal of Lipid Research*, *Molecular & Cellular Proteomics*, and the *Journal of Biological Chemistry*, one of the leading peer-reviewed journals in the life sciences.

Thank you again for considering ASBMB's views on this subject. Please let us know if we can be of further assistance.

Sincerely,
Gregory A. Petsko
President
American Society for Biochemistry and Molecular Biology

asbmb member spotlight

Alberts Honored with Education Award

Bruce Alberts, professor in the Department of Biochemistry and Biophysics at the University of California, San Francisco, has been selected to receive the American Institute of Biological Sciences Education Award. This annual award is presented to an individual (or group) who has made significant contributions to education in the biological sciences, at any level of formal or informal education.

Alberts is currently editor-in-chief of the journal *Science*. He served two six-year terms as the President of the National Academy of Sciences (NAS) and chaired the National Research Council. He continues to serve as an *ex officio* member of the National Academies Teacher Advisory Council, which he initiated. Committed to improving science education, he helped initiate and develop City Science, a program that links UCSF to the improvement of science teaching in San Francisco elementary schools. Alberts was instrumental in developing landmark National Science Education standards that have been implemented in school systems nationwide. He also serves as the co-chair of the InterAcademy Council, a new organization governed by the presidents of 15 national academies of science and established to provide scientific advice to the world.

Alberts is widely recognized for his work in the fields of biochemistry and molecular biology, particularly his extensive studies of the protein complexes that enable chromosome replication. He is also one of the original authors of *The Molecular Biology of the Cell*, which is used widely in U.S. colleges and universities.

Jordan Elected Fellow of UK Academy of Medical Sciences

V. Craig Jordan, scientific director of the Lombardi Comprehensive Cancer Center and professor of Oncology and Pharmacology at Georgetown University Medical School, has been elected a fellow of the Academy of Medical Sciences in the United Kingdom. The induction ceremony took place on June 24th at the Royal Society in London.

In May, Jordan received the Gold Medal of the University of Crete and an honorary Doctor of Medicine degree from their medical school. Jordan is also the recipient of the Jephcott Gold Medal and Lectureship from the Royal Society of Medicine in England, and was elected to the U.S. National Academy of Sciences this past spring.

Jordan has focused his research career on the development of tamoxifen and raloxifene, two selective estrogen receptor modulators (SERMs) used for the treatment and prevention of breast cancer (tamoxifen) and for the prevention of osteoporosis and breast cancer (raloxifene).

Scientifically, he is credited with first recognizing the SERM principle. The biological concept is now being developed for all members of the nuclear receptor superfamily.

Brenner Named Head of Biochemistry

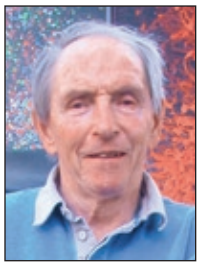
Charles Brenner, professor of genetics and of biochemistry at Dartmouth Medical School, has been named head of the Department of Biochemistry at the University of Iowa Roy J. and Lucille A. Carver College of Medicine. The appointment became effective on July 1.

Brenner is currently scientific director of the Comprehensive Thoracic Oncology Program at Dartmouth-Hitchcock Medical Center and associate director for basic sciences at Norris Cotton Cancer Center in Lebanon, NH.

"We are excited that Dr. Brenner has accepted the position of department head," said Paul Rothman, dean of the UI Carver College of Medicine. "Dr. Brenner is an exceptional scientist who deeply appreciates the critical role of basic research as a foundation for discovery. He has the vision, expertise, and leadership to help us grow our basic research strengths and build bridges to translate research into cures for disease."

Brenner's research focuses on the function of genes that are inactivated in cancer development and metabolic pathways that respond to changes in glucose intake and regulate cellular aging. He uses interdisciplinary approaches, including protein structural analysis, enzymology, human genomics, and yeast genetics to study biochemical pathways.

Schimke Receives Stanford's Sterling Award



This past April, Robert T. Schimke, professor *emeritus* at Stanford University, received the J. E. Wallace Sterling Muleshoe Lifetime Alumni Achievement Award. The award, which is given annually to Stanford Medical School alumni who have made exceptional lifetime achievements, was presented to both Schimke and Paul M. Ellwood for their leadership and commitment to improving health.

Schimke, who received his M.D. from Stanford in 1958, was also chairman of the Department of Pharmacology at Stanford (1969–1972) and chairman of the Department of Biological Sciences (1978–1982). He is best known for showing that protein degradation can act as an enzyme regulatory process and his discovery that gene amplification can result in cellular resistance to cancer chemotherapy drugs.

Schimke is currently professor *emeritus* of Biological Sciences and the American Cancer Society Research professor *emeritus* at Stanford. He was president of the American Society for Biochemistry and Molecular Biology in 1988 and was a member of the editorial board and an associate editor for the *Journal of Biological Chemistry* from 1975 to 1981 and from 1983 to 2002.

Since his retirement, Schimke has devoted much of his time to an old love, painting. In spite of a bicycle accident in 1997 that left him a quadriplegic, confined to a wheelchair and with limited use of his arms and hands, he has been prolific in his art, some of which can be seen on his website (www.stanford.edu/group/schimke).

Pastan Awarded International Feltrinelli Prize for Medicine

Ira H. Pastan of the National Institutes of Health has been declared the recipient of the Accademia Nazionale dei Lincei's 2009 International Feltrinelli Prize for Medicine. Pastan, chief of the Laboratory of Molecular Biology at the Center for Cancer Research, received the prize for his outstanding scientific contributions to the biology of receptors and the development of immunotoxins for cancer therapy.

Pastan's early research focused on elucidating the mechanism of action of polypeptide hormones. He and his colleague Jesse Roth provided the first evidence that there were specific protein receptors on the surface of animal cells and that binding to these receptors was the first action of protein hormones. Pastan went on to characterize the diffusion of hormone-receptor complexes on the cell membrane, their hormone-dependent aggregation, and their pathway of entry into cells, using a variety of tools including video intensification microscopy. Pastan was also among the first to clone and sequence the EGF receptor and to demonstrate that it is amplified in many cancers. Realizing from his receptor studies that powerful toxins, such as *Pseudomonas* exotoxin A, could be targeted to kill specific cells, Pastan and his colleagues later developed a new class of anti-cancer agents called immunotoxins, which are chimeric proteins consisting of an antibody and a toxin.

Jeang Wins Woodrow Wilson Award

This past June, Kuan-Teh Jeang received the Johns Hopkins University Alumni Association's Woodrow Wilson Award, recognizing his contributions to the fields of molecular virology and biology. The Woodrow Wilson Award for Distinguished Government Service honors alumni who have brought credit to Johns Hopkins by their current or recently concluded distinguished public service as elected or appointed officials. Previous winners of the Woodrow Wilson Award have included the former U.S. Secretary of State Madeleine Albright, the former director of the U.S. National Institutes of Health Elias Zerhouni, and the current U.S. Secretary of the Treasury Timothy Geithner.

Since 1985, Jeang has been at NIH. He is currently the head of the Molecular Virology Section in the Laboratory of Molecular Microbiology at the National Institute of Allergy and Infectious Diseases. Jeang has published over 250 peer-reviewed articles. His research interests focus on the gene regulation of HIV and how HTLV-1 causes leukemia. He is the president-elect of the Society of Chinese Bioscientists in America (SCBA), a three-term editorial board member of the *Journal of Biological Chemistry*, an Academician of Academia Sinica, and an elected fellow of the American Association for the Advancement of Science, the American Society for Clinical Investigation, and the Association of American Physicians. Jeang was also a recent past councilor of the ASBMB.

Holick Garners Linus Pauling Prize

Michael Holick, a professor of medicine, physiology, and biophysics at the Boston University School of Medicine, received the Linus Pauling Institute Prize for Health Research. The prize was presented to Holick at a biennial conference, "Diet and Optimum Health," sponsored by the Linus Pauling Institute at Oregon State University. It recognizes international leaders in research on the role of diet and nutrition in health promotion and disease prevention, as well as efforts to disseminate knowledge on diet, lifestyle, and health to enhance public health and reduce suffering from disease.

"Today, Holick is recognized as a world renowned nutritional biochemist/physician whose research has had a global impact on the health of both children and adults," said Nevin Scrimshaw, president of the International Nutrition Foundation, in nominating him for the award.

Holick was the first scientist to isolate the active forms of vitamin D, and in the past three decades, he has become the world authority on the photobiology of vitamin D through synthesis in the skin. In more recent work, Holick has shown links between vitamin D deficiency and the development of preeclampsia in pregnancy.

Lipids, Physiology, and Disease

BY DANIEL M. RABEN AND MARY F. ROBERTS

RABEN

ROBERTS

Lipid Research has become an important component of studies in an expanding number of disciplines. This has ushered in a plethora of new techniques and knowledge in a variety of areas that cover physiology, biochemistry, biophysics, and cell biology. The Lipid Theme for the 2010 ASBMB Annual Meeting, "Lipid Interactions in Physiology and Disease," will highlight emerging concepts in these areas of lipid research.

It is well known that lipids and lipid metabolism play an important role in health and disease. Recently, we have started gaining a new, or perhaps renewed, appreciation for the notion that specific cells and sub-cellular compartments in which lipids and metabolizing enzymes reside are critical to their physiological roles. The first session of the 2010 Lipid Theme will cover emerging concepts in lipid physiology and pathophysiology. For example, regulating apoptosis is a central concept in a number of pathophysiological problems, and the mitochondrion is known to be intimately involved in this process. Valerian E. Kagan (University of Pittsburgh) will discuss new mechanisms and pathways through which cytochrome *c* catalyzes oxidation of cardiolipin, a mitochondria-specific phospholipid, and the role of this process in apoptosis. Lina M. Obeid (Medical University of South Carolina) will present some emerging concepts regarding the role of sphingolipids in cancer, and Lucio Cocco (University of Bologna) will present fascinating data regarding the potential role of nuclear localized phosphatidylinositol phospholipase C-β1 in the progression and prognosis of myelodysplastic syndromes. These discussions will shed light on new and potentially important roles of lipids and lipid-metabolizing enzymes in health and disease.

With the recognition that lipid metabolism in specific cells and sub-cellular compartments needed further investigation came the need to develop new tools and strategies to study this metabolism. Richard W. Gross (Washington University in St. Louis) will discuss some novel approaches for studying lipids and lipid metabolism in membranes to illuminate their potential signaling roles. A particularly difficult yet extremely important question that troubles many lipid researchers pertains to the dynamics of specific lipid-protein interactions. Mary F. Roberts (Boston College) will discuss a potentially powerful approach to this question using high resolution field cycling NMR spectroscopy. To delve further into the analysis of lipids at the single molecule level, Akihiro Kusumi (Kyoto University) will outline some fascinating approaches to track lipids and lipid metabolism enzymes at the single molecule level. This promises to be a very informative tool for studying signaling lipids and the enzymes involved in their metabolism.

The third session will examine lipid movements and compartmentalization within cells. Gerrit van Meer (Utrecht University) will present a bird's eye view of this issue by discussing the general theme of where various membrane lipids are found and how they behave. Brian (Binks) W. Wattenberg (University of Louisville) will discuss new thoughts regarding how the localization of an important lipid metabolizing enzyme, sphingosine kinase-1, is important for its function. One lipid that receives much attention but is also misunderstood is cholesterol. A new way of thinking about the behavior of cholesterol in membranes and its relationship to cholesterol homeostasis will be presented by Yvonne Lange (Rush University Medical Center).

