

HAPPY HOLIDAYS ASBMB MEMBERS

ASBMB

today

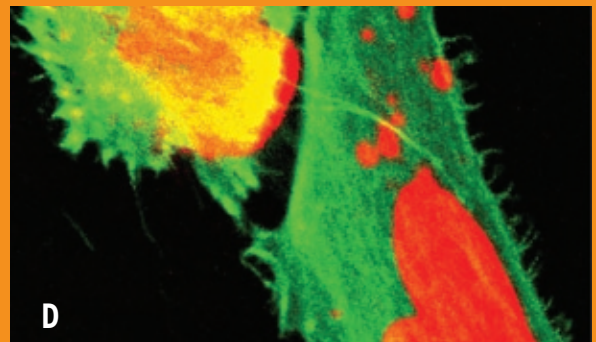
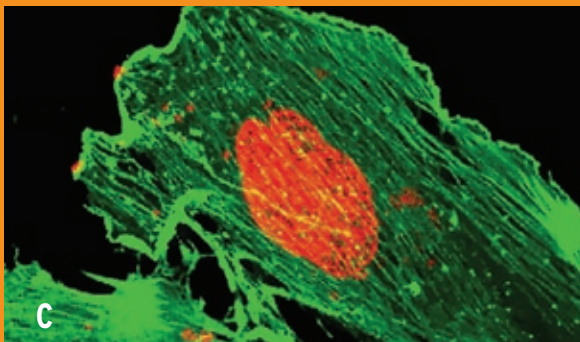
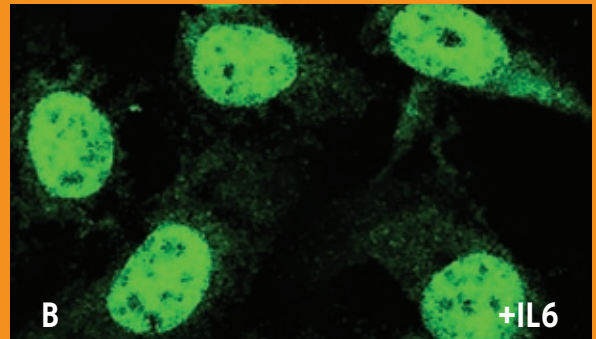
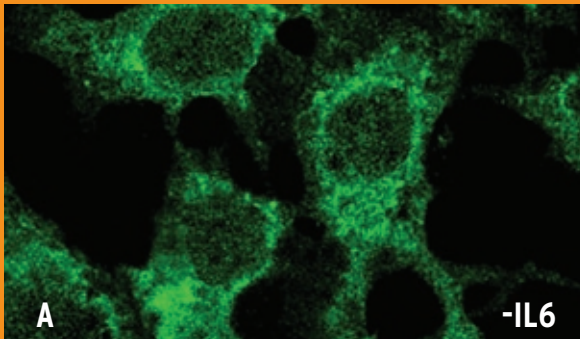
December 2008

***Structure &
Symmetry***

American Society for Biochemistry and Molecular Biology

See Your Proteins

with 37,000 GFP-tagged ORF clones



GFP-tagged TrueORF clones are transfected into HEK293 cells and the tagged proteins are visualized during IL-6 induced nuclear translocation (STAT3, panel A and B) and in filopodia and stress fiber formation (Actin, panel C and D).

TrueORF™

Genome wide ORF clones
for tagged protein expression

- C-terminal tag of GFP
- Sequence verified and guaranteed
- Easily shuttled into 20 destination vectors
- Transfection-ready: 10ug plasmid DNA

OriGene salutes
the GFP pioneers
for their Nobel
Prize award

 **ORIGENE**
Your Gene Company

origene.com/orf



society news

- 2 From the Editor
- 3 President's Message
- 5 Letters to the Editor
- 6 Washington Update
- 12 Retrospective:
Anthony G. San Pietro

special interest

- 13 Science's Role in Foreign Policy
- 14 ASBMB Round Table:
Jim Wells and Mary Woolley
- 16 Keeping Women in Science
- 19 Grammar and Writing Tips

2009 meeting

- 20 The 2009 Fritz Lipmann
Lectureship: Douglas C. Rees
- 21 The 2009 ASBMB Merck
Award: John Kuriyan
- 22 The 2009 FASEB Excellence in
Science Award: Susan Lindquist

science focus

- 30 Sung-Hou Kim: Consummate
Crystallographer

departments

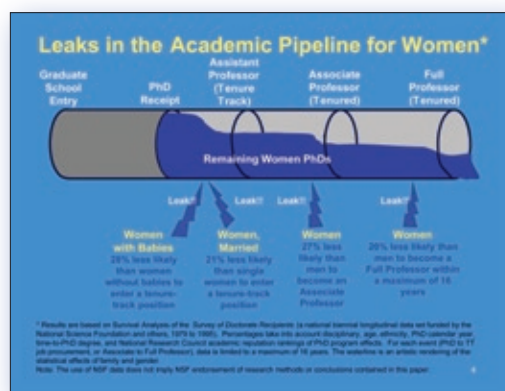
- 7 News from the Hill
- 10 Member Spotlight
- 23 Education and Training
- 26 Minority Affairs
- 28 BioBits

resources

- 34 Career Opportunities
- 36 Calendar

ON THE COVER:
Captivated by the symmetry of molecular structure, Sung-Hou Kim has been a leader in revealing symmetry through his studies in crystallography and structural genomics. 30

FASEB releases new
Breakthroughs in
Bioscience. 6



A leaky pipeline for women scientists.
16

podcast summary

Check out this month's podcast where we talk with contributors to the upcoming JBC Thematic Minireview Series on Alzheimer Disease.

For this and other ASBMB AudioPhiles podcasts go to:
www.asbmb.org/audio.aspx



Officers

Gregory A. Petsko *President*
Heidi E. Hamm *Past President*
Mark A. Lemmon *Secretary*
Merle S. Olson *Treasurer*

Council Members

Dafna Bar-Sagi Alan Hall John D. Scott
Joan A. Steitz Ann M. Stock
Kevin Struhl James A. Wells Adrian Whitty

Ex-Officio Members

Ellis Bell
Chair, Education and Professional
Development Committee
Laurie S. Kaguni
Chair, Meetings Committee
John D. Scott
Chair, Membership Committee
George Hill
Chair, Minority Affairs Committee
Joan W. Conaway
James H. Hurley
Co-chairs, 2009 Program Committee
Ralph A. Bradshaw
Chair, Public Affairs Advisory Committee
Toni M. Antalis
Chair, Publications Committee
Herbert Tabor
Editor, *JBC*
Ralph A. Bradshaw
A. L. Burlingame
Co-editors, *MCP*
Edward A. Dennis
Joseph L. Witztum
Co-editors, *JLR*

ASBMB Today Editorial Advisory Board

Alex Tokor
Chair
Greg P. Bertenshaw Craig E. Cameron
A. Stephen Dahms Irwin Fridovich
Jonathan Gitlin Richard W. Hanson
Elizabeth A. Komives Bettie Sue Masters
Luke A. O'Neill Duanqing Pei
Carol C. Shoulders Robert D. Wells

ASBMB Today

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

Magazine design & production: Amy Phifer

For information on advertising contact
Capitol Media Solutions at 800-517-0610
or Danf@capitolmediasolutions.com



A Year of ASBMB Today

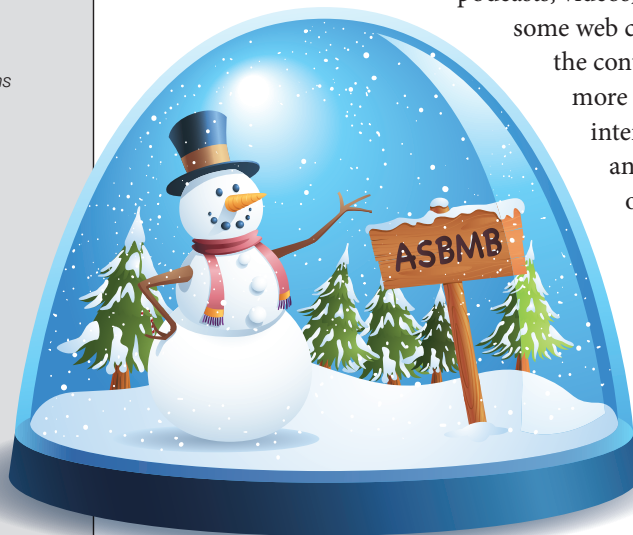
BY NICOLE KRESGE

As this year winds down and the holiday season sets upon us, I can't help but reflect upon what a momentous year 2008 has been for *ASBMB Today*. We've run stories on everything from Carolyn Bertozzi's innovations in glycobiochemistry (February 2008) and a tax primer for postdoctoral fellows (March 2008) to a summary of where Presidential candidates John McCain and Barack Obama stand on issues related to biomedical research (October 2008). This year marked the debut of a new series of articles called *ScienCentric*, which featured the Rutgers Center for Lipid Research (May 2008) and Cornell's Weill Institute for Cell and Molecular Biology (September 2008), and we also started up a new column called *Sci.Comm* (September 2008), which covers the intersection between science communication and communication technology. And finally, we launched an *ASBMB Today* Round Table series by interviewing Nobel laureate and political activist Peter Agre (October 2008).

2008 also marked a huge step for *ASBMB Today* in the electronic world. In January, we unveiled the launch of our new digital magazine—an interactive, vivid replica of the print edition which offers our readers an experience very much like an ink-and-paper magazine delivered electronically. Using this platform, we were able to include online-only features in the magazine, such as a video centerfold featuring movies from presentations at the 2008 annual meeting (June 2008) and a slide show of Cornell's Weill Institute for Cell and Molecular Biology (September 2008). We were also able to provide *ASBMB Today* readers with pop-up links to podcasts related to specific articles, such as a chat with *MCP* Editorial Board Member Robert Chalkley about his trip to the World HUPPO meeting in Amsterdam (November 2008).

And finally, we won a 2008 APEX Award for Publication Excellence in the category of Most Improved Magazines and Journals.

In 2009, we intend to continue improving both the digital and print magazine. We'll take further advantage of the digital platform, offering more podcasts, videos, slide shows, and perhaps even some web chats. We also hope to improve the content of our magazine, adding more articles that cater to our readers' interests. As always, we appreciate any suggestions or comments from our readers, so please send them to asbmbtoday@asbmb.org.
Happy Holidays! ☺



Nicole Kresge



First Impressions, Second Chances

BY GREGORY A PETSKO

By now most of you have probably heard at least something about the reforms to the peer review system that the National Institutes of Health (NIH) is in the process of implementing. I've been interested in this topic for many years and have written extensively about the troubles peer review was going through because of the funding crunch. I also proposed a set of changes to the process, and I'm delighted to see that the committees that recommended the new peer review guidelines seem to have reached many of the same conclusions that I did. But one item in particular that I considered recommending but decided against after long deliberation is a major feature in the new process. It's worth going over the way these reforms were developed, because it will help explain why I think that one of them in particular deserves rethinking.

The assessment of peer review has been going on for over a year now. In June 2007, Elias Zerhouni, then NIH Director, initiated the effort to formally review the NIH peer review system. External and internal working groups, with input from both internal and external communities, considered all aspects of the reviewing process. The year-long effort, which resulted in selected recommendations, included the following phases.

1) Diagnostic Phase

The diagnostic phase involved an in-depth evaluation of the current NIH peer review system. In June 2007, Zerhouni established two working groups: Externally, the Advisory Committee to the Director Working Group (ACD WG), co-chaired by Keith Yamamoto of the University of California, San Francisco, and Lawrence Tabak, Director of the NIH National Institute of Dental and Craniofacial Research (NIDCR); and Internally, the Steering Committee Working Group (SC WG), co-chaired by Tabak and Jeremy Berg, Director of the NIH National Institute of General Medical Sciences (NIGMS). The working groups solicited formal input from key stakeholders before releasing the Final Draft Report on Feb. 29, 2008, which documented the outcome of the diagnostic phase and described a preliminary set of recommendations.

2) Design Implementation Phase

In March 2008, Zerhouni established the Steering Committee Peer Review Implementation Group to draft implementation plans for each recommendation in the Phase 1 report. The committee convened subgroups led by Berg, Tabak, and Story Landis, Director of the National Institute of Neurological Disorders and Stroke (NINDS). Subgroup membership consisted of NIH program and review officers, planning and evaluation experts, and statisticians. Feedback was solicited from both NIH internal and external communities. This feedback, together with careful consideration of the pros and cons of both individual and combined recommendations, was what led to the final decisions on enhancements—that's the word NIH uses; apparently they're nervous about calling them reforms—to the peer review system.

On June 6, 2008, Zerhouni announced the Peer Review Enhancements and Implementation Plan (see the press release at tinyurl.com/6ddu2t), and Tabak presented the Implementation Plan to the Advisory Committee to the Director (ACD).

3) Implementation Phase

In July 2008, Zerhouni established a Peer Review Oversight Committee (PROC)—I know, I know, we ought to declare this an acronym-free column, but believe me, if you deal with Washington, this is the way you have to write to initiate implementation. The PROC, chaired by NIH Deputy Director Raynard Kington, who has just been appointed acting director following the resignation of Zerhouni, established subgroups consisting of NIH program, review, grants management, and evaluation staff to assist with the implementation effort. On Sept. 12, 2008, the PROC and subgroup chairs presented to Zerhouni the first of the preliminary implementation plans for the 2009 through 2010 calendar years. Although specific details of the Implementation Plans continue to be worked through, the first of the preliminary Implementation Plans for the 2009-2010 calendar years are as follows.



Priority Area 1—Engage the Best Reviewers

- **Improve Reviewer Retention:** In 2009, new reviewers will be given additional flexibility regarding their tour of duty, and other efforts will be undertaken to improve retention of standing review members.
- **Recruit the Best Reviewers:** A tool kit, incorporating best practices for recruiting reviewers, will be made available to all ICs in 2009.
- **Enhance Reviewer Training:** In Spring 2009, training will be available to reviewers and SROs related to the changes in peer review.
- **Allow Flexibility through Virtual Reviews:** Pilots will be conducted in 2009 on the feasibility of using high-bandwidth support for review meetings to provide reviewers with greater flexibility and alternatives for in-person meetings. (I didn't recommend this, because I have always hated phone conferences, but having done a few recently I have to admit that the web-based, phone-linked review meetings work better than I thought.)

Priority Area 2—Improve the Quality and Transparency of Review

- **Provide Scores for Streamlined Applications:** In 2009, streamlined applications will receive a preliminary score, unlike in the present system.
- **Shorten and Restructure Applications:** Shorter (12-page research plan) R01 applications (with other activity codes scaled appropriately) will be restructured to align with review criteria for January 2010 receipt dates. The purpose of this is to deemphasize the details of how research is to be carried out, and focus instead on the importance of the problem being investigated and the track record of the investigator(s). This was one of my major recommendations, and I'm delighted to see the committee come to the same conclusion. It's possible to nitpick any proposal to death based on real or perceived imperfections in the research plan, and I hope there will be less of that now.

Priority Area 3—Ensure Balanced and Fair Reviews across Scientific Fields and Career Stages, and Reduce Administrative Burden

- **Review Like Applications Together:** In September 2008, NIH modified the NIH New Investigator Policy to identify Early Stage Investigators. In 2009, where possible, NIH will cluster new investigator applications (including Early Stage Investigators) for review. The same approach will be used for clinical research applications. This recommendation has received some scrutiny. There are a number of people in our Society and in FASEB who are concerned about how this will work in practice and what the unintended consequences might be. I'm cautiously in favor of trying it out, but I wouldn't rule out some detailed comment from the ASBMB and other societies that might lead to reconsideration.

And now, last but certainly not least, the recommendation that I didn't make and that I think should be thought about some more before implementation:

- **New NIH Policy to Fund Meritorious Science Earlier:** To ensure that the largest number of high quality and meritorious applications receive funding earlier and to improve system efficiency, NIH will enhance success rates of new and resubmitted applications by decreasing the number of allowed grant application resubmissions (amendments) from two to one.

That's right, from now on, if this is implemented, you will only get one chance to resubmit a proposal that was turned down for funding. If it is turned down a second time, you must completely rewrite it—it has to be a new grant, essentially—if you are going to try to get the same broad research funded.

I think there are several problems with this. First of all, it treats all rejections as equal, and they're not. A grant that has been triaged is very different from a grant that just missed being funded. I could see a case for not allowing further resubmissions if the first resubmission was triaged. (NIH calls it "streamlined." But dead is dead in any language.) A grant that had a respectable score, it seems to me, is a victim of tight funding or the whim of one or two panelists, and it usually represents quite worthwhile science. To force the PI for such a proposal to rewrite it completely strikes me as draconian, to say the least.

Yes, I know the intent here is to make things easier for the reviewers by trying to hold down the number of applications, but do you really think it's going to do that? It'll make more work for the submitters, that's for sure, but my guess is that most of them will just keep rewriting and submitting because, really, what else can they do? And it's even possible, the Law of Unintended Consequences being what it is, that they will actually submit MORE grants, if they think their chances of getting any one funded have gone down as a result of this rule.

The National Science Foundation (NSF), which is often more sensible about the whole grants business than NIH, has a simpler system. They just treat every proposal as a new submission. Each application is judged on its own merits, and previous reviews are not considered. They tell me this works quite well. I understand that the NIH folks considered this alternative but rejected it. Frankly, I can't see why.

But OK, if they're going to limit the number of times a grant can be resubmitted, I think they are making a huge mistake if they don't cut beginning investigators some slack. Learning how to write good grants often takes quite a bit of time, and a number of rounds of feedback. Again,

continued at the bottom of page 5

Gene-Xer's Making an Impact

To the Editor:

Thank you, Dr. Petsko, for the wonderful exposé on impact factors (*ASBMB Today*, October, 2008). Perhaps you might consider commenting on Jorge Hirsch's H-index that measures a researcher's impact on science, potentially a more appropriate indicator of one's impact in their specific field.

As a Generation X researcher, I find myself in the exciting category of scientists who are actually bridging the gap between the genome and its secret, and the "established" researchers. Unfortunately, it is from this pool of "established" researchers, many of whom wouldn't know the difference between a restriction site and short sight (but who still contribute as co-authors to an impossible number of articles each year), that high-impact journals all too often draw from to review our manuscripts. Do I sound cynical? I

suppose I do, and for that I apologize. I do not mean to generalize as there is fantastic work being done by some of the "big" labs. However, it is a sad fact, but a consensus amongst many of us Gene-Xer's, that we and our graduate students spend a disproportionate amount of time (and hard-gained operating funds!) wading through a literature that is quite often flawed (or perhaps simply over-interpreted because of pressure to publish? I mean, really! Why are there researchers who still adhere to the misguided notion that cell signalling cascades are linear?). Of course, the biggest challenge is in convincing journal editors and reviewers (with much tongue-biting, but great diplomacy, I might add!) that our data and the interpretation thereof, is indeed correct. Geographical and institutional bias renders this an even greater challenge; I am from the University of Saskatchewan. Did I hear you say "Saskatchewan"?

Gene-Xer's tend to live by Eric Hoffer's adage, "In times of change learners inherit the earth; while the learned find themselves beautifully equipped to

deal with a world that no longer exists." However inspiring this sounds, Hoffer's philosophy is not the best formula for success in this impact factor-driven environment, where we all too often have to deal with *learned* grant application and journal reviewers who apparently fear the evolution of concepts and who choose to ascribe to the comforting ostrich-head-in-the-sand, "What, me worry?" mind-frame championed by that other notable philosopher of the 20th century, Alfred E. Neuman.

*Darrell D. Mousseau, Ph.D.
Cell Signalling Laboratory
University of Saskatchewan
Canada*

Tell Us What You Think

We appreciate receiving letters that are suitable for publication regarding issues of importance or comment on articles appearing in ASBMB Today. Letters should be sent to the editor at the address found in the masthead. Letters must be signed and must contain the writer's address and telephone number. The editor reserves the right to edit all letters for clarity and length. Opinions expressed in letters do not necessarily reflect ASBMB policy.

continued from on page 4

unless the second resubmission is triaged, I think investigators who have never had an NIH grant should be given the option of a third resubmission. If study sections do their jobs, the additional CONSTRUCTIVE criticism should be very valuable to a young scientist.

Do you have a different opinion? Good, then let NIH know about it. If we want things to improve, we all need to take an interest in what is happening. Because the funding situation is not going to get much better any time soon—I think the recession we're already in is going to be deep and dark compared with the last few—it is imperative that peer review, the jewel in the crown of American science, works as well as possible.