> **"One lipid that receives much attention but is also misunderstood is cholesterol."**

The fourth and final topic will focus on some current thoughts on the structure and regulation of lipid transporters and metabolizing enzymes. Lipid transporters are gaining increasing attention as they play important roles in lipid homeostasis as well as drug delivery and metabolism. Frances J. Sharom (University of Guelph) will present some new ideas on lipid transporters and membrane proteins that bind sterols. Understanding the enzymology and regulation of lipid-metabolizing enzymes is central to our

ability to understand signaling lipids. Two lipid second messengers that are emerging as essential players in a number of physiological and pathophysiological processes are diacylglycerol and phosphatidic acid. The enzymes responsible for metabolizing these signaling lipids once generated are critical to regulating their levels. Daniel M. Raben (Johns Hopkins University School of Medicine) will outline new ideas regarding the regulation of a mammalian diacylglycerol kinase (DGK-θ), which converts diacylglycerol to phosphatidic acid. Phosphatidic acid is itself metabolized by specific enzymes. One class of such enzymes is phosphatidate phosphatases. George M. Carman (Rutgers University) will highlight recent discoveries regarding the structure, regulation, and physiology of these enzymes.

These presentations will be complemented by 12 short talks selected from submitted abstracts. The organizers have a strong interest in finding abstracts from young investigators, postdoctoral fellows, and graduate students to give them an opportunity to present their work to the lipid community. Please encourage these young folks to submit an abstract! We are hoping this meeting will stimulate ideas and increase enthusiasm for lipid research.

In addition to the symposia noted above, there will be a new award, the Avanti Young Investigator Award in Lipid Research, which will be presented at this meeting. This award will be given to a young investigator selected for their novel and innovative work in the area of lipid research. The awardee, who will be asked to present a lecture at one of the Lipid Theme sessions, will receive a plaque, $2,000, and transportation support to the ASBMB meeting. For more information, go to www.asbmb.org/lipidcorner.

There will also be a workshop, "Lipidology—From Basics to Biofuels and Cancer Therapeutics," that is aimed at those who are interested in, but not necessarily expert practitioners of, lipidology. Small roundtable discussions guided by experts will accompany a general overview of different aspects relevant to working with lipids and membranes. If lipids didn't excite you before, they should after seeing how useful a little lipidology can be!

We look forward to what promises to be a very exciting and enlightening meeting.

Daniel M. Raben is a professor of Biological Chemistry at Johns Hopkins University School of Medicine and can be reached at draben@jhmi.edu. Mary F. Roberts is a professor of Chemistry at Boston College and can be reached at mary.roberts@bc.edu.

Lipid Interactions in Physiology and Disease

SYMPOSIUM: EMERGING CONCEPTS IN THE PHYSIOLOGY AND PATHOLOGY OF LIPID METABOLISM

Nuclear Inositide Signaling: Role of PI-PLCβ1 in MDS and AML, *Lucio Cocco, University of Bologna*

Cardiolipin and Its Redox Interactions with Cytochrome c in Apoptosis, *Valerian E. Kagan, University of Pittsburgh*

Bioactive Sphingolipids in Inflammation and Cancer, *Lina M. Obeid, Medical University of South Carolina*

SYMPOSIUM: NOVEL APPROACHES FOR STUDYING LIPID SIGNALING, METABOLISM, AND MEMBRANES

Multidimensional Mass Spectrometry Using Shotgun Lipidomics to Identify Alterations in Lipid Signaling and Metabolism in Disease States, *Richard W. Gross, Washington University in St. Louis*

Signal Transduction by Lipid-anchored Molecules as Revealed by Single-molecule Tracking, *Akihiro Kusumi, Kyoto University*

High Resolution Field Cycling for Analysis of Lipid Dynamics in Membranes, *Mary F. Roberts, Boston College*

SYMPOSIUM: CELLULAR LIPID MOVEMENT AND COMPARTMENTALIZED METABOLISM

How Cells Sense and Set Their Cholesterol, *Yvonne Lange, Rush University Medical Center*

Sphingolipids on the Move, *Gerrit van Meer, Utrecht University*

Sphingosine Kinase-1 Localization Drives Differential Metabolism of Sphingosine-1-phosphate, *Brian (Binks) W. Wattenberg, University of Louisville*

SYMPOSIUM: STRUCTURE AND REGULATION OF LIPID TRANSPORTERS AND METABOLIZING ENZYMES

Regulation of Human and Yeast Phosphatidic Acid Phosphatase Enzymes, *George M. Carman, Rutgers University*

Regulation of DGKθ, *Daniel M. Raben, Johns Hopkins University School of Medicine*

Sterol Binding and Transfer by NPC1, *Frances J. Sharom, University of Guelph*

Dealing with Insults: Genome Stability in the Face of Stress

BY ELLEN FANNING AND THOMAS A. KUNKEL

FANNING

KUNKEL

More than half a century has passed since Watson and Crick's (*Nature* 171,737) famous understatement, "It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material." Research in the ensuing years has demonstrated that the machinery required to replicate DNA with the accuracy needed to maintain genetic information over many generations is very complex. This complexity partly reflects the need to deal with DNA damage. Indeed, by the time you finish reading this brief article, the DNA in every cell in your body will be damaged many times. How the replication machinery is coupled to the processes that first sense problems generated by environmental stress and then coordinate removal or tolerance of lesions in DNA is therefore also of great interest, even more so because failure of these processes is associated with cytotoxicity, mutagenesis, and diseases. At the 2010 ASBMB Annual Meeting, four symposia in the "DNA Transactions" theme will consider current research aimed at understanding how genomes are replicated and stably maintained in the face of constant insults.

The theme begins with a Sunday symposium titled "DNA Synthesis and Mutagenesis." Thomas A. Kunkel (National Institutes of Health) will describe studies of DNA replication fidelity, with emphasis on characterizing the leading and lagging strand replication machinery in yeast. Graham C. Walker (Massachusetts Institute of Technology) will describe the elegant regulation and control of evolutionarily conserved, highly specialized DNA polymerases that perform trans-lesion DNA synthesis. One mechanism that is central to controlling lesion bypass is the timing and spacing of protein ubiquitinylation, a subject of intense interest that will be considered by Helle D. Ulrich (Cancer Research UK).

The DNA Transactions theme continues with a symposium on Monday titled "Replication Fork Dynamics." This session will focus on the intricacies of normal replication forks. James M. Berger (University of California, Berkeley)

DNA Transactions

SYMPOSIUM: DNA SYNTHESIS AND MUTAGENESIS

Eukaryotic DNA Replication Fidelity, *Thomas A. Kunkel, National Institutes of Health*

Timing and Spacing of Ubiquitin-dependent DNA Damage Bypass, *Helle D. Ulrich, Cancer Research UK*

Function and Control of Trans-lesion Synthesis Polymerases, *Graham C. Walker, Massachusetts Institute of Technology*

SYMPOSIUM: REPLICATION FORK DYNAMICS

Structural Mechanisms for Initiating DNA Replication, *James M. Berger, University of California, Berkeley*

Molecular Hand-off in Viral DNA Replication, *Ellen Fanning, Vanderbilt University*

Structural Mechanisms of Bacterial Replication, *James L. Keck, University of Wisconsin-Madison*

SYMPOSIUM: DNA DAMAGE SIGNALING AND REPAIR

Genome Maintenance by the DNA Damage Response, *David Cortez, Vanderbilt University School of Medicine*

RecQ Helicase and RPA Regulate Fork Stability under Control of the ATR Kinase, *Susan M. Gasser, Friedrich Miescher Institute*

Regulated Proteolysis of a Trans-lesion DNA Polymerase on DNA, *W. Matthew Michael, Harvard University*

SYMPOSIUM: THE 3RS, GENOME INSTABILITY, AND DISEASE

Defects in Mitochondrial DNA Replication and Human Disease, *William C. Copeland, National Institutes of Health*

Title to be announced, *Penny A. Jeggo, University of Sussex*

DNA Repair Gone Wrong: Mechanisms of Trinucleotide Expansion, *Cynthia T. McMurray, Mayo Clinic Rochester*

will begin by describing structural mechanisms for initiating DNA replication. Ellen Fanning (Vanderbilt University) will then present her latest research aimed at understanding molecular handoff in viral DNA replication. James L. Keck (University of Wisconsin-Madison) will report on his most recent research using structural approaches to dissect the mechanisms that regulate bacterial DNA replication.

"...by the time you finish reading this brief article, the DNA in every cell in your body will be damaged many times."

Tuesday's contribution will be a symposium titled "DNA Damage Signaling and Repair." David Cortez (Vanderbilt University School of Medicine) will present a talk focused on how the DNA damage response contributes to genome maintenance. W. Matthew Michael (Harvard University) will then consider regulated proteolysis, a critical mechanism by which cells keep trans-lesion DNA polymerases from operating at the wrong place or time. The next speaker, Susan M. Gasser (Friedrich Miescher Institute), will cover the important topic of how forks are given enough time to do the right thing, *i.e.* by describing how the RecQ helicase and RPA regulate fork stability under control of the ATR kinase.

Wednesday's final symposium in the DNA Transactions theme, titled "The 3Rs, Genome Instability, and Disease," will consider some of the many known disease consequences of DNA transactions gone awry. First, Cynthia T. McMurray (Mayo Clinic Rochester) will consider how proteins involved in DNA repair can be subverted to expand trinucleotide repeats, a cause of several hereditary diseases. William C. Copeland (National Institutes of Health) will then discuss the latest research revealing how defects in mitochondrial DNA replication result in a large number of degenerative human diseases. Finally, Penny A. Jeggo (University of Sussex) will report on the impact of higher order chromatin structure on the damage response to DNA double strand breaks, defects which are also associated with disease.

The four symposia will also include 12 speakers chosen from submitted abstracts and will be complemented by poster sessions that cover DNA replication, repair, and DNA damage responses. Obviously, these DNA transactions are highly coordinated with other cellular processes that will be considered at the meeting, including chromatin dynamics, transcription, post-translational gene regulation, and protein turnover. Thus, scientists interested in how organisms, from viruses to man, can replicate and stably maintain their genomes in the face of constant environmental insults can satisfy their appetites for some of the best and most recent research by attending the 2010 ASBMB Annual Meeting.

Ellen Fanning is the Stevenson Professor of Molecular Biology in the Department of Biological Sciences at Vanderbilt University and can be reached at ellen.fanning@vanderbilt.edu. Thomas A. Kunkel is a principal investigator in the DNA Replication Fidelity Group at the National Institute of Environmental Health Sciences (NIH) and can be reached at kunkel@niehs.nih.gov.

Insights into the Biological Chemistry of RNA

BY MARTHA J. FEDOR AND SARAH A. WOODSON

FEDOR

WOODSON

The recent explosion of new RNA functions and structures is revising our view of biological regulation and evolution. Modern combinatorial chemistry, high-throughput sequencing, structural biology, and genetics are producing exciting discoveries in the roles of RNA in gene expression and their assembly into cellular machines. Theme organizers Martha J. Fedor and Sarah A. Woodson invite you to a series of talks on the "Biological Chemistry of RNA" that highlight emerging insights into the assembly, structure, and biological function of RNA-protein complexes, as well as technical and therapeutic applications of RNAs with novel functions.

The "Post-transcriptional Gene Regulation" session will be chaired by Melissa J. Moore (Howard Hughes Medical Institute (HHMI)/University of Massachusetts Medical School). Moore's research has shown how the exon junction complex, a protein complex that assembles onto precursor mRNAs during splicing in the nucleus, accompanies mRNAs into the cytoplasm to influence mRNA localization, translation, and turnover. The title of her talk will be "mRNAs with a Complex: The Long-term Consequences of a Nuclear Upbringing." Jeffrey S. Kieft (University of Colorado Denver School of Medicine) will focus on critical RNA structure-function relationships in viral replication and pathogenesis in his talk, titled "Structural Mimicry at the Heart of Translation Initiation by a Viral IRES." Kimberly Mowry (Brown University) will describe the molecular mechanisms through which mRNAs and proteins localize to specific regions of the cell cytoplasm in her presentation titled, "RNA Transport in the Cytoplasm: How to Get There from Here."

> **"...these RNA-themed symposia are bound to change your view of the role of RNA in modern biology."**

As the ribonucleoprotein machine responsible for protein synthesis, the ribosome is the engine of cellular growth and adaptation. The "Ribosome Assembly and Function" session, chaired by Sarah A. Woodson (Johns Hopkins University), will showcase recent progress in understanding bacterial ribosome assembly and function both *in vitro* and in bacteria. Woodson and James R. Williamson (The Scripps Research Institute) use a combination of biophysical approaches to characterize assemblies of large ribonucleoprotein complexes. Woodson's talk, titled "RNA Folding during Assembly of the 30S Ribosome" will present studies of structural changes in the rRNA during assembly of ribosomal subunits. In his talk, titled "Cellular Physiology of Bacterial Ribosome Assembly," Williamson will describe ribosome assembly as it occurs in bacteria. Harry Noller (University of California, Santa Cruz) has elucidated key features of ribosomal RNA interactions with ribosomal proteins, tRNAs, and translation initiation and elongation factors; provided compelling evidence that ribosomal RNA participates directly in peptide bond formation; and produced the first high resolution crystal structure of a 70 S bacterial ribosome. In a talk, titled "Structure and Dynamics of the Ribosome," Noller will present insights into how ribosome function arises from its three-dimensional structure.

Precursor mRNA splicing is the process that excises introns from primary RNA transcripts and joins the exons that encode amino acid sequences to generate mature, protein-coding mRNAs. The capacity to generate different exon combinations through alternative splicing generates a human proteome that is far more diverse than the genome, and splicing defects are said to be responsible for the majority of hereditary human diseases. The "Splicing Mechanism and Regulation" session, chaired by Douglas L. Black (HHMI/University of California Los Angeles), will cover recent progress in understanding splicing mechanisms and regulation. Black's talk, titled "Alternative Splicing and the Regulation of Neuronal Gene Expression," will describe molecular mechanisms that control the changes in splicing patterns during development and function

of the mammalian nervous system. Magda Konarska's (The Rockefeller University) talk, titled "Spliceosome Dynamics and Their Impact on the Fidelity of Splice Site Selection," will focus on interactions between precursor mRNAs and the small ribonucleoprotein complexes (snRNPs) that are crucial for maintaining a continuous open reading frame. Jonathan P. Staley's research (University of Chicago) focuses on the RNA rearrangements that regulate the activity of splicing machinery in yeast. He will expand on the theme of the fidelity of splice site selection in his talk, titled "Constraining Errors in Splice Site Choice."

The chemical transformations in translation and precursor mRNA splicing are most likely catalyzed by the RNA components of ribosomes and spliceosomes. The final session in the "Biological Chemistry of RNA" theme will focus explicitly on RNA catalysis. Martha J. Fedor (The Scripps Research Institute), chair of the "Ribozyme Structure and Function" session, will describe the use of fluorescent nucleobase analogs to probe the mechanism of the self-cleavage reaction catalyzed by the hairpin ribozyme. Hiroaki Suga (The University of Tokyo) and Dipankar Sen (Simon Fraser University) use *in vitro* evolution to explore the catalytic potential of RNA. RNA enzymes that catalyze the same reaction as the aminoacylases that charge tRNAs with amino acids in preparation for protein synthesis will be the focus of Suga's talk, titled "Structure and Catalysis of Flexizymes, Flexible tRNA Acylation Ribozymes, and Their Technical Potentials." Sen will describe novel RNA enzymes selected for their ability to use thiamine as a catalytic cofactor in his talk, titled "Towards Thiamine-utilizing Ribozymes."

There will also be 12 short talks, which will be selected from the submitted poster abstracts.

Sarah A. Woodson and Martha J. Fedor look forward to welcoming you to these RNA-themed symposia that are bound to change your view of the role of RNA in modern biology.

Martha J. Fedor is a principal investigator at The Scripps Research Institute and can be reached at mfedor@scripps.edu. Sarah A. Woodson is a professor of biophysics at Johns Hopkins University and can be reached at swoodson@jhu.edu.

Biological Chemistry of RNA

SYMPOSIUM: POST-TRANSCRIPTIONAL GENE REGULATION

Structural Mimicry at the Heart of Translation Initiation by a Viral IRES, *Jeffrey S. Kieft, University of Colorado Denver School of Medicine*

mRNAs with a Complex: The Long-term Consequences of a Nuclear Upbringing, *Melissa J. Moore, HHMI/University of Massachusetts Medical School*

RNA Transport in the Cytoplasm: How to Get There from Here, *Kimberly Mowry, Brown University*

SYMPOSIUM: RIBOSOME ASSEMBLY AND FUNCTION

Structure and Dynamics of the Ribosome, *Harry Noller, University of California, Santa Cruz*

Cellular Physiology of Bacterial Ribosome Assembly, *James R. Williamson, The Scripps Research Institute*

RNA Folding during Assembly of the 30 S Ribosome, *Sarah A. Woodson, Johns Hopkins University*

SYMPOSIUM: SPLICING MECHANISM AND REGULATION

Alternative Splicing and the Regulation of Neuronal Gene Expression, *Douglas L. Black, HHMI/University of California, Los Angeles*

Spliceosome Dynamics and Their Impact on the Fidelity of Splice Site Selection, *Magda Konarska, The Rockefeller University*

Constraining Errors in Splice Site Choice, *Jonathan P. Staley, University of Chicago*

SYMPOSIUM: RIBOZYME STRUCTURE AND FUNCTION

Active Site Purines and Catalysis of RNA Self-cleavage, *Martha J. Fedor, The Scripps Research Institute*

Towards Thiamine-utilizing Ribozymes, *Dipankar Sen, Simon Fraser University*

Structure and Catalysis of Flexizymes, Flexible tRNA Acylation Ribozymes, and their Technical Potentials, *Hiroaki Suga, The University of Tokyo*

The Department of Biological Chemistry at Johns Hopkins School of Medicine: 100 Years of Excellence

BY RALPH A. BRADSHAW

In November 2008, the Department of Biological Chemistry at Johns Hopkins School of Medicine celebrated its 100th birthday, making it one of the oldest departments of its kind. The event was marked with a symposium featuring six distinguished guest scientists, followed by a gala banquet attended by several hundred friends and associates. The department has enjoyed a century of remarkable accomplishments by its faculty and leaders, including many "firsts" (and with many significant connections to ASBMB) that are in keeping with the great traditions of Johns Hopkins University.

The Medical Department (which eventually became the Medical School) at Johns Hopkins University in Baltimore, Maryland opened its doors in 1893 under the combined leadership of four giants in the field of medicine: William Welch (pathology), William Halsted (surgery), William Osler (medicine), and Howard Kelly (gynecology). Among the innovative ideas that characterized the department's new curriculum was the teaching of chemistry to the medical students. This was originally to have been done by the Department of Chemistry, but it was ultimately entrusted to John Jacob Abel, professor of pharmacology. Abel, who later founded the *Journal of Biological Chemistry* in 1905 and the American Society of Biological Chemists (which eventually became ASBMB) in 1906, had a lifelong interest in the chemistry of biology and certainly would have been influential in making this decision. In the words of Welch, who was the first dean of the medical school:[1] "Physiological chemistry means much more than what is usually taught in our medical schools as medicinal chemistry, which includes little more than the chemical analysis of certain fluids of the body for diagnostic purposes."

This statement demonstrates the increasingly popular and much broader view, particularly as had been enunciated by Felix Hoppe-Seyler, one of the pioneers in the development of biochemistry, that to truly understand the molecular basis of physiology, it was essential to understand the underlying basic chemistry.

Abel, with the aid of several assistants, took up the task of teaching physiological chemistry to the medical students as a separate course (but not as a separate department) for the next several years. One of these individuals was Walter Jones, a native Marylander, who obtained his Ph.D. in chemistry from Johns Hopkins. He had joined Abel as an assistant in 1896 and rose to associate and then associate professor, all in physiological chemistry. In 1908, Jones was promoted to professor. This event was accompanied by the formation of the Department of Physiological Chemistry and the naming of Jones as its director (the title used for chair). In 1923, as the result of an unusual bequest from Capt. Joseph DeLamar, who was not a chemist and had no direct connection with Johns Hopkins University, the position was endowed, and Jones and all subsequent directors have held the title of DeLamar Professor. (The accompanying $4 million gift did not, however, find its way into the departmental coffers.)

Jones worked most of his life on nucleic acids, in particular, the enzymes that modified the bases. He developed this interest during a short stay in Germany in the laboratory of Albrecht Kossel, who, following in the footsteps of Friedrich Miescher, had become one of the leaders in this field. During this time he met and became close friends with Phoebus A. Levene, who was also an important contributor to the field of nucleic acid research. Levene, like Jones, was a founding member of the *JBC* and the Society. Jones eventually became the eighth president of the ASBC (1915–1916). He passed away in 1935.

One of the more impressive aspects of the history of the department, which changed its name to the Department of Biological Chemistry in 1984, is that, including Jones, there have only been five directors in its 100-year history, two of whom are still active there. In 1927, Jones retired,

Over the past 100 years, there have only been five directors of the Department of Physiological Chemistry (Biological Chemistry) at the Johns Hopkins School of Medicine: (*left* to *right*) Walter Jones, William M. Clark, Albert L. Lehninger, M. Daniel Lane, and Gerald Hart.

For more ASBMB history go to www.asbmb.org/history

largely due to health reasons, and he was succeeded by William Mansfield Clark. Clark was born in 1884 and was also a graduate of Johns Hopkins University, having received his doctorate in chemistry there in 1910. During this training period, he worked summers at the U. S. Bureau of Fisheries laboratory at Wood's Hole with both Carl Alsberg and Donald D. Van Slyke, who were the 9th and 11th presidents of the ASBC, respectively. It was here that Clark became interested in acidity and the measurement of hydrogen ion concentration, which eventually led, during his subsequent tenure at the United States Department of Agriculture (USDA), to his famous book, *The Determination of Hydrogen Ions*, published in 1920. Before returning to Johns Hopkins as the second DeLamar Professor, he also held a post at the U. S. Public Health Service, where he developed his interests in oxidation-reduction reactions, particularly involving organic dyes.[1]

Clark was essentially a physical chemist and protested at the time of his appointment as director that "[he] had had no formal training in biochemistry, had an inadequate appreciation of the needs of medical students, and [had] inherited laboratory equipment and space totally deficient for my research and student instruction."[1] The latter problem was soon corrected, and he quickly rectified his lack of knowledge in biochemistry and medical instruction. He proved to be an outstanding teacher and leader and held the post of director until 1952. However, he continued as *emeritus* DeLamar professor and as a research professor in chemistry until his death in 1964. He was the 18th president of the ASBC (1933–1934).

Clark was succeeded as director by the third DeLamar professor, Albert L. Lehninger. Lehninger, who was born in 1917, trained at the University of Wisconsin and spent six years at the University of Chicago before moving east. During his tenure there, he made seminal discoveries concerning fatty acid oxidation (some with his student, Eugene P. Kennedy, who became the 47th president of the ASBC in 1970) and the involvement of ATP that led to the appreciation that cellular metabolism was compartmentalized. Lehninger went on to make great contributions to the understanding of oxidative phosphorylation and energy-coupling with electron transport and the role of the mitochondrion in respiration, energy metabolism, and the regulation of calcium distribution in cells and tissues.[1] However, to several generations of biochemists, Lehninger is probably best known for his textbook, *Principles of Biochemistry*, that was widely adopted and was one of the most heavily used in medical and graduate teaching for many years. Perhaps reflecting his early collegiate interest in English, he authored several other books on the mitochondrion and bioenergetics that were equally authoritative. Lehninger was the 49th president of the ASBC (1972). He stepped down from his position at Johns Hopkins in 1978 and passed away in 1982.