Meanwhile, I think the best advice to give young scientists, who are the ones we all need to be most concerned

about (they are, after all, the lifeblood of our profession), is not to pay attention to rumors about queuing, which might make you think you should just get in line with an imperfect proposal and try to fix it in the first revision. Personally, I've not seen much evidence for queuing in the way proposals are ranked, at least in the study sections that I participate in. And if NIH is not going to make allowances for beginning investigators and sticks with the one resubmission-only policy across the board, it's important that the first submission be as close to fundable as possible. Besides, I think a young investigator should make the strongest case he or she can, by writing the best possible proposal, so that the study section has the best possible impression of them the first time it encounters them. Second chances are all well and good, but as my mother was fond of saying: "You never get a second chance to make a first impression." ❧

FASEB Releases Neural Prosthetics Publication

BY CARRIE WOLINETZ

FASEB recently announced the release of the publication “Building Electronic Bridges to Bionics: The Basic Science of Neural Prosthetics,” the latest article in the Breakthroughs in Bioscience series. The Breakthroughs in Bioscience series is a collection of illustrated articles, published by FASEB, that explain recent developments in basic biomedical research and how they are important to society. FASEB distributes this series, free of charge, to members of Congress, patient advocacy groups, educational organizations, members of the press, and research advocacy partners. We highly encourage members of the FASEB societies to use these materials in their own advocacy and education activities. The entire series is available online at opa.faseb.org/pages/Publications/breakthroughs.htm or in hardcopy form by contacting the FASEB Office of Public Affairs at opa.faseb.org. Recent titles in the series have included:

- **Viruses, Cancer, Warts and All: The HPV Vaccine for Cervical Cancer**
- **Breathtaking Discoveries: How Basic Research Led to Treatments for Asthma**
- **Science, Serotonin, and Sadness: The Biology of Antidepressants**
- **Breast Cancer, Tamoxifen, and Beyond: Estrogen and Estrogen Receptors**
- **Finding Chinks in the Viral Armor: Influenza, AIDS, and Antiviral Therapies**


FASEB also welcomes suggestions for new topics from member societies if scientists have ideas that meet the objective of the series: basic research discoveries that have resulted in effective treatments or diagnostics for medical conditions. The Breakthroughs series is overseen by a subcommittee of the FASEB Science Policy Committee, chaired for the past decade by ASBMB and Peptide Society member Fred Naider, who will be succeeded this winter by James Barrett. The subcommittee is planning its next article, to be focused



on biomaterials, for publication in early 2009. Suggestions for topics may be submitted directly to Carrie Wolinetz at cwolinetz@faseb.org.

This new article explores the cutting-edge science of neural prosthetics, from cochlear implants to artificial retinas to bionic arms, and describes the roots of these devices in centuries of fundamental research. Today, millions of Americans use neural prostheses, whose origin can be traced back to the 18th century physicist, Luigi Galvani. Galvani’s discovery of

“animal electricity” in frogs was later identified as the electrical nerve impulse, which is the basic signaling mechanism that nerves use to communicate with tissues and organs. By the 19th century, research was being conducted on the cochlea as the main organ for sound, and following in Galvani’s footsteps, Princeton psychologists E. Glen Wever and Charles Bray showed that electrical impulses were involved in hearing speech from this organ. NIH-funded research in California enabled scientists to discover exactly how the cochlea transmits speech sounds to the brain, and by the 1970s, the first cochlear implant made its debut.

The success of cochlear implants encouraged researchers to study other neural processes, including sight and the use of limbs. Many disciplines such as physics, physiology, ophthalmology, computer sciences, mathematics, and engineering contributed to further breakthroughs in neural prosthetics. Collectively, these scientists fostered the development of bio-engineered devices that can close crucial gaps in nerve signaling so that the deaf can hear, the blind can see, and amputees can have artificial limbs that feel and act like their missing limbs. 

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.



Obama Wins Presidency, Democrats Increase Majorities in the House and Senate

BY PETER FARNHAM

As the polls closed in every state but Alaska, at 11:00 pm Eastern time on Nov. 4, 2008, major news organizations around the country called the presidential race for Senator Barack Obama. Senator John McCain made it close (and interesting) in several key states, but for the Republican candidate, it did not matter in the end.

As President, Obama is expected to be friendly toward science. He recruited a very solid team of top scientists to advise him during the campaign, headed up by Nobel Laureate and ASBMB member Harold Varmus, President of Memorial Sloan-Kettering Cancer Center in New York. He also described his views on science issues in detail in his responses to a series of 14 questions sent to both candidates earlier in the campaign by a group called Scientists and Engineers for America. The October issue of *ASBMB Today* also has information on Obama's positions on certain key science issues.

Unfortunately, Obama will be limited in what he can do early in his presidency. The nation faces massive fiscal problems: the wars in Iraq and Afghanistan, a \$11 trillion national debt, annual budget deficits in the hundreds of billions, growing Social Security spending needs due to the aging "baby boomer" population, a new and expensive drug benefit under Medicare Part D, and the recent \$700 billion bailout of the investment banking and insurance industries (which may rise to \$1 trillion or more before the rescue is finished). The continued fiscal fallout of the subprime mortgage collapse will likely exacerbate these problems. Some of this involves mandatory spending required by law. This leaves very little money left to pay for domestic discretionary spending without resorting to some combination of unpalatable alternatives: increased

deficit spending and/or raising taxes. Thus, the chances of large spending increases on biomedical and other scientific research in the near future, even with an otherwise sympathetic administration and Congress, may be limited.

Congressional Results

Obama will be assisted by a more Democratic Congress. The Democrats entered Election Day with a slim 51-49 majority that included two Independents—former Democratic Vice Presidential candidate Joe Lieberman and Socialist Bernie Sanders of Vermont. The results solidified Democratic control of the chamber, as they picked up at least five seats; the new majority is 54 Senators (plus Lieberman and Sanders, who were not up for reelection this cycle). As of this writing, three seats are still undecided, although the GOP leads in all three cases. However, the Democrats appear not to have reached the magic number of 60 seats; this is the number that would have allowed them to invoke cloture and thereby cut off a filibuster. The ability to filibuster is the GOP's sole remaining check on a greatly strengthened Democratic majority.

It is also enormously helpful to biomedical research that Sen. Tom Harkin (D-IA) won reelection easily; his seat was never in doubt, but, since he is one of biomedical research's two staunchest champions in the Senate, it was reassuring to see that he prevailed.

It is not entirely clear what the final count will be in the House, but Democrats are on track to pick up between 20 and 25 seats. Albeit a healthy gain, it does not rise to the levels predicted by some pundits in the days leading up to the election. A democratic majority in the range of 250-260 seats is thus expected once the final



results are in, with the GOP relegated to approximately 175 seats.


The day after the election, several leadership struggles had already begun to break out in the House. The most relevant to ASBMB's interests is that Rep. Henry Waxman (D-CA) is expected to take on Rep. John Dingell (D-MI) for the chairmanship of the powerful Energy & Commerce Committee, which oversees NIH.

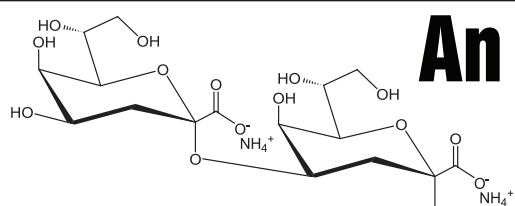
Other Developments

As of this writing, Obama has offered the White House chief of staff position to Rahm Emanuel, a Democrat who sits on the House Ways and Means Committee's Health Subcommittee. During his three terms on the Hill, Emanuel has sponsored legislation on prescription drugs, public health campaigns for influenza vaccinations, and expansion of a visa waiver program, suggesting that he may be familiar with some issues of interest to the ASBMB community. ASBMB, along with the coalitions it works with—which include FASEB, the Coalition for Life Sciences, and the Coalition for National Science Funding—will be pushing the incoming administration to appoint knowledgeable individuals to key staff positions and to give greater consideration to issues that affect biomedical research.

Speaker of the House Nancy Pelosi (D-CA) has issued yet another call for a lame duck session of Congress—a final meeting of the 110th Congress, to occur prior to the inauguration—to pass another economic stimulus package as quickly as possible. No details are available at this time, but ASBMB has joined the rest of the biomedical community to call for additional funding of scientific research in the prospective package.

Finally, there were a variety of ballot initiatives around the country, including Michigan's Proposition Two, which amends the state constitution to permit human embryonic stem cell research with certain restrictions. According to the initiative, the embryos must have been created for fertility treatment purposes; research may only be performed on embryos that would have otherwise been discarded; and the embryos may not be used more than 14 days after cell division has begun. The initiative was approved by a margin of 53, or 47 percent.

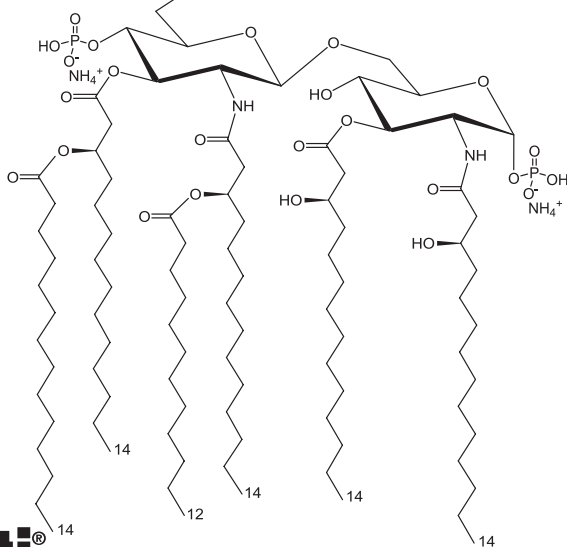
While Democrats have many reasons to celebrate the outcome of the 2008 election on purely partisan grounds, biomedical researchers should also take heart in the knowledge that, regardless of the amount of funding available next year, science is likely to be given greater weight in the next administration. 



An Endotoxin to replace LPS

Kdo₂-Lipid A from Avanti[®]

Kdo₂-Lipid A
Avanti Number
699500



A new preparation of the saccharolipid glycan, Kdo₂-Lipid A, is a nearly homo-geneous Re lipopolysaccharide (LPS) sub-structure with endotoxin activity equal to that of native LPS. Kdo₂-Lipid A is comparable to LPS and its activity is reduced by >10³ in cells from TLR-4 deficient mice.

The advantage of Kdo₂-Lipid A over LPS is that it is a reproducible, defined natural product, and it can be detected by ESI/MS at the low concentrations used to stimulate animal cells. The purity of Kdo₂-Lipid A should also facilitate the structural analysis of its complexes with signaling receptors, such as TLR-4/MD2.

Reference
Kdo₂-Lipid A of *Escherichia coli*, a defined endotoxin that activates macrophages via TLR-4. Raetz, C.R.H. et al. (2006) *J. of Lipid Res* 47:1097-111.



Phone 800-227-0651 (205-663-2494 International) or Email info@avantilipids.com for details of Avanti's selection of lipids of unparalleled purity visit www.avantilipids.com

FROM RESEARCH TO cGMP PRODUCTION - AVANTI'S HERE FOR YOU

Paul Rogers, “Mr. Health,” Passes Away at 87

BY PETER FARNHAM

Paul Rogers, known as “Mr. Health” for his 24 years’ work as a Florida congressman, died unexpectedly in mid-October. Hundreds of friends and colleagues turned out on Oct. 20 to mourn him at a memorial service at Washington National Cathedral, a fittingly grand setting for a man who will be sorely missed by biomedical advocates everywhere.

Rogers entered Congress in 1954 and served in 11 consecutive Congresses, until Jan. 3, 1979. He chose not to run for reelection to the 96th Congress, even though he had won his previous election with 91 percent of the vote.

Rogers served as chair of the Subcommittee on Health and the Environment from 1971 to 1979. He was a key architect of the adoption of the National Cancer Act of 1971, the Medical Device Amendments Act of 1976, The Health Maintenance Organization Act, the Emergency Medical Service Act, the Medicare-Medicaid Anti-Fraud and Abuse Amendments of 1977, the Clean Air Act of 1970, and the Safe Drinking Water Act.

After leaving Congress, Rogers joined the Washington D.C. law firm of Hogan & Hartson, and in addition to his law practice, was very generous with his time, participating in many charitable causes that advanced his passions for health and quality of life. This passion led him to work very hard with the Campaign for Medical Research, of which ASBMB was a part, in the late 1990s to double the NIH’s budget, conducting hundreds of meetings between scientists and members of Congress to advocate for the doubling plan. In recognition of his contributions to the nation’s health, the main plaza at NIH was named in his honor in 2001.

Rogers was eulogized at his memorial service by several people who knew him well, including his friend and former law partner, Chief Justice of the Supreme Court John G. Roberts Jr., who lauded him as an extraordinarily gracious man. As Justice Roberts said, “No one would exit an elevator after him or go through a doorway behind him.”

In a statement released upon news of Rogers’ death, NIH Director Elias Zerhouni noted that “All of us at NIH are deeply saddened...We have lost one of our true champions for biomedical research. His dedication, intellect, and disarmingly warm style reaped many successes

over his long career. People around the world can be thankful for all that he did on behalf of public health.”

The former chairman of ASBMB’s Public Affairs Advisory Committee, Bill Brinkley, was attending a recent Institute of Medicine meeting when word of Rogers’ death was announced. As Brinkley told *ASBMB Today*, “During the campaign to double NIH funding, Paul would take me by the arm and usher me into the congressional offices of both friends and staunch opponents with his big smile and say, ‘This is Dr. Bill Brinkley, a scientist from the great Texas Medical Center down in Houston, and he wants to tell you why we need to double the budget for health research at NIH!’” After one such meeting with a staunchly conservative senator initially opposed to the doubling, Rogers told Brinkley that the meeting was so successful that even this senator “has come over to our side—now that is something; we are really making progress!”

Kevin Mathis, a lobbyist who worked with Rogers on the campaign to double NIH’s funds, gave a glimpse of Rogers’ puckish sense of humor. After a meeting with Rep. John Spratt (R-SC), Rogers noted, “That was Jack Spratt.” After a perfectly timed pause, he added, “He can eat no fat!”


Research!America President Mary Woolley spoke eloquently of Mr. Roger’s legacy at his memorial service. “Please join me in taking a deep breath. And join me in savoring that breath. We can savor a deep breath of air this morning because the air we’re breathing is clean.

“And we can savor the water we drink; we can revel in our nation’s priceless lakes and rivers, because our water is clean.

“We can rejoice in the lives of children who have overcome diagnoses of cancer.

“We can celebrate octogenarians who flourish in ways unthinkable only a few decades ago.

“For all these blessings, and for many more, we have Paul Grant Rogers to thank.”

Rogers’ attitude toward basic biomedical research can be summed up best by one of his favorite remarks: “Without research, there is no hope.” 

Peter Farnham is public affairs officer of the Society. He can be reached at pfarnham@asbmb.org.


Brady Honored with National Medal of Technology and Innovation



Roscoe O. Brady, Scientist Emeritus at the National Institute of Neurological Disorders and Stroke at NIH, was honored with a 2007 National Medal of Technology and Innovation.

President Bush presented Brady, five other individuals, and two corporations, with his medal at a White House ceremony in September. The medal is the highest

honor for outstanding contributions to the nation's economic, environmental, and social well-being through the development and commercialization of technology products. The medal was created by Congress in 1980 and has been presented by the President of the United States since 1985.

Brady was honored for his discovery of the enzymatic defects in hereditary metabolic disorders such as Gaucher disease, Niemann-Pick disease, Fabry disease, and Tay-Sachs disease. These studies led to Brady's development of diagnostic, carrier detection, and prenatal tests for several of these disorders. He and his co-workers also developed effective enzyme replacement therapy for patients with Gaucher disease and Fabry disease. Brady is currently investigating substrate depletion and molecular chaperone therapy for patients with metabolic storage disorders. 

Bruice Honored with Linus Pauling Medal




Thomas C. Bruice, Professor of Chemistry and Biochemistry at the University of California, Santa Barbara, has been awarded the 2008 Linus Pauling Medal.

The medal is given annually by the Oregon, Portland, and Puget Sound Sections of the American Chemical Society; it recognizes outstanding accomplishments in chemistry in the spirit of and in honor of Linus

Pauling, a native of the Pacific Northwest.


Bruice has published over 530 research papers in 32 discernable areas related to biochemical problems. He was involved in inventing the term "bioorganic chemistry" and helped to define the field. Significant advances have been made in his laboratory in the elucidation of the catalytic processes in acyl and phosphate transfer reactions, the mechanisms of cofactor reactions (pyridoxal, flavins, lipoic acid, and dihydronicotinimides), and metalloporphyrin chemistry. More recent areas of investigation include the design, synthesis, and study of putative anti-sense and anti-gene agents as well as the use of computational methods in the study of reaction mechanisms and in particular enzyme catalysis and drug design.

Bruice is a member of the National Academy of Sciences, the American Academy of Arts and Sciences, a Guggenheim Fellow, and a fellow of the Royal Society of Chemistry. 

Costello Named HUPPO Discovery Award Winner



Catherine E. Costello, Director of the Boston University School of Medicine Mass Spectrometry Resource, was awarded the Human Proteome Organization's Discovery Award in Proteomics Sciences. She received the award for her contributions "to the structural elucidation of glycolipids and lipids and of post-translational modifications that are involved in the onset and progress of infectious and parasitic diseases, protein misfolding, disorders, and cardiovascular disease."

Costello is an internationally known leader in glycomics and glycoconjugate analysis. Her research focuses on developing the initial techniques and applications of high performance tandem mass spectrometry for glycan and glycolipid analysis. She was the first to apply matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry for site-specific profiling of glycoprotein glycans and for the direct analysis of glycolipids from thin-layer chromatographic plates. To address the problems caused by metastable decomposition of MALDI-generated ions, she and her colleagues developed the high-pressure MALDI source for fourier transform ion cyclotron resonance mass spectrometry (FTMS) and applied it to the analysis of thin-layer chromatography-separated glycolipids and protein digests. She has also made contributions to the structural elucidation of glycolipids and lipids, and of protein post-translational modifications that are involved in the onset and progress of infectious and parasitic diseases, protein-misfolding disorders, and cardiovascular disease. 


Stroud to Receive Anatrache Membrane Protein Award



Robert Stroud, Professor of Biochemistry & Biophysics and Professor of Pharmaceutical Chemistry at the University of California, San Francisco, has been selected to receive the Biophysical Society's 2009 Anatrache Membrane Protein Award.

The Anatrache Membrane Protein Award was established to recognize an outstanding investigator who has made a significant

contribution to the field of membrane protein research. Stroud was selected to receive the award for his contributions to transmembrane biology and for pioneering new methods that allow membrane proteins to become tractable. He will receive the award at the annual Biophysical Society meeting in Boston this spring.

Stroud's research has focused on elucidating the molecular mechanisms of biological processes at the protein level. His lab studies several integral membrane proteins including aquaporins, the ammonia channel, and glycerol channels. Stroud is also the Director of the Membrane Protein Expression Center (MPEC) and the Center for Structures of Membrane Proteins, both at UCSF. 



Karger Awarded Torbern Bergman Medal




Barry L. Karger, Founder of the Barnett Institute of Chemical and Biological Analysis at Northeastern University, was recently awarded the Torbern Bergman Medal by the Analytical Division of the Swedish Chemical Society. Karger, who is also the James L. Waters Chair in Analytical Chemistry at the Barnett Institute, received the medal in recognition of his work in

aiding the development of separation science as a tool for the analysis of biological molecules.

The Bergman Medal, which is presented every other year to a single recipient, is among the most prestigious analytical chemistry awards. It is given to those working to make a "paradigm shift in life science" through mass spectrometry.

Among his career-defining accomplishments, Karger helped develop polymer matrices used in the Human Genome Project. His current research focuses on the integration of modern separation systems with mass spectrometry for proteome and biomarker analysis.


Karger was also recently elected as an honorary member of the Hungarian Academy of Sciences, an honor rarely extended to non-Hungarian citizens and named recipient of this year's Csaba Horvath Medal. 

Stubbe Presented with Kirkwood Medal



JoAnne Stubbe, Novartis Professor of Chemistry and Professor of Biology at Massachusetts Institute of Technology, was presented with the 2008 Kirkwood Medal this past spring. Stubbe received the award for her work in mechanisms of enzymatic reactions and biosynthetic pathways. The award, which is presented biennially by Yale University and the American Chemical

Society New Haven Section, honors the late John G. Kirkwood, former Sterling Professor of Chemistry and Chairman of the Department at Yale.

Stubbe's major research efforts have focused on the mechanism of nucleotide reductases. Her work has led to the design and synthesis of several nucleotide analogs that have potential anti-tumor, anti-virus, and anti-parasite activity. Currently, Stubbe has four main research interests: 1) the mechanism of natural product DNA cleavers; 2) the mechanism and regulation of ribonucleotide reductases; 3) polyester biosynthesis; and 4) the mechanism, structure, and regulation of the purine biosynthetic pathway. She has a long list of awards and honors, including election to the National Academy of Sciences. 

Prestwich Wins Volwiler Research Achievement Award




Glenn D. Prestwich, Presidential Professor of Medicinal Chemistry and Special Presidential Assistant for Faculty Entrepreneurism at the University of Utah College of Pharmacy, received the Volwiler Research Achievement Award from the American Association of Colleges of Pharmacy. Prestwich was honored for his outstanding research and contributions to

the field of pharmaceutical sciences.

Prestwich's research focuses on new reagents for lipid signaling in cell biology and cancer treatment, and biomaterials for wound repair, cartilage repair, stem cell culture, tissue engineering, scar-free healing, and toxicology and xenograft models.

"Glenn is an exceptional leader and teacher. He is not only known for his incredible contributions to pharmaceutical education, but for a commitment to research that is vital to the academic community," explained Lucinda L. Maine, AACP executive vice president and CEO. "It is an honor to present him with this prestigious award."


Prestwich also holds adjunct appointments in the Departments of Chemistry, Biochemistry, and Bioengineering at the University of Utah. During his 32 years as a faculty member, he has published more than 600 technical papers, patents, and book chapters, including popular articles in *National Geographic* and *Scientific American*. 

White Recipient of Avanti Award



Stephen H. White, a Professor at the University of California, Irvine, will receive the Biophysical Society's 2009 Avanti Award in Lipids at the Society's annual meeting in Boston this spring. White was selected to receive the award for his novel findings in the areas of membrane structure and protein insertion into membranes.