The fourth director of the department was M. Daniel Lane, a native of Chicago. Unlike his predecessors, he had been recruited to the department several years before taking over as director and was thus an internal appointment. Lane received his doctorate from the University of Illinois in 1956 and held faculty positions at Virginia Polytechnic Institute and State University in Blacksburg, Virginia and

The current faculty of the Department of Biological Chemistry reflects the variety of sub-disciplines found in biochemistry: standing (*left* to *right*) Pierre A. Coulombe, Natasha Zachara, Susan W. Craig, Denise Montell, Craig Montell, Joel Pomerantz, Mollie K. Meffert, Akhilesh Pandey, David R. Shortle, Michael Wolfgang, Michael Caterina, Robert N. Cole, and Jennifer van Eyk; seated (*left* to *right*) Barbara Sollner-Webb, Daniel M. Raben, Albert S. Mildvan, M. Daniel Lane, Gerald W. Hart, Peter L. Pedersen, Paul T. Englund, Stephen J. Gould, and George Sack.

New York University before moving to Johns Hopkins in 1970. He served as director and DeLamar Professor from 1978 to 1997. He is presently the Distinguished Service Professor in the department. Lane continued the tradition of excellence in both research and teaching set by his predecessors. His own work has focused on understanding the molecular basis of fatty acid synthesis and adipogenesis and their relationship to obesity and other conditions, including the nature of differentiative processes in adipocytes. He is also a world leader in insulin signaling and the mechanisms underlying diabetes.[2] He served as the 67th president of the ASBMB (1990).

The department is currently headed by Gerald Hart, the fifth director and DeLamar Professor. Hart received his doctorate from Kansas State University and was a post-doctoral fellow in the department at Johns Hopkins under William J. Lennarz (the 66th president of the ASBMB, just before Lane), where he contributed significant detail to the understanding of the formation of *N*-linked carbohydrates. In 1992, he moved to the University of Alabama at Birmingham as chair of biochemistry and molecular genetics but eventually returned to Johns Hopkins to assume the directorship in 1997. Hart is best known for his discovery of *O*-linked *N*-acetylglucosamine (*O*-GlcNAc), an intracellular modification of proteins on serine and threonine residues. This modification is clearly related to a variety of metabolic and disease conditions and will likely form the basis of important cellular regulation mechanisms.

Today's department is a varied group of outstanding investigators that reflects the expansion and diversification of biochemistry as a discipline. This was manifested in the birthday symposium, entitled "The Biology of Molecules, the Chemistry of Life," where presentations on Wnt signaling (Marc W. Kirschner, Harvard Medical School), centromeres (Don Cleveland, University of California, San Diego), cell motility (Thomas D. Pollard, Yale University), small RNPs (Joan A. Steitz, Yale University), prion proteins (Susan Lindquist, Massachusetts Institute of Technology), and insulin action (C. Ronald Kahn, Harvard University) were featured. By its nature (and title), the symposium emphasized the founding principles of Abel and the subsequent directors (and their many faculty colleagues) that were and are focused on the chemistry of biology.

The ASBMB and Johns Hopkins University Department of Biological Chemistry have enjoyed common origins and purposes throughout their 100-year histories. As both head into their second century, one can expect this close and productive relationship to continue.

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Honoring the Biochemist's Biochemist: NIH Hosts the Stadtman Symposium

BY NICK ZAGORSKI

When asked once what he would consider an ideal birthday present, Earl Stadtman replied, "A great day of science." That simple desire was a strong statement about the nature of Stadtman, one of the great biochemists of the 20th century, who passed away on January 7, 2008 at the age of 88 (see the February 2008 issue of *ASBMB Today* for a retrospective). His wish, though, was remembered in the halls of the National Institutes of Health, where he spent most of his career, and through the efforts of his colleagues, this past April 29 saw a great day of science come together at the Stadtman Symposium held in Bethesda, MD.

The Symposium, brought to fruition by former Stadtman postdocs and current National Heart, Lung, and Blood Institute researchers Rod Levine and Boon Chock (who made sure to note the immense contributions of Merry Peters and Nadia Nimley) kicked off with a presentation by historian Buhm Soon Park (who, in 2004, set up an exhibit dedicated to Earl and his wife Thressa called "The Stadtman Way: A Tale of Two Biochemists at NIH, http://history.nih.gov/exhibits/stadtman). Park recalled some of Stadtman's scientific journey, from his days on the high school debate team to his early work during World War II looking at preventing the browning of dried apricots, and his more noted work at the NIH with glutamine synthetase.

Park pointed out that Stadtman greatly valued the importance of training others during a career in which he mentored over 100 scientists—including two Nobel winners, over a dozen members of the National Academies, and numerous other giants in academia and industry. Following Park's talk, the attendees had a chance to hear lectures from some of these noted trainees who cut their scientific teeth in Stadtman's lab, including Michael Brown (who jokingly thanked Joseph Goldstein for this rare opportunity to speak alone), Sue Goo Rhee, Brian Hemmings, and Stanley Prusiner. Also presenting was Susan Taylor, a frequent visitor to Stadtman's lab at Building 3 on the NIH campus, who described herself as "a surrogate member of Earl's family."

In between the talks and the short breaks to allow old colleagues a chance to catch up, the symposium featured comments and reflections about Stadtman from many of the scientists whose lives he touched, from the Pasteur Institute's Georges Cohen, who had been a close colleague for over five decades, to Gabriela Viteri, the most recent postdoc hired by Stadtman just a few years before he died. These short reflections proved to be some of the most informative and emotional moments of the symposium, where the attendees learned about Stadtman's loves of dancing, fine wine, and poker. "Earl took the same approach to poker as research," said Alfred Alberts, a scientist who helped develop the statin drugs Lovastatin and Zocor. "He was thoughtful and deliberate, though in the case of poker he wasn't always successful."

And while the symposium did come to an end, capped off by a dinner and reception featuring a talk by former postdoc and former Merck President Roy Vagelos, Stadtman's legacy will live on. Starting in 2011, ASBMB will present the Earl and Thressa Stadtman Award during the Annual Meeting, which will honor one great scientist each year in the biochemistry field. It was also revealed that Thressa Stadtman had recently deeded over five acres of the bucolic property she and Earl owned to form an expansion of Rock Creek Regional Park in Maryland, an area known as "The Stadtman Preserve." Said Levine, "The Stadtmans are leaving a legacy to the people of Montgomery County as strong as the legacy they left to science."

During his talk, Park noted that Stadtman had once said, "I hope all my trainees remember me in the same high regard as I remember them." Well, judging from the strong scientific presence at this symposium and all that was said, his hopes have come true.

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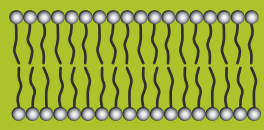

Understanding Plant Lipids

BY XUEMIN (SAM) WANG AND RUTH WELTI

One of the goals of the ASBMB Lipid Research Division is to provide a forum for lipid scientists to hear from colleagues working in a wide variety of lipid research disciplines. In this contribution to "Lipid News," Xuemin (Sam) Wang (University of Missouri-St. Louis) and Ruth Welti (Kansas State University) describe their perspective on the current state of plant lipid research.

When hearing the words "plant lipids," most people think of vegetable oils. However, in addition to the energy-dense oils stored in seeds, plant lipids play myriad structural and regulatory roles in plant growth, development, and response to abiotic and biotic stresses. Plant lipids are a diverse group of non-water-soluble compounds that include the pigments capturing sunlight for photosynthesis; essential oils attracting pollinators or repelling predators; and plant hormones and intracellular signaling messengers mediating plant response to environmental factors, such as water, temperature, and nutrient status. Substantial progress has been made in recent years toward understanding and appreciating the importance of lipids in plant growth and the regulation of that process. As in animal systems, the roles of lipids hydrolytically released from membranes and acting to regulate enzymes and transcription are being revealed. However, there are significant gaps in our knowledge of chemical structures, pathways of production, and mechanisms of action for regulatory lipids in plants.

One such gap is in our understanding of the pathways and regulation of seed oil biogenesis and partitioning of photosynthetic carbon among lipids, carbohydrates, and proteins. This is an important area because plant-derived oils are a major source of calories and essential nutrients for humans and animals. In addition, vegetable oils can be used as renewable fuels and as industrial feedstock. The interest in plant lipids as bio-renewable resources continues to increase as the supply of nonrenewable petroleum decreases. Although there have been some important successes in improving fatty acid composition to meet food, nutritional, and industrial applications, increasing oil content remains a challenge.

With the current national and international focus on energy, the environment, and the economy, this is a time of opportunity and challenge for the plant lipid researcher. One impediment to plant lipid research is the lack of comprehensive systematic analyses at the lipid level. Significant progress has been made in the analyses of polar glycerolipids, sphingolipids, oxylipins, and cuticle lipids. However, a robust lipidome-wide analysis that can be used in a systems biology context is yet to be realized. Technological innovations and interdisciplinary collaborations are needed to develop comprehensive and specialized enabling technologies to advance plant lipid research. Creativity and collaboration within and beyond the lipid community promise new fundamental knowledge that will be applied to increase plant productivity and quality for food and industrial uses.

> **"...plant-derived oils are a major source of calories and essential nutrients for humans and animals."**

The international plant lipid scientific community is a highly collaborative and cooperative community that assembles at least annually. Since 1974, there has been a biannual international symposium on plant lipids organized by this community. The next meeting is in Cairns, Australia in July 2010. During odd-numbered years, there are smaller meetings in North America and Europe. In particular, a Gordon Research Conference, entitled "Plant Lipids: Structure, Metabolism, and Function," was successfully launched in February 2009. Future Gordon Conferences on plant lipids have been planned biannually. All of these gatherings provide excellent opportunities for networking as well as rapid inroads for beginning investigators and newcomers to plant lipid research.

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Four Ways to Fund Your Postdoc

BY WEIYI ZHAO

Finding a postdoctoral position that fits your research interests, career goals, and family needs in a lab that can afford to pay you can often pose a challenge. In this fluctuating economy, getting the right postdoc experience is even more crucial, given the weak job market and uncertainty in funding.

A handful of small, elite postdoctoral fellowship programs worth looking into offer prestigious fellowships in the life sciences. The Helen Hay Whitney Foundation, the Damon Runyon Cancer Research Foundation, the Jane Coffin Childs Memorial Fund, and the Life Sciences Research Foundation are four such organizations that award funding to postdocs and allow them the flexibility to choose where to work and what type of research to conduct.

The Helen Hay Whitney Foundation awards postdoctoral fellowships to applicants who have had no more than one year of postdoctoral research experience. The foundation was established in 1947 to support research in the area of rheumatic fever and rheumatic heart disease. It has since expanded its research interests to include all basic biomedical sciences. Both M.D.s and Ph.D.s are eligible to apply but must have received their degrees within the past three and two years, respectively. The fellowship selection process involves both an application screening and a personal interview. The deadline for this year's award is July 15, 2009.

Established in 1946, **The Damon Runyon Cancer Research Foundation** supports postdoctoral fellows who are engaged in cancer research. Candidates must have completed their M.D., Ph.D., M.D./Ph.D., D.D.S., or D.V.M. and must apply for their very first postdoctoral fellowship under the guidance of a scientific mentor. Applicants are selected based on the quality of their research proposal, qualifications, experience, and the quality of their research training environment. The 2010 award deadlines are August 17, 2009 and March 15, 2010.

The Jane Coffin Childs Memorial Fund awards fellowships to M.D. or Ph.D. degree holders with less than one year of postdoctoral experience. The Fund was established in 1937 and supports a wide range of scientific inquiry, such as carcinogens of organic and inorganic origins, virus studies, endocrinology, microbiology, gene isolation, and growth control. Applications are due every year on February 1.

In comparison to the three foundations described above, **The Life Sciences Research Foundation (LSRF)** has no endowment and must therefore raise money each year from sponsors. Established in 1981, LSRF awards fellowships to graduates with M.D., Ph.D., D.V.M., or D.D.S. degrees. The foundation's mission is to support high quality young scientists in all areas of the life sciences. Candidates are judged based on the quality of their research, and all fellows must do their proposed research at a nonprofit institution. Donald Brown, a member of ASBMB, directs LSRF along with Douglas Koshland. The peer review process is administered by Jim Broach and Tom Silhavy at Princeton University's Department of Molecular Biology.