White's laboratory focuses on biophysical problems related to the folding and stability of membrane proteins and is part of the UCI Structural Biology and Molecular Biophysics graduate program. Specifically, he looks at the following areas: membrane protein folding and stability, energetics of protein-bilayer interactions, experimentally determined hydrophobicity scales, translocon-assisted folding of membrane proteins, structure of fluid lipid bilayers, molecular dynamics simulations of membranes and proteins, and antimicrobial peptides.

White, who served as the President of the Biophysical Society from 1996 to 1997, has received many other honors and awards in the past, including the Kaiser-Permanente Award for Excellence in Teaching (1975 and 1992) and the Biophysical Society Distinguished Service Award (1999). 

Retrospective: Anthony G. San Pietro

Anthony G. San Pietro, professor emeritus at Indiana University, passed away on Sept. 13, 2008, at the age of 86.

Born on Apr. 22, 1922 in Brooklyn, NY, San Pietro originally aspired to become a singer. When he was in high school, he purchased booklets of song lyrics from street vendors and emulated the popular singers of the time. Despite his obvious talent, however, he instead chose a career path in scientific research and education. He graduated from New York University in 1942, after which he entered the Army Specialized Training Program where he studied electrical engineering. Upon completing the program, he joined the Manhattan Project in Los Alamos, NM, as a member of its Biochemistry Group.

After finishing his military service, San Pietro enrolled in graduate school at Columbia University and received his Ph.D. in Biochemistry in 1951. He then did a two-year postdoctoral fellowship at Johns Hopkins University, after which he became an assistant professor in Biology at the McCollum-Pratt Institute. He was promoted to associate professor in 1959.

During his time at Johns Hopkins University, San Pietro isolated an enzyme from chloroplast extracts that was needed for the photochemical reduction of NADP and suggested it be named "photosynthetic pyridine nucleotide reductase" (PPNR). Several years later, it was shown that PPNR and a new electron carrier called "ferredoxin," discovered in the hydrogenase system of *Clostridium pasteurianum*, were functionally similar. Thus, PPNR became known as ferredoxin.


San Pietro continued his work on photosynthesis and later isolated transhydrogenase, the enzyme that transfers hydrogen from NADPH, formed by photosynthetic pyridine nucleotide reductase, to NAD. This was the basis of his Transhydrogenase Theory, which states that illuminated grana reduce NADP in the presence of photosynthetic pyridine nucleotide reductase and transhydroge-



nase, then reduces NAD using reduced NADP. In 1962, San Pietro joined the Charles F. Kettering Research Laboratory in Yellow Springs, OH, where he was involved in the creation of a first-rate laboratory in Photosynthesis and Nitrogen Fixation Research. While at the Kettering lab, he extended his research to include chromatophores of photosynthetic bacteria and also made time to teach a biochemistry course at Antioch College.

San Pietro moved to Indiana University, Bloomington in 1968 to chair the Department of Plant Sciences, a position he held until 1977. While serving as chairman, he maintained an active laboratory for investigating the mechanisms of the light-dependent reactions of photosynthesis and published over 160 papers. In 1975, San Pietro was given the title of distinguished professor of Plant Biochemistry, and in 1980, he was appointed science adviser to the Office of the President of Indiana University. In 1983, he was honored by election to the National Academy of Sciences. San Pietro was also awarded an honorary doctor of science degree by Purdue University in 1992, the same year he retired from the Indiana University faculty.

During his 50 years in science, San Pietro traveled extensively and collaborated with scientists from Japan, Europe, England, and Israel. He also edited several of the photosynthetic volumes of *Methods in Enzymology* and served on the Editorial Board of the *JBC*.

After his retirement, San Pietro continued to make contributions to the educational and scientific communities, participating in Indiana University's Faculty and Staff for Student Excellence (FASE) mentoring program until 2003. As a consultant to the Vice-Chancellor for Undergraduate Education at Indiana University-Purdue University Indianapolis, he helped guide the University's efforts to develop a community, state, and national alliance for enhanced minority enrollment in science and engineering education. 

Science's Role in Foreign Policy

BY ALLEN DODSON

The world of foreign policy has seen “shuttle diplomacy” and “ping pong diplomacy,” but is it ready for biochemical diplomacy? The new Center for Science Diplomacy at the American Association for the Advancement of Science (AAAS) held a conference in Washington titled, “Science, Diplomacy, and International Cooperation” to address this question. The event focused primarily on how collaboration between scientists can help broaden foreign policy goals, and called for increased cooperation between scientists and policymakers. Speakers agreed that, regardless of popular opinion of American policy in general, the world continues to hold our science and technology advances in high esteem and wants to establish collaborations with our scientists and institutions.

Improving Relations through Research

Rep. Brian Baird (D-WA), chair of the Research and Science Education subcommittee of the House Science Committee, gave opening remarks. He emphasized that the personal and professional relationships formed between scientists can span borders and help deal with global issues like climate change, food supplies, and drug-resistant infectious diseases. However, he also warned that these goals may need to be accomplished with little or no additional funding, because of the ongoing financial crisis and the other long-term financial commitments on the nation's books.

The conference featured several testimonials about cases in which collaborations started by scientists to pursue research have the potential to improve foreign relations. For example, Stuart Thorson from Syracuse University summarized ongoing collaborations between his institution and a North Korean university, and the New America Foundation's Patrick Doherty described a delegation of U.S. scientists seeking approval from the United States to travel to Cuba.

Science and Biosecurity Regulations

In discussions on biosecurity, participants agreed that there needs to be better communication and understanding between the intelligence and scientific communities. Currently, many security experts are concerned that scientists fail to do enough to safeguard sensitive information, and

many scientists view security regulations with a lack of confidence and distrust. Keynote speaker John Hamre, a former Deputy Secretary of Defense, argued that increased cooperation could help eliminate ineffectual regulations, noting that the intelligence community often doesn't know what questions to ask and that scientists are, in some cases, taking the necessary security precautions on their own. Hamre suggested that scientists have a role to play as sentinels over dual use technologies, which have legitimate research applications but could also be exploited by terrorists. Vaughan Turekian, Chief International Officer of AAAS, agreed that scientists should be involved in drafting protections against this “dark side” of biomedical research to produce regulations that are both manageable and effective. As Hamre put it, the goal should not be loosening rules but rather re-writing them to ensure that the rules that remain on the books are there because of their importance to U.S. security.

Regulations and International Collaboration

Issues related to visas were mentioned repeatedly during the conference. Numerous panelists noted that foreign nationals face hurdles applying for visas, work permits, or even visits to the United States. Hamre observed that we have closed our doors just as other nations are investing more in order to build local capacity and attract their expatriate scientists home. Funding was also discussed; currently many funding agencies do not fund overseas collaborators, even when the amounts of money in question are small and would further the work of funded American researchers. It was also noted that international policies can impact universities in major ways.

The New Administration

The next few months present an opportunity to re-evaluate policy roles at the start of a new administration. Although we hope for improvements in the state of research and education, perhaps it is also time to anticipate a new role as ambassadors—official or informal—in a scientific enterprise that transcends borders. 

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

ASBMB Round Table: *Jim Wells and Mary Woolley*

BY NICK ZAGORSKI

Jim Wells, University of California, San Francisco chair and professor of Pharmaceutical Chemistry and professor of Cellular and Molecular Pharmacology, and Mary Woolley, president of Research!America, have both been long-time advocates of improving the global health system. This past summer, they each caught the attention of *Science* Editor-in-Chief Bruce



Alberts, who suggested they join their unique perspectives—Wells' firsthand knowledge of drug research and development and Woolley's 25 years of editorial, publication, and outreach efforts—for an editorial in the journal. Together, they laid out some of the problems in the worldwide health arena and suggested that a populist movement, à la Al Gore's environmental crusade, might be needed for public health as well¹. The two recently sat down at the ASBMB round table and gave some more insight into their populist proposal.

ASBMB: *One of the ways that the climate change movement got momentum was through the vivid images of shrinking glaciers highlighting the downward trend of our environment over the past 50 years. However, in regards to public health, most people probably think we are better off than we were 50 years ago (longer lifespans, better vaccines, etc.). Will that make it more difficult to convince them that we are, in fact, on the precipice of a crisis?*

WOOLLEY: Well, I think the “it’s not so bad attitude” may be exactly the way most people felt about climate change when the scientific experts first brought it up—well before Al Gore brought it to the masses—because for both global warming and global health, the majority of the problems initially lay below the surface like an iceberg. So, things appear all right, but you can see many disturbing signs about our health if you know where to look: the rising obesity epidemic, the emergence of SARS and other diseases, and even scientific reports that suggest average lifespan might be plateauing out.

WELLS: Another way to look at it is that our health situation is not necessarily better, only some of the diseases have changed. One hundred years ago, if an individual got infected with polio, his family would just accept it as a matter of course—it was God’s will or something. Today, we certainly wouldn’t accept an explanation like that. But, say your father gets diagnosed

with congestive heart failure, the cardiologist might tell you, “Well, I guess his heart is just wearing out.” And 50 years from now, someone will look back and say, “I can’t believe they used to give such crazy explanations.”

ASBMB: *For those people already cognizant of the looming problem, one of their biggest worries may be the threat of a new pandemic rivaling the Spanish Flu of 1919. But do you both believe that another potentially serious crisis could arise as well?*

WELLS: Definitely. As our population ages, we’re going to wind up with many more people with diabetes, Alzheimer’s, cancer—all diseases that, under our current model, will require long periods of care and treatment, and thus will be a huge financial burden.

WOOLLEY: I agree. In addition, one important looming problem that we did not have a chance to expand on in the editorial is the economic cost of a deteriorating health system, and it’s big. And tough economic times are inherently linked with healthcare costs, which we can see now. People are avoiding refilling their drug prescriptions or not visiting referring physicians because they’re worried about the cost.

ASBMB: *Despite the many effects (and victims) of climate change, polar bears have become one of the more popular symbols of the crisis; do you see some particular disease that might strike a similar chord to captivate the public? Or do you think focusing too narrowly might be detrimental to advocating for global health as a whole?*

WELLS: I think it's great that some people or places bring attention to specific diseases, for example, St. Jude's Children's Hospital and all the great work they've done for childhood cancers. But, it's vital that these individual lobbyists make sure to highlight that the underpinnings of all these diseases are interconnected, like the links between obesity and diabetes or cancer and inflammation.

WOOLLEY: I agree with Jim; using examples can certainly help illustrate the problem, but we don't want to overshadow the big threat to our well-being, which is that health for everybody is not where we need to be.

ASBMB: *In looking for the Al Gores of public health, what kind of individual would you envision as ideal? What traits should he or she have for the best chance of success? And perhaps most importantly, should the spokesperson be a scientist or not?*

WELLS: I've discussed this at many meetings, and I believe that we definitely should not have a scientist as the key champion. The reason is that we're not looking for a Carl Sagan-type of figure, someone to inspire and fascinate us about science. We need someone who understands science but has to come in and communicate the vulnerability of the global health situation, point out the medical, economic, and global security risks, and call people out to action. In that regard, a pure scientist-spokesperson may lead to a perception that he or she has an underlying self-interest for funding.