LSRF awards are highly competitive. Application submissions for 2009 open on September 10 and close on October 1. With approximately 800 applicants each year, only the top 5 percent are chosen as finalists and considered for funding. All applications are reviewed by LSRF's large and diverse peer review committee, whose members span the life sciences and whose sole interest is choosing the very best young scientists. ASBMB President Greg Petsko is a member of the LSRF peer review committee. Once finalists are selected, LSRF works with individual sponsors to find the candidate who best matches the sponsor's research interests. Once a year, LSRF brings together sponsors and fellows for an annual meeting. This provides an opportunity for sponsors to interact with their fellows.

All four fellowship programs described above offer three-year fellowships that are open to both U.S. citizens and international applicants. International fellows must conduct their research in laboratories within the United States. Some awards also provide dependent child allowances and travel support in addition to an annual stipend. Although these small fellowship programs will never solve the problem of funding for the thousands of postdocs in this country, they play an important role in training successful scientists and are worth investigating by both potential postdocs and sponsors. As Brown puts it, "sponsoring an LSRF fellow is the best bang for the philanthropic buck imaginable."

Links for all four foundations can be found online at www.asbmb.org/fellowships.

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Postdocs and the Recovery Act—What the ARRA Means to You

BY STACY GELHAUS

On February 17, 2009, the American Recovery and Reinvestment Act (ARRA) was signed into law. This act was designed to stimulate our struggling economy and to save and create millions of jobs, but how does this short-term stimulus bill benefit the postdoctoral scholar? Because the federal government funds 70 percent of postdocs, we can look to NIH and the NSF as the forecasters of the current postdoc climate.[1]

Few scientists would deny that the additional funding given to NIH and NSF this year is helpful. Stimulus money is saving the jobs of numerous researchers across the country whose labs were on the brink of closure, as well as funding those whose excellent science did not quite make the cut. According to Arden L. Bement, Jr., director of NSF, funding grants currently in the pipeline is the best possible use of the $3 billion in stimulus funding. In fact, the NSF does not expect to have any of this Recovery Act funding available in research and related activities for expenditure on fiscal year (FY) 2010 awards. In this regard, postdoctoral positions will only continue to be funded, or additional positions created, by increasing the number of grants funded by NSF.

NIH took a different approach with the $10 billion it received through the ARRA. Several new funding mechanisms have been developed in addition to the $7.4 billion appropriated among the 27 institutes and centers that will use this to fund two-year proposals, many of which just missed the cut last year. The NIH director's office was allotted $800 million, and about two-thirds of this is divided among four competitions: $200 million for Challenge Grants, another $200 million for Grand Opportunities (GO) Grants of at least $1 million, $100 million for new faculty hiring at core academic facilities, and $21 million for summer research experiences for students and teachers.

So how does this increase in funding benefit postdocs? While none of the money has been allotted to increase the number of awarded F or K training grants, postdocs will benefit through increased funding on current grants via the creation of new postdoc positions or at least the extension of current contracts. Probably the best indication that NIH is concerned about the ever-increasing decline in the number of postdocs entering faculty positions is the $100 million allotted to fund new faculty positions. Awarded under a P30 (program center) mechanism, these grants will be used to fund approximately 117 faculty positions across the United States. The funding will be granted to academic institutions and organizations and be used to support the hiring of newly recruited faculty to develop research projects within the context of biomedical core centers. Those who receive these positions will be responsible for creating jobs within their core centers. Although less than 1 percent of the stimulus funds have been allotted to this program, there are still indications that NIH is aware that after two years, these faculty positions must be sustained. One could view this as a responsible start: addressing an issue on the minds of many current and former postdocs.

Challenge grants are another new mechanism to be funded by the director's office. Although usually lacking Principal Investigator (PI) status, postdocs may be eligible to apply if they have institutional support. However, due to the highly competitive nature of these awards, successful applicants will lose their new or young investigator status and thus not be eligible to apply for any pathway to independence or transition awards pertaining to new investigators. NIH also issued a request for administrative supplements, which allows for additional funding to active NIH Research Grants and Research Program and Center Grants (P), as well as Career Development Awards (K), Institutional Training Grants (T), Cooperative Agreements (U), and Educational Development Awards. Again, this will help postdocs by increasing funding and resources for positions including additional funded time for those under the K99/R00 mechanism, as well as employment for new postdocs, and extended support for senior postdocs. Each institute has established its own guidelines, so keep in mind that eligibility may vary among the institutes.

The National Postdoc Association (NPA) is actively involved in addressing the current and future needs of postdocs in this economic climate. When the ARRA was announced, the NPA applauded the administration for its recognition of the dire need for increases in scientific funding. Including the scientific enterprise in the stimulus bill is a start in the right direction, and the NPA hopes to see continued, stable funding in future budgets of federal granting agencies. The NPA was invited by the National Institute of General Medical Science (NIGMS) to provide input regarding how the Institute's funding should be allocated. The Executive Committee of the NPA Board of Directors composed a letter, and in addition to responding to the request of NIGMS, letters were also sent to several other institutes at

NIH. These letters enumerated four suggestions for programs that would use ARRA monies in a manner that would benefit postdoctoral scholars. These four points were: increased funding for training, increased support for grants supporting minority fellowships, development of a postdoc mentoring program, and the development of a support program for postdoc offices (PDOs) and associations (PDAs).

I. Increase Funding for Training

The NPA recommends an increase in funding for the Kirschstein NRSA award programs by at least 20 percent. This increase in funding could be used to raise stipends/salaries and/or support more awards. In the same vein, the NPA suggests that a portion of the increase in postdoctoral positions could be administered by fully funding current T32 institutional programs. Because actual funding is often lower than levels requested, T32s rarely support the number of postdoc positions applied for. Thus, increasing T32 funding could fund many "open" postdoc positions. Most postdoc positions are only for a few years, so supporting them will fit with the time limitations of the ARRA funding.

The NPA believes that an increase in funding for training is necessary for a transient period. An effort to hold more postdocs in these programs through September 2010 could ensure that the human resources needed for future economic growth are retained in the U.S. research enterprise. If the economy slows further, the job market for these highly trained and highly qualified scientists will dry up, and the field will be in danger of losing a generation of postdoctoral scholars to fickle economic forces.

II. Postdoctoral Fellowship Pilot Program for Minorities

The NPA recommends the development of a pilot program to examine the role of institutional postdoctoral fellowships in establishing and retaining new minority Ph.D. degree-holders. Preferably, these pilot programs would emphasize acquisition of academic tenure-track positions at top-tier research universities. Such pilot programs would provide fellowships for qualified minority postdoctoral scholars, as well as support for orientation and mentoring over an 18-month period. It would also require quantitative and qualitative evaluation and dissemination of lessons learned. Ideally, participating institutions would convene to share best practices at the end of the pilot project.

Such a short-term project would be an excellent use of ARRA funds, because it would immediately create new fellowships for minority postdoctoral scholars and have a long-term meaningful impact on the success of minority-targeted fellowship programming in academic institutions.

III. Pilot Initiative to Involve Senior Researchers in Postdoctoral Mentoring

The NPA recommends the establishment of a new program to provide funding for senior researchers to serve as full-time mentors to postdoctoral scholars.[a] These are the scientists who, in today's volatile science career environment, must examine all career options available and build the necessary transferable skills. This project would first require training for the mentors with regard to career options and would require support programs to which the mentors could refer postdoctoral scholars (*e.g.* training in cross-platform communication, media awareness, or development of leadership skills). The ARRA funds would provide an opportunity to establish a short-term pilot program for this endeavor.

Should the pilot prove successful and the program instituted, such an initiative would provide employment and transition funding for Principal Investigators from research to retirement. Thus, it could help address one of the recent phenomena highlighted as a reason for the lack of positions for new investigators as well as increased competition for R01 grants: scientists are increasingly waiting longer to retire.

IV. Support the Supporters

Many institutions have PDOs comprised of administrators who support postdocs, and/or PDAs composed of postdoc leaders. Both provide career and professional development and guidance to new scientists. The NPA believes that the current economic times call for an increase in such efforts if we are to retain this generation of postdoctoral scholars in the scientific workforce. We suggest a new funding initiative for the development of PDO- or PDA-based professional development programs at institutions.

The NPA continues to submit letters to NIH institutes and centers regarding the ARRA, and we will also continue to respond to any other legislation that may impact postdocs. It is through the establishment of relationships with granting agencies, Congress, and professional societies that we hope to influence the direction of science and the future of postdocs. For updates on the NPA and the ARRA, please visit the website: www.nationalpostdoc.org/recovery.

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FOOTNOTE

a. This idea was mutually developed with members of the FASEB Office of Public Affairs.

Accepting the Responsibilities of Our Degrees

BY PHILLIP A. ORTIZ

We live in difficult times. In the United States and beyond, there is a growing separation between political ideologies. During such times it would be easiest to take the path of least resistance, but the easy way is not necessarily the right way. Difficult times call for strong leaders. Not only do we need to dig deep within ourselves to summon courage and strength, but we need to look across our populace and recognize that the next generation of leaders will be more diverse than any before. Many Americans thought that they would never live to see a black man in the White House, but I believe that this is only one in a natural progression of events in which merit and intelligence will overwhelm stereotypes and birthrights.

The next generation's battles will occur in unusual places, including our classrooms. We have already seen battles over curricula in which the lines between religion and science have been blurred. Members of ASBMB, including President Gregory Petsko, have been fierce advocates for education and have been instrumental in leading informed discussions. Similarly, there have been battles over affirmative action in which laws have been overturned. It is ironic that these same battles were fought in 1991 when Clarence Thomas, arguably one of the most influential people to ever get a job he didn't deserve in the name of affirmative action, was appointed to the Supreme Court.

We, as highly educated scientists and teachers, should be on the leading edge of educational equity and social justice. In many years of attending graduations, I have been struck by the words of the college presidents as they confer the degrees and inform the students that they have earned all the "rights and privileges" that accompany the degrees. From the first time I heard those words it struck me that a key element was missing: the *responsibilities* that come along with their accomplishments.

Among my many roles at my institution, I serve in college governance. Thus, I engage regularly in conversations with my colleagues on a number of difficult topics. At times there are differences between the objectives of the faculty and those of the administration. To be certain that the correct decisions are made, it is necessary to first have an understanding of the complexities of the issues; second, honest conversations; and third, the strength of commitment.

As someone who regularly participates in college faculty reviews, I am acutely aware of the freedom that comes with tenure. As a unique aspect of educational employment, tenure was conceived as a means to protect faculty from political tides. It is at once a tool to provide the freedom to teach controversial ideas and, perhaps far more importantly, it embodies the *responsibility* to do so. In particular, I am very wary of anyone who promises to speak up only once they have tenure, as my experience has been that their behavior rarely changes.

Let me focus on *personal responsibility*. It can take many forms, and I'd like to share my story with you. My father, mother, brother, sister, and I earned our degrees at public universities, and several of us have since gone on to become educators—all at public institutions. Why is it that we have invested ourselves so much in the education of others? The answer is simple—because we ourselves have seen and experienced the transformative power of education. My parents both came from humble beginnings—first generation Americans and first generation college students. With each succeeding year, they were able to offer more and more to their children and their community. Not because of an inheritance or lottery winnings, but because they invested in themselves through education and encouraged and enabled their children to do the same. Their legacy will persist in that they have changed the lives of their children. Furthermore, by putting energy into becoming educators, we will hopefully touch the lives of many other people who will themselves pay it forward.

I know that some people may see the responsibilities of their degree as a burden and a distraction. But, as has been pointed out by others, we are facing a "quiet crisis" in which education is being eroded and undervalued, and, although we have begun to see the effects of this situation, it will take many years for the full effects to be apparent. It will take the work of many people to rise to this challenge. For too long we have been quiet for fear that we will be singled out as the "educated liberal elite;" and now we

should let it be known that "liberal" can also mean "liberated," in the sense that our eyes have been opened, and we see a new world of possibilities.