WOOLLEY: Yes, the face of our effort has to convey both integrity and plausibility. In looking at possibilities, what Al Gore brought to the table was political savvy as well as a long-standing history of effort in the climate arena, platforms that should not be overlooked. The kind of people that have been equally as stunning in the health area already include Bill Gates, Mike Bloomberg, and Hillary Clinton. Bono provides another good example; while his efforts are more specific to global poverty, he does exemplify someone dedicating his life's work to a cause.

ASBMB: *Besides increased funding for research, a big aspect of a populist endeavor is education and service; i.e. what can you do to help? Do you have any thoughts on getting a good education message across, especially considering many current efforts at health education (healthy diet, regular screenings, etc.) seem to have limited effect?*

WOOLLEY: I do believe health messages have been having positive effects; it's just been at a slow pace. It's important to understand that real behavioral change takes time and a combination of efforts. Take seat belts, for example; first, we had to prove conclusively that they save lives, then we

had to convince Congress to pass a law mandating seat belts in all cars, then we still had to convince motorists to wear them as an act of habit. There have been similar initiatives in health education, like having fast food restaurants display their nutritional information, but we really haven't even begun to scratch the surface of things we can do.

WELLS: I think that also brings up an important point; one of the amazing things about the environmental movement is that Al Gore said that it may take a century of work to halt the global warming crisis, but that didn't deter any enthusiasm. So we need to stress, to the public and policymakers, the similar need for time to bring about changes in health. Unfortunately, both research scientists and pharmaceutical companies have been doing a lousy job relaying their expectations, often setting unreasonable goals, and that can sour the public when you don't meet them.

ASBMB: *Speaking of pharmaceutical companies, do you think these industries could be an obstacle in a global health movement? Or, is it important to have Pharma on hand as an ally in this endeavor to go from 'crisis management' to 'cure'?*

WOOLLEY: I think Pharma is an ally. We will always need treatment advances before we get to cures, themselves often Pharma-based, as are preventions such as vaccines. However, the Pharma pipeline is in trouble right now, and there are also regulatory and litigation challenges hindering progress. We need a combination of innovation and business savvy, smarter public policy, and advocacy by patient groups and others to bring the promise of research for global health to fruition.

WELLS: I know pharmaceutical companies frequently get maligned and vilified and sometimes for good reasons. But I've been in the pharmaceutical business, so I know that the rank and file researchers, their hearts are in the right place, trying to develop better drugs to help people. And we're definitely going to need them, because these still are the people that have the knowledge and resources to develop drugs, although it's encouraging to see academia beginning to work more with this area.

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

REFERENCE

1. Wells, J., and Woolley, M. (2008) A Populist Movement for Health? *Science* 322, 15.

Keeping Women in Science

BY NICOLE KRESGE

Recent data has shown that while equal numbers of women and men enroll in graduate school and earn doctoral degrees in the biomedical sciences, women only comprise about 25 percent of tenured faculty. The cause of this phenomenon, often referred to as “the leaky pipeline,” has garnered much investigation over the past several years, including the National Academy of Sciences’ *Beyond Bias and Barriers* report. Proposed explanations for this trend include reasons such as: women leave the workforce to act as caregivers and raise families; women are less competitive than men; women devote more time to teaching and mentoring than men; and lastly, that women don’t have many female role models in science.

One of the latest attempts to fix the leaks in the pipeline came in the form of a workshop this past September called, “From Doctorate to Dean or Director: Sustaining Women through Critical Transition Points in Science, Engineering, and Medicine.” The workshop was organized by the National Academies of Sciences’ Committee on Women in Science, Engineering, and Medicine (CWSEM) and was sponsored by the National Institutes of Health’s Office of Research on Women’s Health and the Kauffman Foundation. The premise of the workshop was that women were leaving the sciences at key transition points in their careers, such as the step from postdoctoral fellow to assistant professor, and if these “leaks” were fixed, more women might be retained in higher level positions in the sciences.

Assessing Gender Differences and Providing Support

The workshop started with a presentation by Claude Canizares, vice president for research and associate provost at Massachusetts Institute of Technology and the Bruno Rossi professor of Physics. Canizares spoke about an upcoming report on a study by the National Research Council titled, “Assessing Gender Differences in the Careers of Science, Engineering, and Mathematics Faculty.” Due to NRC rules, Canizares couldn’t divulge the results of the study until it was published, but he did explain that the congressionally mandated report was based on two surveys of faculty and departments at research I universities in the fields of biology, chemistry, civil engineering, electrical engineering, mathematics,

and physics. One survey collected information on departmental policies, recent tenure and promotion cases, and recent hires in almost 500 departments. The other survey gathered information from a stratified, random sample of about 1,800 faculty members on demographic characteristics, employment experiences, the allocation of institutional resources such as laboratory space, professional activities, and scholarly productivity.

Canizares closed by saying that he believes that one of the reasons women are leaving science is the prolonged amount of time it takes to obtain a faculty position, due to the increasing length of postdoctoral fellowships and the time to tenure. The system is problematic, he believes, and we need to examine the underlying structure of the profession to see if we can adjust it. One way to do this, Canizares suggested, is to involve professional societies in the discussion and encourage them to implement change.

Joan Girgus, professor of psychology and special assistant to the dean of the faculty for issues concerning faculty diversity at Princeton University, followed Canizares’ presentation by turning the focus to a meeting that occurred at MIT in 2001, between the leaders of nine research universities. This meeting focused on how universities dealt with the professional lives of women, and the meeting attendees agreed to analyze the salaries and university resources provided to women faculty, work toward a faculty that reflects the diversity of the student body, and to reconvene in one year.

The MIT nine universities have been meeting every year since then, but more recently, their focus has turned from the professional lives of faculty to how faculty members, postdoctoral fellows, and graduate students can juggle work and family. She argued that all three groups need additional support and suggested we provide a variety of resources to choose from, such as maternity leave, tenure clock extension, workload relief, dependent care travel funds, and on-campus child care. By implementing these programs, institutions are making it clear that it’s okay to want both a thriving career and a family. Girgus concluded by stating that universities must think of these supports as essential for a stimulating work environment and find the funds to provide them, or we may end up losing our best and brightest women and men.

Women and Medicine

June Osborn, president emerita of the Josiah Macy, Jr. Foundation, then gave a presentation on the 2007 Macy Foundation's Report on Women and Medicine. She explained that although the state of women participating in medicine is better than that of women participating in research science, the number of women faculty members participating in academic medicine is still low. She believes that a lack of visible female leadership has caused a runoff of women.

The president of the Association for Women in Science (AWIS), Phoebe Leboy, followed Osborn's presentation with a discussion on the decline in women involved in basic science in academic medicine. She presented statistics which revealed that there is a 50 percent decrease in the number of women during the transition from postdoc to assistant professor. This decline is occurring because women are not applying for assistant professor positions, Leboy explained; instead, women are leaving the academic workforce for more women-friendly professions, such as science writing and consulting. Leboy believes that women are encountering obstacles in the pipeline, including family issues; a chilly, isolating climate for women; and a culture designed for, and by men. In order to alleviate this problem, she recommended that institutions implement mentoring and networking programs, develop more family-friendly policies, decrease sexist behavior, and provide a more welcoming workplace culture for women.

Some Personal Stories

The next part of the workshop featured a panel of women who spoke about the transition points in an academic career. Pardis Sabeti, a new faculty member at Harvard University and the "proud mother of a new lab" talked about transitioning from postdoc to assistant professor. She had a lot of advice for young scientists including: figure out ahead

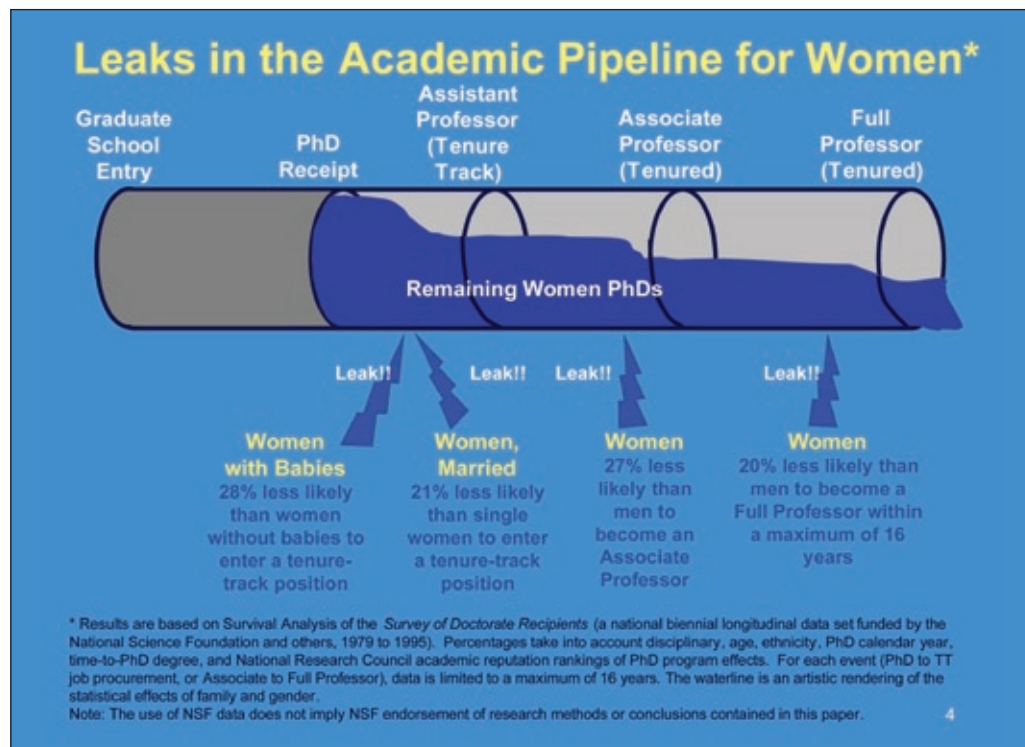


Figure 1

of time what you want and negotiate for it, don't be passive aggressive, and finally, find out what is expected of you in your new position.

Susan Wessler, a professor at the University of Georgia, spoke next about making the transition from assistant professor, to associate professor, to professor. She asserted that the negative perception that it is difficult to have a family and a career at the same time leads to a leaky pipeline. Her solution was to promote the idea of academic research as a family-friendly job that allows flexibility.

A second panel addressed careers in industry. Elizabeth Donley, chief executive officer at Stemina Biomarker Discovery, Inc., Andrea Vergara-Silva, senior scientific liaison at Astellas Pharma U.S., Inc., and Lydia Villa-Komoraff, chief executive officer at Cytonome, Inc. spoke of their career paths and the compromises they made to raise their families. Despite the fact that industry is by far more family-friendly than academia, all three women revealed that they encountered glass ceilings and were discriminated against at certain points in each of their careers.