We need many excellent educators, role models, and mentors to inspire, guide, and support one another, and, to quote Shirley Jackson (a physicist and college president), "carry with them who they are" to transform this crisis into an opportunity. I am asking you, the members of ASBMB, not only to be leaders, but also to be informed and enlightened followers. Do not be afraid to ask the hard questions as well as answer them. Follow those who are worthy. And, when you feel ready, lead.

I would be remiss if I didn't point out that sometimes the best leaders are also the best followers. There will be times when someone else has the great idea or has begun the fight. At those times we need to be willing to recognize the good ideas and bravery of others and to stand beside them as they take the brunt of the counterattack. As Martin Luther King once said, "Our lives begin to end the day we become silent about things that matter," and thus, it is imperative that we engage our colleagues and students at every opportunity. We need to stand beside them when we believe that they are correct, guide them when they are wrong, and encourage them to seek truthful knowledge.

So, I encourage you to do what you can to give back to your communities, honor the investment others have made in you, contribute to our understanding of the world, empower yourselves and those around you, be agents of change, and most of all, embody the courage and dedication it will take to meet the challenges ahead.

The bottom line is that taking responsibility requires hard work, knowledge, courage, and the understanding that nothing good has ever come from ignorance, cowardice, and fear. Your educations have liberated you; you must look into yourselves, find your strength, and follow your hearts. There is no doubt that such a path is difficult. But there is also no doubt that it is right and worth doing. Moving down this path is your ultimate achievement.

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Matchmaking in Science

BY BARBARA PRESTON

After doing undergraduate research projects, working in a university lab, getting my Master's degree, working at NIH, earning my Ph.D. from Cornell University, and doing a four-year postdoc, I had burned out at the bench. I needed a break and decided to take time to work with friends in a marketing business. There, I discovered that I liked working with people, but I missed science. I wondered how I could combine the two.

Then I saw the ad. It said: "Still like science but tired of the bench?" "Yes. That's me," I thought. I read further and discovered that the ad was for a company that was looking for scientific recruiters to match scientists with biotechnology and pharmaceutical companies. I knew I had found my niche. I had long ago gotten over the disdain many of us in science have for sales. Even though we have to sell our ideas, hypotheses, and research to funding agencies, investors, department heads, or the public in general, we often hold sales or marketing people in contempt. But I enjoyed finding and offering solutions to people's problems as much as finding the answer to scientific questions. Why not help companies solve drug discovery questions by identifying and attracting top scientists with the appropriate laboratory skills and knowledge? I knew the area, I knew a range of scientists from my professional associations, and I understood the techniques and disciplines. It was matchmaking. Easy!

Except that nothing worth doing is ever easy. The company that placed the ad rejected my application and not just once! The vice president of human resources himself wrote to confirm their disinterest. Even though I had never heard of scientific recruiters before, I knew that it was what I wanted to do. But how would I start? I searched for a company that would train me. Even if I had to work for a recruiting agency in a non-scientific industry and switch to life science after learning the ropes, I would have. Eventually, I found a company that would take me; and they were actually looking for someone like me, with an advanced scientific degree to build that aspect of their biomedical recruiting office.

I immediately saw the potential of the position. Recruiting offered several things I wanted: an ability to stay in touch with life science research; lots of interaction with people; a way to feel that I was contributing (both to an individual's career advancement and the discovery of new therapeutics); freedom that comes with a job that can be done anywhere with phone and internet service; and an income based on my own initiative and productivity. But it wouldn't come cheaply. The learning curve in recruiting is steep and often painful. Sometimes companies that are looking for scientists haven't really identified what the right needs are for the position or haven't acknowledged the challenges it entails. As scientists, we often don't plan out our careers or identify what we want as our next step. Until I learned, as a recruiter, to walk people through those thought processes and confront difficult questions, I experienced more disappointment and frustration than success or reward. Too much of that causes most people to give up, which is a possible reason why so few scientists become recruiters.

For recruiters, companies are our clients. They are the ones with the need as well as the ability to pay for help. They need someone to contribute techniques, knowledge, and scientific interactions appropriate to their goals and culture. But companies, HR departments, and staff (rightfully) want to use every network of their

Preston

Barbara Preston made the transition to her current role as a scientific "talent scout" after many years as a research scientist. She obtained her B.S. and M.S. in microbiology at the University of Maryland, learned molecular biology at NIH, and earned her Ph.D. in pharmacology at Cornell University. She subsequently did her postdoctoral studies in neuroscience with the chair of the Department of Pharmacology at the University of California, San Diego. After a period of working in marketing, she joined the biomedical recruiting company MIS International. In 2003, she co-founded PharmaScouts, Inc. where she continues attracting top talent for biomedical companies.

own before using recruiting budgets for outside help. And as someone whom hiring managers or HR directors do not know, it is challenging to even get the opportunity to help fill a position.

Once a position opens up, there's plenty of research to do before any recruiting can begin. My approach to finding appropriate candidates to recruit is to find the right companies that have the right technology with the right programs, where the right scientists could be working. Most of my prospective recruits are somewhere on the continuum between "I love my job, the people, the rewards," and "I hate my job and dread going to work." It's important for me to find the person who has the right skills and the appropriate personality, who is ready to make a change for the right reasons, and to determine whether the position I'm working on can fit this individual's needs and goals. As a long-term thinker, I try to learn what's important to a person and build a relationship that will continue, even beyond this moment or opportunity. Everyone fits somewhere at some time.

> **"Recruiting offered several things I wanted: an ability to stay in touch with life science research; lots of interaction with people; a way to feel like I was contributing;... freedom that comes with a job that can be done anywhere with phone and internet service; and an income based on my own initiative and productivity."**

No one wants another job, but everyone wants an opportunity for something. It's that something that I try to identify and match between a company's need and a candidate's future. Ultimately, it is about finding someone who can come in, hit the ground running, and begin contributing quickly but who also has room to grow personally and professionally. That makes for long-term satisfaction—a good match—for everyone.

news from the hill *continued from page 7*

2009. This reflects the Administration's continued commitment to increasing science and technology spending. NSF also received $3 billion in stimulus money under the ARRA in March, so it faces a funding "cliff" as well.

The NSF proposed increase for 2010 was largely concentrated in Research & Related Activities, where ASBMB has traditionally focused its attention. These are the core research programs at the agency. R&RA went up 9 percent over 2009 to $5.642 billion, an increase of $459 million.

The full committee adopted the subcommittee bill on June 9.

There is no announced date yet for a markup of the L/HHS appropriations bill (which funds NIH) but rumor has it that it won't be taken up until July at the earliest. This bill is traditionally one of the most contentious. Chairman Obey has declared his intention to clear all 12 regular appropriations bills before the August recess. This is a very tall order, but with Democrats firmly in control of both houses of Congress and the White House, it may be possible.

Fauci Briefs Hill Staff on ARRA

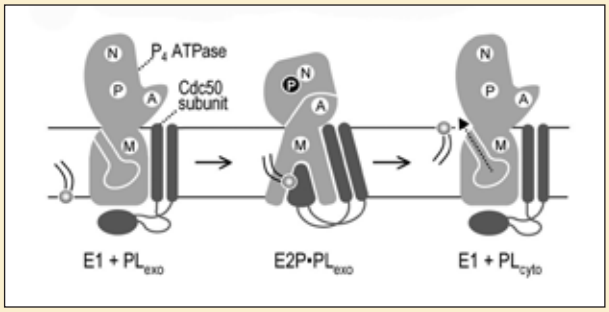
NIAID Director Tony Fauci gave a standing-room-only briefing for Congressional staff in June, detailing the Institute's plans for its stimulus funds. The briefing indicated that HIV/AIDS and influenza prevention projects will receive a good deal of the money. A video of the complete talk is available through the Ad Hoc Group for Medical Research Funding, at www.aamc.org/research/adhocgp/news.htm.

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

**Allen Dodson contributed to this article.*

"Flipping" the P-type ATPase Family

While most P-type ATPases pump small ions like calcium across membranes, growing evidence suggests that the P4 subfamily of these proteins catalyzes the transmembrane transport of phospholipids. Considering the fact that structural studies show that the mechanism of transport is conserved across the P-type family, a major challenge is uncovering how P4 ATPases adapt to accommodate phospholipids as opposed to small ions. P4 ATPases form complexes with Cdc50 proteins, and in this study, the researchers show that these Cdc50 subunits play a crucial role in the reaction cycle. The affinity of the yeast P4 ATPase Drs2p for its Cdc50 binding partner fluctuates during lipid transport, with the strongest interaction occurring at the point where the enzyme is loaded with phospholipid ligand. Looking at a purified Drs2p-Cdc50 complex, the researchers also find that catalytic activity relies on direct and specific interactions between the subunit and transporter. A general belief is that P4 ATPases evolved from ion transports to flippases, and this study provides evidence that acquiring these Cdc50 subunits might be a key step in that evolution.



Cartoon model of the reaction cycle-dependent transporter/subunit rearrangements of the P4 ATPase/Cdc50 complex.

Cdc50p Plays a Vital Role in the ATPase Reaction Cycle of the Putative Aminophospholipid Transporter Drs2p

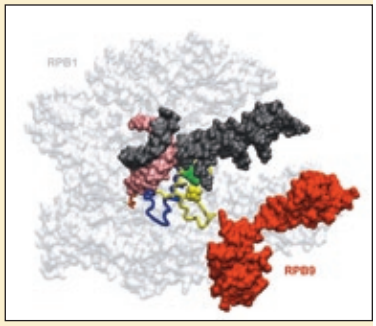
Guillaume Lenoir, Patrick Williamson, Catheleyne F. Puts, and Joost C. M. Holthuis

J. Biol. Chem., published online May 2, 2009

jbc

Polymerase II: Now Twice as Faithful

Maintaining enzyme fidelity is perhaps the most crucial concern for DNA transcription. The fidelity of the RNA transcription polymerase (Pol) II, for example, has been shown to be mediated by the trigger loop, a mobile structural element within the large Rpb1 subunit, during nucleotide isomerization. There is some evidence to suggest, though, that the peripheral and non-essential Rpb9 subunit may also be involved in transcription fidelity. In this study, the researchers provide more solid evidence for this by establishing a genetic interaction between Rpb9 and the trigger loop. They demonstrate that Rpb9-deficient Pol II results in a significant decrease in fidelity *in vitro*, while deletion of the *RPB9* gene in yeast shows synthetic lethality when combined with the low-fidelity *rpb1-E1103G* mutation. Further analysis revealed that *RPB9* deletion promotes the sequestration of NTPs in the polymerase active center prior to the formation of phosphodiester bonds, leading the researchers to suggest that the Rpb9 subunit controls transcription fidelity by delaying the closure of the trigger loop on the incoming NTP.



Structure of *Saccharomyces cerevisiae* Pol II showing how RPB9 might stabilize the open conformation of the trigger loop (shown in *yellow*; closed conformation is shown in *blue*) to help ensure proper transcription fidelity. (The DNA backbone and RNA are shown in *dark gray* and *pink*, respectively.)

RPB9 Subunit Controls Transcription Fidelity by Delaying NTP Sequestration in RNA Polymerase II

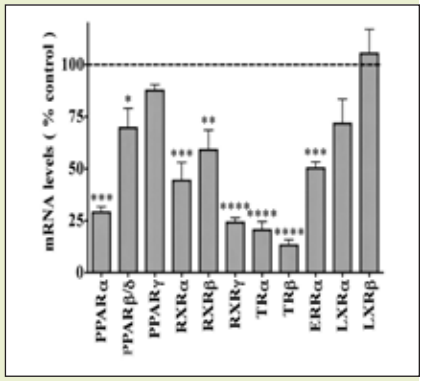
Celine Walmacq, Maria L. Kireeva, Jordan Irvin, Yuri Nedialkov, Lucyna Lubkowska, Francisco Malagon, Jeffrey N. Strathern, and Mikhail Kashlev

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

jbc

Oxidation and Ventilation

Respiratory failure is a major cause of mortality due to septic shock, in part due to decreased contraction of ventilatory muscles like the diaphragm. This contraction failure might occur as a result of abnormalities in fatty acid oxidation, a major metabolic pathway for these muscles with high energy demands. In this study, the researchers demonstrate that treatment with lipopolysaccharide (LPS) or zymosan, good models of septic shock, decreased the expression of several nuclear hormone receptors and other proteins required for fatty acid uptake and oxidation in the diaphragms of mice: the affected proteins include LPL, FATP1, CPT-1β and PPARα/β/δ. In PPARα-deficient mice, though, CPT-1β and FATP-1 levels were already decreased and were not further affected by LPS, suggesting that the PPARα signaling pathway plays a pivotal role in inducing some of the observed changes in protein expression. The decreased fatty oxidation in the diaphragm likely arises from the body's attempt to generate additional VLDL particles to combat infection, which, however, puts an increased burden on the diaphragm and creates an increased risk of respiratory failure.



LPS infection can reduce the expression of several nuclear hormone receptors in the diaphragms of mice.

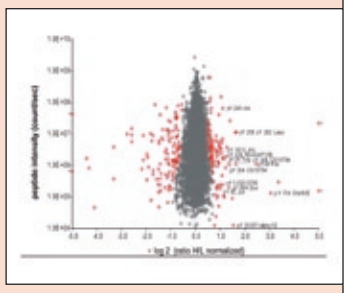
Infection Decreases Fatty Acid Oxidation and Nuclear Hormone Receptors in the Diaphragm

Kenneth R. Feingold, Arthur Moser, Sophie M. Patzek, Judy K. Shigenaga, and Carl Grunfeld

J. Lipid Res., published online May 14, 2009

The Depth of Ptp61F Loss

Signal transduction, particularly phosphorylation-based signaling, regulates almost all aspects of biological function in metazoans and contributes to countless diseases when defunct or aberrant. Analyzing perturbations in phosphorylation-based signaling networks is typically conducted through a hypothesis-driven approach, but in this study, the researchers applied a high-resolution mass spectrometry-based approach to determine the systems response to the elimination of *Drosophila* phosphatase Ptp61F—the ortholog of mammalian PTB1B. Following RNA interference (RNAi) knockdown of *Drosophila* Schneider cells, they used stable isotope labeling by amino acids in cell culture (SILAC)-based quantitation to find that Ptp61F deficiency minimally affected the proteome; apart from the phosphatase, only 288 of 6,478 high confidence phosphorylation sites changed significantly (217 serines, 45 threonines, and 26 tyrosines). The alterations include previously described Ptp61F substrates such as Stat92E and Abi, as well as up-regulated phosphotyrosine sites on GTPase regulating proteins (RhoGAP15B and Vav) and constituents of focal adhesions (Paxillin and Lasp), which expand the proposed involvement of Ptp61F into the regulation of cytoskeleton organization.



Scatter plot of normalized ratios of all quantified phosphorylation sites against their summed heavy and light peptide intensities upon RNAi knockdown of Ptp61F.

Systems-wide Analysis of a Phosphatase Knockdown by Quantitative Proteomics and Phosphoproteomics

Maximiliane Hilger, Tiziana Bonaldi, Florian Gnad, and Matthias Mann

Mol. Cell. Proteomics, published online May 9, 2009

Britton Chance: Former Olympian and Pioneer in Enzyme Kinetics and Functional Spectroscopy

BY NICK ZAGORSKI

In the heart of historic Philadelphia lies the headquarters of the American Philosophical Society (APS), a learned society that offers a testament to the incredible thinkers, past and present, who have helped shape the United States. Not too far away, on the campus of the University of Pennsylvania, one of the society's members is busy at work, offering his own testament to longstanding scholarly excellence. For even at 95 years of age, there is no slowing down for Britton Chance, the Eldridge Reeves Johnson University professor *emeritus* of Biophysics, Physical Chemistry, and Radiologic Physics at Penn.

Born in nearby Wilkes-Barre, PA in 1913, Chance, occasionally referred to as the "father of modern biophysics," has been making contributions to science, medicine, and engineering ever since producing his first practical invention as a teenager.

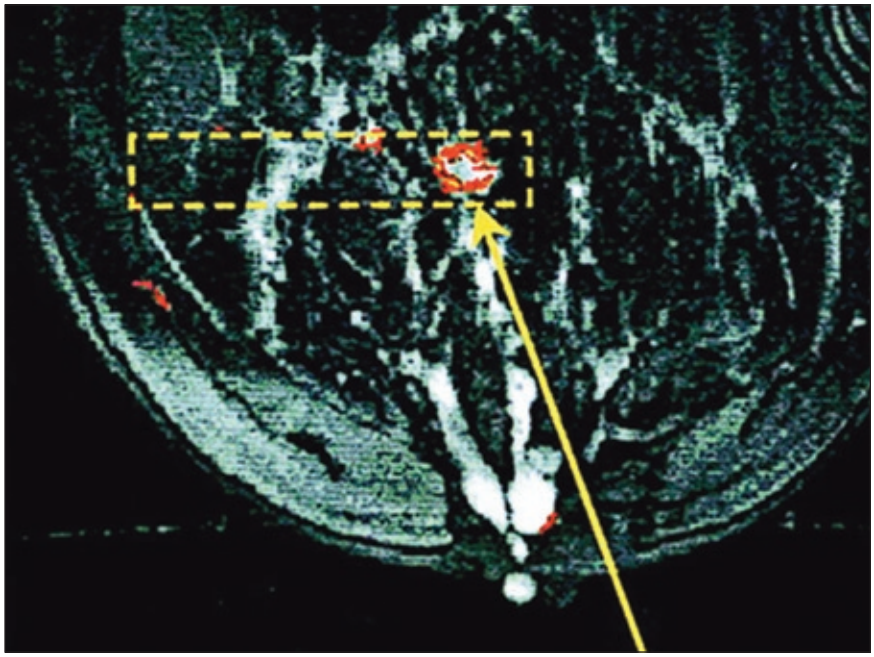
From his elucidation of enzyme-substrate compounds, to his insights into mitochondrial physiology, Chance helped bring forth a renaissance in biochemistry research, while his studies into photon migration through tissues and his advances in magnetic resonance spectroscopy have transformed the field of biomedical optics. His countless scientific honors include memberships in the APS, the National Academy of Sciences, and the Royal Society of London. He has also received the National Medal of Science, the Pennsylvania Award for Excellence in Life Sciences, and the APS Benjamin Franklin Medal for Distinguished Achievement in the Sciences.

Yet just think, all of these scientific achievements may never have happened, if not for Chance's love of a few of nature's simple gifts: the sun, the sea, the wind, and a sail to catch it.

Sailing for the Stars

For Britton Chance, science and sailing have been intertwined for as long as he can remember, and he may not have achieved greatness in one area if not for the other. His love of the sea dates back to some of the earliest summers of his youth, when he went sailing and fishing with his family throughout the Caribbean and Latin America.

His enthusiasm for sailing grew rapidly, as did a competitive spirit to excel, and in the years since his early sailing adventures, Chance has challenged his sailing skills throughout the world, from the local waters outside Philadelphia to exotic locales such as Indonesia, Tahiti, and the Galapagos Islands. His talents even took him to the pinnacle of the sport; in 1952, Chance was part of the three-man



Chance has been a pioneer in the field of biomedical optics, including studies combining near-infrared diffuse optical tomography (DOT) and magnetic resonance imaging (MRI) to identify tumors in breast tissue, like the ductal carcinoma above.
Vasilis Ntziachristos et al., *PNAS* (2000) **97**, 2767-2772.

Besides the laboratory, there is no place Chance loves more than a sailboat on the open sea.

> *"...even at 95 years of age, there is no slowing down for Britton Chance..."*

crew, along with Edgar and Sumner White, which won the Olympic gold medal in the 5.5-meter class sailing event at the Helsinki games.

That spirit continues to this day, and Chance, who considers life without sailing unendurable, is always just steps away—figuratively—from his boat, ready to set sail. (It's an infectious spirit as well; Chance's son, Britton Jr., has followed in his father's wake. He has become a renowned ship designer and has been an integral part of many America's Cup yachts.)

Long before his Olympic victory, however, Chance's passion for sailing proved to be the catalyst for his first major contribution to science. At the tender age of 13, Chance, the son of an engineer, used his burgeoning mechanical skills to design and build an autosteering device that detected deviations in a ship's course and generated a feedback signal to redirect and correct the ship's steering—a simple yet elegant invention that would forever shape the course of Chance's career.

The Enzyme Enigma

In 1931, Chance enrolled at Penn to study chemistry and engineering, and after receiving his B.S. in 1935, he stayed on to conduct graduate studies in enzyme kinetics. Enzymes were an elusive beast at this time—there were many theories about how they worked but no experimental data to back any of them up. Chance, who always enjoys a challenge, took on this enzyme mystery. As he points out, "I used elements of engineering, electronics, and mechanics to build my automatic feedback circuit, and studying enzyme kinetics required those exact same skills and more."

Chance was intrigued with the theory put forth by Leonor Michaelis and his graduate student, Maud Menten, in 1913, which proposed that enzymes actually combined with their substrates to form an intermediate complex. "The trick," says Chance, "was finding a method to observe this combination within an extremely rapid reaction." Two separate events would lead him to the solution. First was his own observation that adding hydrogen peroxide to a crude extract of horseradish peroxidase could produce a colored compound; the second was reading about a stop-flow apparatus developed by Cambridge University researcher Glenn Millikan that could measure the rate of formation of oxymyoglobin.

Chance believed he could modify Millikan's apparatus to study more rapid reactions by measuring colorimetric output; so, in 1937, he started building a "rapid-flow" apparatus, incorporating some features from his own photoelectric autosteering device. Not long after, the British General Electric Company offered Chance a contract to test out his autosteerer on a ship sailing from London to New Zealand and Australia. Chance took this opportunity to introduce himself to Millikan and ask if he could study with him. Millikan agreed, and after Chance returned from his seafaring

adventure, he and Millikan constructed a second rapid-flow apparatus and tested it with preliminary studies on luciferase reactions.

In 1940, Chance returned home to visit his parents, but this temporary trip became permanent following the continued escalation of World War II. Unable to continue his work with Millikan, Chance resumed his studies at Penn and began building a third version of the rapid-flow apparatus. The design involved emptying two syringes, one filled with peroxide and a chemical reagent called leuco-malachite green (MG) and the other filled with peroxidase, into a narrow tube that flowed towards a photocell. Inside the cell, peroxidase would convert leuco-MG to malachite green, which could be measured with a spectrometer.

By varying the peroxide or leuco-MG concentrations, Chance could determine any changes in reaction rate or equilibrium and thus assay the kinetics of the reaction. "And, by comparing my results with Michaelis and Menten's predicted results on a point by point basis, I was able to provide the proof to their theory," he says. In 1950, Chance received the Paul Lewis Award in Enzyme Chemistry for these groundbreaking studies, the first of many scientific honors he would receive.

> *"…these scientific achievements may never have happened, if not for Chance's love of a few of nature's simple gifts: the sun, the sea, the wind, and a sail to catch it."*

Helping the War Effort

While Chance's development of the stop-flow method for measuring enzyme kinetics would usher in a new era of biochemistry, he hardly had time to celebrate. In 1941, with war continuing to rage and with U.S. involvement drawing ever nearer, Chance left Penn—and his newly appointed assistant professor position in the Department of Biophysics and Physical Biochemistry—to participate in secret government research at the MIT Radiation Laboratory. Here, Chance became part of an international team focused on improving nascent radar technology for defense efforts.