Interdisciplinary Science

The final workshop panel looked at the rise of interdisciplinary science and how it affects women and their careers.

Alice Agogino, the Roscoe and Elizabeth Hughes professor of Mechanical Engineering at the University of California, Berkeley, began by remarking that many fields have “entrenched” the status quo by making it difficult for women to succeed. Fortunately, over the past several years, new interdisciplinary areas such as bioengineering and environmental engineering have emerged, and women have ventured into these new fields of science that have little or no entrenched gender bias.

The next panelist was Stacey Gabriel, director of the Genetic Analysis platform and the National Center for Genotyping and Analysis at the Broad Institute. She talked about the Broad Institute as a new model of collaborative science that brings together scientists from MIT, Harvard, and other institutions to work on problems in genomic medicine. Although there are more male research faculty members than female members at the institute, Gabriel pointed out that equal numbers of men and women hold the role of director.

The final panelist of the workshop was Eugene Orringer, a professor of Medicine at the University of North Carolina-Chapel Hill. He talked about the Building Interdisciplinary Research Careers in Women’s Health (BIRCWH) Program, which was created by the Office of Research on Women’s Health at NIH. BIRCWH awards are given to individual institutions and are designed to identify junior faculty scholars whose primary focus was women’s health research and then train them in an interdisciplinary manner. Of the BIRCWH program scholars, 79 percent are female and 21 percent are


male. The current UNC-Chapel Hill BIRCWH program contains 22 women and two men from a diverse array of fields including pathology, psychology, health education, and oncology.

Having a Career and a Family

A final presentation by Kathleen Christensen of the Alfred P. Sloan Foundation addressed the fit between family and career. Christensen used some statistics from a University of California, Berkeley survey to point out that although 40 percent of assistant professors at the University are women, this number falls sharply to 18 percent when looking at the number of full female professors. She claims that having a family affects career formation and pointed out that women with babies are 28 percent less likely than women without babies to enter a tenure-track position (Figure 1), and that while 70 percent of male tenured faculty are married with children, only 44 percent of female tenured faculty are married with children.

Christensen feels part of the problem is that academic careers are thought of as straight-line trajectories when in reality, they are more jagged paths with plateaus, accelerations, and decelerations. As a solution, she suggests we make careers more flexible and realign the academic career path to fit the needs of an increasingly diverse workforce. Her suggested career flexibility policies include extending the time to tenure, adding on and off ramps through leave policies, including slow-down periods with reduced appointments, allowing delayed entry to foster later-than-usual career starts, and implementing phased retirement.

The Future

The workshop concluded with a summary of findings, themes, and next steps. Workshop attendees agreed that most of the issues discussed impact both men and women, just not at the same level or in the same manner. It was suggested we look at what we can apply from successful fields and institutions and involve both men and women in future discussions. Some of the next steps identified by workshop coordinators included strengthening the mechanisms of information dissemination, regularly engaging representatives from professional societies, and addressing basic issues impacting career transitions overall, such as the time it takes to earn a degree, and then focusing on issues impacting women in particular. 

Nicole Kresge is the editor of *ASBMB Today*. She can be reached at nkresge@asbmb.org.

Resources

- The workshop program and findings, as well as the individual presentations, can be found at: www7.nationalacademies.org/cwsem/
- The text of *Beyond Bias and Barriers: Fulfilling the Potential of Women in Academic Science and Engineering* can be read online at books.nap.edu/catalog.php?record_id=11741
- The National Research Council Report, “Assessing Gender Differences in the Careers of Science, Engineering, and Mathematics Faculty” will be published by the end of the year and can be ordered at books.nap.edu/catalog.php?record_id=12062
- The Macy Foundation Report on Women and Medicine can be found at: www.josiahmacyfoundation.org/index.php?section=publications

Grammar and Writing Tips

Have you ever wondered why an accepted manuscript submitted to the *JBC* doesn't necessarily read quite the same when returned in proof form for your review? Scientific research demands accuracy; thus, scientific writing itself should reflect this with razor-sharp precision and clarity. Cadmus Communications works to clarify manuscripts for the reader by reviewing and, if necessary, correcting grammar, spelling, and punctuation. We try to enforce consistency throughout an article so as not to "jar" the flow of the article. Below are four topics that Cadmus editors would like to share with *ASBMB Today* readers—in essence, a few reasons why we do what we do! These editorial "tidbits" may provide authors with some explanations why certain editorial revisions have been made to their articles.

Tip 1: Verb Tense

JBC authors may have encountered an author query similar to the following: "?/Author: Verb tense: The past tense is used for what was done and observed in your experiments; the present tense is used for established facts (already published work) or general truths. Therefore, XXX has been changed to ZZZ."

As they do when they are speaking, journal authors frequently alternate between the past and present tenses when writing an article. Here is a good tip for authors to follow: when quoting or discussing previously published work, an author should use the present tense in the "Introduction" and "Discussion" sections. When referring to your own work, however, *which has not yet been published*, results should be discussed in the past tense, *i.e.* in the "Introduction," "Materials and Methods," and "Results" sections. Another useful rule of thumb: "previously" and "recently" are excellent hints that a sentence may be written in the past tense!

Tip 2: Queries

The Cadmus editors may insert queries to ensure that we have not altered the author's meaning in any way. We are not science experts, but we want to be sure the information is presented in a clear, easily understandable manner. As an author, please be sure to answer all queries in the manuscript, even to approve a change that the editor has made.

Tip 3: Compound Sentences

"These particles do not bind nucleic acid and plasmid DNA remains in the supernatant."


The above sentence is missing something. Cadmus copyeditors would change this to be grammatically correct. This compound sentence needs a comma before "and." Otherwise, readers may "stumble" at first glance, mistakenly believing that the particles do not bind nucleic acid and plasmid DNA. But wait— isn't plasmid DNA a nucleic acid? Instead of accidentally forcing your audience to reread a sentence containing two independent thoughts, a comma should be placed before the "and" in all compound sentences, leaving the reader free to enjoy the rest of your article.

Tip 4: Subject/Verb Agreement

"Furthermore, the relative expression and the spectrum of growth factors present in the individual microenvironment *is* not defined..."

The subject and verb should always agree with each other, *not with a word that comes in between them*. The correct sentence follows: "Furthermore, the relative expression and the spectrum of growth factors present in the individual microenvironment *are* not defined..." Both the relative expression and the spectrum are not defined; therefore, the plural form is correct. Watching out for when to use a singular verb ("is," "either," or "was") versus a plural verb ("are," "both," and "were") is easier than you may have thought!

So, the next time you submit an article to the *JBC* for review (or any science journal for that matter), take a step back and ask yourself the following questions:

- Are the verbs clear and recognizable?
- Will the reader have trouble understanding the meaning of the text?
- Am I making my readers work too hard to understand the concepts in the article?
- Have I been consistent throughout the text when using abbreviations, hyphens, and capitalization? 

The 2009 Fritz Lipmann Lectureship: Douglas C. Rees

Douglas C. Rees, a Howard Hughes Medical Institute investigator and professor of Chemistry at the California Institute of Technology, will give the Fritz Lipmann Lectureship at the 2009 ASBMB Annual meeting. This lectureship recognizes investigators who make conceptual advances in biochemistry, bioenergetics, and molecular biology. Rees will present his award lecture in New Orleans on Sunday, Apr. 19 at 8:30 a.m.


Rees has been an HHMI investigator since 1997 and is the Roscoe Gilkey Dickinson professor of Chemistry at the California Institute of Technology as well as an adjunct professor of Physiology at the University of California, Los Angeles, School of Medicine. He received his B.S. degree in Molecular Biophysics and Biochemistry from Yale University in 1974 and his Ph.D. in Biophysics from Harvard University in 1980, working with William Lipscomb. From 1980 to 1981, he was a postdoctoral fellow at Harvard and from 1981 to 1982, he was a postdoctoral fellow at the University of Minnesota with James Howard. He then joined the faculty at the University of California, Los Angeles before moving to Caltech in 1989.

Rees has made pivotal contributions to understanding the structure of integral membrane proteins, membrane transport mechanisms, and metalloenzyme structure and mechanism. His research focuses on structural bioenergetics, which is the description of biological energy transduction processes at a molecular level. One of his group's major goals is to characterize the structures and mechanisms of ATP-dependent transduction systems, including membrane proteins that catalyze energy transduction processes associated with transport, mechanosensation, and respiration-linked electron transfer reactions.

Rees' graduate training was in x-ray crystallography, and while studying as a postdoctoral fellow at Minnesota, he became interested in how ATP and other large molecules are used for energy in the body. One way in which organisms harness this energy is via ATP binding cassette (ABC) transporters, which use the binding and hydrolysis of ATP to pump molecules against concentration gradients across cell membranes. When Rees started as an independent investigator, no structure of an ABC transporter had been determined. Rees surveyed several ABC transporters from a variety of organisms before deciding that BtuCD,

the protein that imports vitamin B12 into *Escherichia coli*, would be appropriate for his structural studies. Rees and his colleagues were able to produce crystals of the transporter and solve its structure. Based on their results, they proposed a model for the transporter's molecule pumping ability. This initial structure also enabled them to crystallize and solve the structure of the intact, nucleotide-free HI1470/1 transporter from *Haemophilus influenzae*, a member of the family of binding protein-dependent bacterial ABC transporters that mediate the uptake of metal-chelate species, including heme and vitamin B12.

Since solving these structures, Rees has added many other projects to his repertoire, including:

- **Nitrogenase:** The biological conversion of dinitrogen to ammonia is catalyzed by the nitrogenase enzyme system, which consists of two component proteins, the iron (Fe-) protein and the molybdenum-iron (MoFe-) protein. Rees and his colleagues have determined the structures of both proteins and their metal centers and are currently developing mechanistic models for the nitrogenase reaction.
- **Extremely Thermostable Metalloproteins:** Rees determined structures of the tungsten-containing aldehyde ferredoxin oxidoreductase and a rubredoxin from *Pyrococcus furiosus*, an archaeon that grows optimally at 100° C. He is now using these structures to identify the origins of the proteins' thermostability.
- **Membrane Proteins:** Structural and sequence analyses of membrane proteins indicate that the same general structural and energetic considerations govern the three-dimensional structures of both water-soluble and membrane proteins. Currently, Rees and his colleagues are looking at the structures of succinate quinone oxidoreductase and photosynthetic reaction centers to assess the generality of this conclusion and to establish the structural organization of the redox centers.
- **Fibroblast Growth Factors (FGF):** These proteins stimulate the growth and development of many different cell types. Rees has solved the structures of two members of the FGF family and recently determined how the anti-ulcer drug, sucrose octasulfate, and heparin fragments bind to FGF. 