Chance recalls those eventful years at MIT: "I was working 80-hour weeks, trying to oversee a 300-person lab, with the Army, Navy, and Air Force constantly breathing down my neck." Still, the efforts were for a great cause, and they ultimately proved successful: Chance notes that over 5,000 planes in both the Pacific and European theaters employed the technology his lab helped develop, including the aircraft involved at the beaches of Normandy.

After the war concluded, Chance went to the Karolinska Institute in Stockholm to work alongside the renowned Hugo Theorell, one of the greatest contributors to our knowledge of oxidative enzymes like peroxidases. (Theorell would later win the Nobel Prize in Medicine for this work in 1955.) "Mr. Guggenheim was offering his fellowships to individuals who had given up their own careers for the war effort, which was extremely nice, and I was lucky enough to receive one," Chance notes. Together with Theorell, Chance refined his stop-flow apparatus design and used it to elucidate the role of NAD in the cellular oxidation of alcohol, a reaction that would later be dubbed the Theorell-Chance mechanism.

Following his fellowship, Chance returned to Penn in 1947, grateful that the university had been kind enough to retain his faculty post during his long absence. He would definitely repay that gesture over the next 60 years as he helped place Penn at the forefront of biochemical and biophysical research with his extraordinary work.

Renewed Energy

Following his sailing success at the 1952 Olympics—"that was the one year where sailing took complete priority over science," Chance notes, "but it also helped invigorate my research. Having conquered the waters, I was ready for an even bigger challenge, tackling the great unknowns of biochemistry."—Chance decided to shift the focus of his enzyme studies to look at oxidative phosphorylation and electron transfer in mitochondria. For someone with a lifelong interest in athletics and staying fit, the study of bioenergetics seemed a natural choice.

Using his inventive mind yet again, Chance worked out a method to separate mitochondria from cells while preserving their metabolic activity and also designed a dual wavelength spectrophotometer (a machine still often used today) that could measure ATP synthesis in the isolated mitochondria. With these techniques, Chance carried out a long series of experiments that revealed previously unknown details about the nature of various electron transport coenzymes, the localization of respiratory chain components, the effects of altering oxygen concentra-

Chance receives an honorary degree from Huazhong University of Science and Technology in April 2009.

tion, and the role of molecules like calcium and manganese.

These studies also led to one of the most surprising moments of Chance's career: the discovery of electron tunneling in biological systems. "This idea had never even been hypothesized, let alone tested," he says. "Yet, we were studying photosynthesis in bacteria, and we observed electron transfer at liquid nitrogen temperatures, which meant the transfer couldn't be a thermal process; it had to be physical. It really shook the hell out of me."

Medical Miracles

In the 1970s, Chance began wondering if he could broaden his bioenergetic spectroscopy studies to look at whole tissues or even organs. His idea stemmed from a research group at Oxford who had found that phosphorous NMR (which measures the chemical shifts of the phosphorous isotope ^{31}P) could track metabolites in living tissue. Chance then set out to improve the use of NMR technology in living systems, and soon his lab produced groundbreaking observations of active metabolism and cellular respiration in whole animal organs such as brain, heart, and liver, as well as in living leg muscle of a human subject. (In an interesting coincidence, Edward Purcell, who discovered NMR in 1946, also worked on radar development at the MIT Radiation Lab.)

Chance's leg muscle subject also became the first human patient diagnosed with the aid of NMR technology. "That particular individual happened to have a genetic deficiency in phosphofructokinase, which prevents skeletal muscle from properly metabolizing carbohydrates," says Chance, "and we were able to describe it and eventually remedy it. That patient has lived a happy and healthy life ever since."

"Now, clinical studies have always been of interest to me," says Chance, who was director of the Elridge Reeves Johnson Foundation at the Penn School of Medicine from 1949 to 1983, "but the success of treating that bioenergetic defect certainly spurred me on to look at other biomedical applications for optical spectroscopy."

Over the years, Chance has done exactly that, first with NMR and later moving on to near infrared (NIR) spectroscopy. Through his group's efforts, physicians now have access to non-invasive diagnostic equipment that can analyze cancer progression, brain oxygenation, internal bleeding,

and even changes in muscle activity during strenuous exercise. In recognition of these efforts, Chance was appointed president of the Medical Diagnostic Research Foundation (MDRF) in Philadelphia in 1995.

A Journey East

Britton Chance has observed, frequently firsthand, some of the great advances in scientific knowledge in the 20th century. So what does he think the next century holds in store in the areas of biophysics and spectroscopy? "I certainly think microelectronics, or more specifically, microoptics, will invade all parts of the body."

Just recently, Chance himself, along with collaborator Ata Akin at Drexel University, invented a hand-held device—not much bigger than a cell phone—that can detect breast cancer by measuring the differences in blood oxygen ratios of normal breast tissue and angiogenesis-rich tumors. Considering the improvement over the bulky devices employed just a generation ago, one can understand how micro-sized devices may indeed be a part of our near future.

With scientists in Asia taking a prominent role in the field of microoptics, Chance has now added "diplomat" to his repertoire of titles that includes scientist, educator, inventor, and sailor. He has helped set up labs and collaborations in Taiwan (National Cheng Kung University in Tainan), China (the Britton Chance Center for Biophotonics in Hunan), and Singapore (Biopolis Biomedical Research Center) to advance these efforts and has just embarked on a several-month-long trip to these sites to share his expertise. (though officially an *emeritus* professor since 1983, Chance has remained very active in both his lab and at the University level.)

Of course, it's not going to be all business. The waters of South Asia—Singapore, Malaysia, Indonesia—happen to be some of Chance's favorites, so he'll definitely find some time to take in a peaceful sunset sail and reflect upon his outstanding career.

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

Still Going Strong: Chance Wins 2009 IUBMB Medal

Les Dutton, a former Chance postdoc and his successor as director of Penn's Johnson Foundation, notes that his former mentor "has an international view on life." This view can be seen in Chance's own endeavors in spreading and advancing science in China and Singapore, the geographically diverse scientists who have come to study with him over the years, and even the highly multidisciplinary nature of his studies. When taking all three measures into account, it is perhaps fitting that at the 21st International Union of Biochemistry and Molecular Biology (IUBMB)/ 12th Federation of Asian and Oceanian Biochemists and Molecular Biologists (FAOBMB) Congress this August in Shanghai, Britton Chance will be presented with the IUBMB Medal (IUBMB President Angelo Azzi, who will present the medal, is a former Chance postdoc).

In honor of this event, the IUBMB Congress will feature a symposium in tribute to Chance's legacy and accomplishments that will include noted speakers George Radda and Aaron Ciechanover, among others. Dutton stresses, however, "this symposium is not a retrospective; Brit does not like that term." Rather, the Britton Chance symposium will encompass the themes of Chance's many scientific discoveries—from myoglobin/hemoglobin oxygenation to optical diagnostics—in a contemporary framework, highlighting where Chance's discoveries have led researchers today, and where they're going in the future. Much like Britton Chance, this will be a forward-looking affair.

Out of Focus: Speaking of Medals

While the IUBMB Medal will be the newest addition to Chance's long and deserved list of honors, it may surprise some to learn what Chance considers one of his favorite awards. "I think receiving the Gold Medal of the American Roentgen Ray Society [in 2006], which I received for my work on non-invasive breast cancer imaging, was the most pleasantly surprising," he says. As to why recognition by the oldest radiological society (founded in 1900) in the U.S. is so noteworthy, Chance notes that "they're a pretty closed shop, so being honored as a non-radiologist was exciting."

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ORGANIZER:
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Eugene Koonin, NCBI, NIH
Gregory Petsko, Brandeis University

Friday, October 23 — METABOLISM
Valérie de Crécy-Lagard, University of Florida
Eric Gaucher, Georgia Institute of Technology
Vadim Gladyshev, University of Nebraska
Carole Lartigue, J. Craig Venter Institute

Saturday, October 24 — STRUCTURE
John-Marc Chandonia, Lawrence Berkeley National Laboratory
Aled Edwards, University of Toronto
Nick Grishin, UT Southwestern - HHMI
Alexey Murzin, MRC Laboratory of Molecular Biology, Cambridge, UK

Sunday, October 25 — NETWORKS
Arcady Mushegian, Stowers Institute for Medical Research
Frederick Roth, Harvard University
Andrey Rzhetsky, University of Chicago
David Sprinzak, California Institute of Technology

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www.gerli.com/rennes2009english.htm

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

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SWLA 4th Annual Scientific Forum
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JULY 25–29, 2009
BOSTON, MA
www.proteinsociety.org

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

AUGUST 2009

3rd EU Summer School in Proteomic Basics: Protein Modification and Quantification
AUGUST 2–8, 2009
SOUTH TYROL, ITALY
www.proteomic-basics.eu

21st IUBMB and 12th FAOBMB International Congress of Biochemistry and Molecular Biology
AUGUST 2–7, 2009
SHANGHAI, CHINA
www.iubmb-faobmb2009.cn/iubmb/page/index.jsp#

11th International Congress on Amino Acids, Peptides, and Proteins
AUGUST 3–7, 2009
VIENNA, AUSTRIA
www.meduniwien.ac.at/ICAAP09

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

Gordon Research Conference: Molecular, Biophysical, & Biomechanical Understanding of Skin Barrier Formation, Function, & Disease
AUGUST 9–14, 2009
WATERVILLE VALLEY, NH
www.grc.org/programs.aspx?year=2009&program=barrier

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

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

Gordon Research Conference: Mechanisms of Cell Signaling
AUGUST 23–28, 2009
OXFORD, UNITED KINGDOM
www.grc.org/programs.aspx?year=2009&program=mechcell

9th International Symposium on Mass Spectrometry in the Health and Life Sciences: Molecular and Cellular Proteomics
AUGUST 23–27, 2009
SAN FRANCISCO, CA
www.msf.ucsf.edu/symposium

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

SEPTEMBER 2009

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

British Atherosclerosis Society Meeting on Genetics of Complex Diseases
SEPTEMBER 17–18, 2009
CAMBRIDGE, UNITED KINGDOM
www.britathsoc.org

MWLA Annual Scientific Forum
SEPTEMBER 25–27, 2009
CINCINNATI, OH
www.lipid.org

HUPO 8th Annual World Congress
SEPTEMBER 26–30, 2009
TORONTO, CANADA
www.hupo2009.org/default.htm

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

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

OCTOBER 2009

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

SACNAS National Conference: Improving the Human Condition: Challenges for Interdisciplinary Science
OCTOBER 15–18, 2009
DALLAS, TX
www.sacnas.org/confnew/confclient

7th Euro Fed Lipid Congress
OCTOBER 18–21, 2009
GRAZ, AUSTRIA
www.eurofedlipid.org/meetings/graz/

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

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

2009 Swiss Group for Mass Spectrometry Meeting
OCTOBER 28–29, 2009
BEATENBERG, SWITZERLAND
www.sgms.ch

NOVEMBER 2009

Annual Biomedical Research Conference for Minority Students
NOVEMBER 4–7, 2009
PHOENIX, AZ
www.abrcms.org/index.html

7th Annual World Congress on the Insulin Resistance Syndrome
NOVEMBER 5–7, 2009
SAN FRANCISCO, CA
www.insulinresistance.us

Annual Meeting of the Society for Glycobiology
NOVEMBER 12–15, 2009
SAN DIEGO, CA
www.glycobiology.org

American Heart Association Scientific Sessions 2009
NOVEMBER 14–18, 2009
ORLANDO, FL
www.scientificsessions.org

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

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

DECEMBER 2009

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

FEBRUARY 2010

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

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

APRIL 2010

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

JUNE 2010

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

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

AUGUST 2010

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

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

APRIL 2011

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

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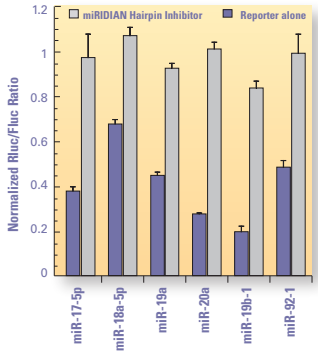

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