The 2009 ASBMB Merck Award: John Kuriyan

John Kuriyan, Howard Hughes Medical Institute investigator and Chancellor's professor at the University of California, Berkeley will be honored with the 2009 ASBMB Merck Award for his exceptional achievements in and contributions to structural biology. Kuriyan is one of the world's leading researchers on the structure and function of protein kinases, and his studies of c-Src, c-Abl, and Ca²⁺/calmodulin-dependent protein kinase (CaMKII) have provided exciting new insights into the structure and function of molecular systems that are similar to those found in many other biological contexts. He will present his award lecture at the ASBMB annual meeting in New Orleans on Tuesday, Apr. 21 at 8:30 a.m.


Kuriyan received his B.S. in Chemistry from Juniata College in Huntingdon, Pennsylvania before attending graduate school at the Massachusetts Institute of Technology. Working as a computational chemist with mentors Gregory A. Petsko (MIT) and Martin Karplus (Harvard University), he received his Ph.D. in Physical Chemistry in 1986 with a thesis titled "The Structure and Flexibility of Myoglobin: Molecular Dynamics and X-ray Crystallography." After graduating, Kuriyan became a postdoctoral fellow at Harvard University, continuing his work with Karplus and Petsko.

In 1987, Kuriyan became an assistant professor at Rockefeller University and climbed up the ranks to eventually become the Patrick E. and Beatrice M. Haggerty Professor and Associate Dean of Graduate Studies at Rockefeller. In 2001, he left Rockefeller to become divisional deputy for structural biology at the Advanced Light Source Physical Biosciences Division at the Lawrence Berkeley National Laboratory, as well as Chancellor's professor of molecular and cell biology and chemistry at the University of California, Berkeley. In 2007, Kuriyan was promoted to head of the Division of Biochemistry and Molecular Biology in the Department of Cell and Molecular Biology at Berkeley.

Kuriyan has made several major contributions to the area of cell signaling, starting with his determination of the first crystal structure of an Src homology 2 (SH2) domain bound to a tyrosine-phosphorylated peptide. This led to his explanation for the sequence-specific recognition of phosphotyrosyl peptides by SH2 domains. Kuriyan then decided to look at multi-domain proteins involved in tyrosine kinase

signaling and solved the structure of the auto-inhibited Src-family cytoplasmic tyrosine kinase (Hck). This structure explained nearly a century of research on the oncogenic v-Src gene and its normal counterpart. Kuriyan has also shown how the signaling pathways that operate downstream of tyrosine kinases are controlled, solving the structures of a signal transducer and activator of transcription (STAT) factor and the nucleotide exchange factor that activates Ras, Son-of-Sevenless (SOS), bound to Ras. He also solved the structure of the Abl tyrosine kinase catalytic domain bound to the small molecule inhibitor STI571 (Gleevec), showing how the drug selectively inhibits the kinase. More recently, Kuriyan has determined the structure of auto-inhibited ZAP-70, a tyrosine kinase that plays a critical role in T-cell activation and has determined the auto-inhibitory mechanism of CaMK-II.

In an entirely separate line of research, Kuriyan's laboratory has made pioneering discoveries in the field of processive DNA replication, most notably by determining the structure of the sliding clamp of *E. coli* DNA polymerase III, which established the principle that chromosomal replicases achieve high processivity by utilizing a circular "sliding clamp" protein that provides a mobile tether on DNA. This was followed by the determination of the structures of the clamp loader complexes from *E. coli* and yeast. Most recently, his laboratory has determined the first structure of the catalytic subunit of a bacterial DNA polymerase, resulting in the discovery that the prokaryotic DNA polymerases are related in structure to nucleotidyl transferases rather than eukaryotic DNA polymerases, providing support for the idea that DNA replication may have arisen independently in the major branches of life.

"John is arguably the preeminent structural biologist of his generation," says Tony Hunter of the Salk Institute. "Through his elegant crystallographic and modeling studies, John has made truly seminal contributions to our understanding of how signals are transduced in mammalian cells and how DNA replication processivity is achieved in both bacterial and mammalian cells. John's structural work and biochemical follow-up is characterized by its elegance and clarity of thought. He selects important problems that will be illuminated by structural insights and seems to come up with an exciting new principle each time." 

The 2009 FASEB Excellence in Science Award: Susan Lindquist

The 2009 FASEB Excellence in Science Award will be presented to Susan Lindquist, a Howard Hughes Medical Institute Investigator and Professor of Biology at Massachusetts Institute of Technology (MIT). The award, which is sponsored by Eli Lilly and Company, recognizes women whose outstanding career achievements in biological science have contributed significantly to further our understanding of a particular discipline by excellence in research. Lindquist will receive her award and present an award lecture at the ASBMB annual meeting in New Orleans on Tuesday, Apr. 21 at 2:10 p.m.

Lindquist received her undergraduate degree in microbiology from the University of Illinois and her Ph.D. in Biology from Harvard University in 1976. After a postdoctoral fellowship at the University of Chicago she became an Assistant Professor of Biology at the University of Chicago. She was promoted to Associate Professor of Biology in 1984, became a full professor in 1988, and was named the Albert D. Lasker Professor of Medical Sciences in 1999. In 2001, she became the director of the Whitehead Institute for Biomedical Research. She held that position until 2004 and remains a member of the Whitehead Institute today.


Work in Lindquist's laboratory covers a broad range of topics unified by one theme, the protein-folding problem. She and her colleagues have used a variety of organisms and techniques to investigate different aspects of protein folding including folding mechanisms, impediments to correct folding, and consequences of misfolding on biological systems.

One of the areas Lindquist studies is prion assembly and inheritance. Prions propagate via conversion of one domain of the protein into an amyloid fold. This conversion occurs through a molten oligomeric intermediate. Lindquist and her colleagues have identified the critical nucleating contacts involved in the conversion of the yeast prion protein Sup35. Using peptide arrays, they determined that the intermolecular contact region controls the species specificity of protein interactions (and hence the species barrier) and also the formation of distinct prion strains. Lindquist and her colleagues have also discovered that a regulatory protein that plays an important role in synaptic plasticity, cytoplasmic polyadenylation element-binding protein (CPEB), also behaves as a prion in yeast. CPEB maintains synapses by promoting the local translation of mRNAs. Lindquist

believes that the self-perpetuating folding of its prion domain acts as a molecular memory. She is currently attempting to identify the structural core of the CPEB amyloid and to pinpoint regions involved in nucleating prion formation.

Lindquist's laboratory also focuses on the molecular chaperone Hsp90 (heat-shock protein 90), which promotes the maturation of signal transducers, proteins regulating a multitude of processes controlling life, death, growth, and development. Lindquist found that Hsp90 buffers the effects of a multitude of silent polymorphisms at normal temperatures in *Drosophila melanogaster*, but when the organism is stressed, the effects of these polymorphisms are exposed. Selection can then act on the traits these polymorphisms produce. Lindquist hypothesizes that Hsp90 is a capacitor for morphogenetic evolution, allowing organisms to accumulate mutations that remain silent under optimal conditions and releasing their effects during stress when they might provide a survival advantage.

Lindquist and her colleagues are also using yeast models to investigate neurodegenerative diseases that have been linked to protein misfolding and the accumulation of protein aggregates such as Parkinson and Huntington disease. Using a yeast model of Parkinson disease expressing inducibly toxic levels of human α -synuclein, they performed high-throughput chemical, genetic, and cyclic peptide screens for modifiers of toxicity. In this study, Lindquist and her colleagues discovered that several of these modifiers could specifically reverse toxicity in neuronal cell cultures and animal models of Parkinson disease. They are also using a model of Huntington disease to screen for chemical and genetic modifiers and are generating additional yeast models of protein-folding diseases as well. Their results suggest that the approach of expressing a toxic human disease protein in yeast will be broadly applicable to a range of neurodegenerative diseases.

Lindquist has also found that eliminating HSF1, the dominant regulator of the heat-shock response, protects mice from tumors induced by oncogene mutations. Ironically, activation of the heat-shock response is a double-edged sword in the prevention of deadly diseases; although it can prevent the protein aggregation associated with degenerative diseases of aging, it also puts tissues at risk for cancer. 



ASBMB Targets Secondary Education

BY ELLIS BELL

Promoting the molecular life sciences at the K-12 level has always been a priority for ASBMB. In the coming months, the society will initiate two new programs that target middle and high school science.

The first is an awards program for middle and high school science fairs in which ASBMB will offer prizes and recognition for biochemistry- and molecular biology-related projects. The awards will be administered by local chapters of the Undergraduate Affiliate Network (UAN). If you are a UAN Faculty Advisor and would like to get involved in sponsoring science fair awards in your area, you can get details from your UAN Regional Director.

The second initiative is a grade 7-12 teachers' summer research program. This new program, which will run for two years on a trial basis, will pair grades 7-12 teachers and students with UAN faculty mentors and undergraduates for a two-summer research experience. Through this program, we hope to promote research-based educational activities by building connections between teachers and students in secondary schools and colleges. Moreover, we hope the program will present grades 7-12 students with role models and provide UAN faculty and their students with meaningful service-learning opportunities.

In the pilot program, we will pair one grade 7-12 school teacher and student with a UAN faculty mentor and student in each of our UAN regions. The teams will work together for two years (two summers and one academic year) to:

- Conduct scientific research for a minimum of four weeks each summer.
- Develop a classroom activity or a science museum activity related to the research.
- Develop a multimedia tie-in with the State Standards of Learning guides.
- Develop a multimedia vignette of a career involving science aimed at K-12 students.
- Maintain contact throughout the year via classroom visits by the undergraduate faculty and students, science fair activities, etc.

Each summer, the secondary school teachers will receive a \$4,000 award, and the students will receive \$1,000. The UAN faculty mentors will also receive \$200 in support.


To apply to be a mentor for this program, UAN faculty should submit the following materials by Feb. 1, 2009:

- The name of a grade 7-12 teacher and a letter from the teacher indicating interest in participating in the program.
- Evidence of support for summer undergraduate student(s). This could be institutional or grant support—no support for summer undergraduate students is provided by ASBMB.
- A brief overview of research that will be conducted.
- Plans for year-round involvement of faculty and undergraduates with the grade 7-12 teacher and their class during the school year, including plans for science fair activities.
- Plans for assessment of outcomes in terms of impact of both the grade 7-12 classroom and the undergraduate students.

The above materials should be discussed with a UAN Regional Director before submission. Final materials should be sent electronically to the appropriate UAN Regional Director. Email address and contact information can be found on the Undergraduate Affiliates Network website (tinyurl.com/5vkt68).

The UAN faculty mentor will be expected to submit both an interim and final report. The second year of funding depends upon successful submission and review of the interim report.

The whole team (secondary and undergraduate teacher, faculty, and students) will be invited to participate in the ASBMB Small Education Meeting in early August 2009 to discuss what worked and what problems were encountered. As part of that meeting, the teacher and faculty member will attend an assessment and grant writing workshop.

The UAN faculty member will also be encouraged to submit an abstract describing his or her program and its outcomes at subsequent ASBMB annual meetings. 

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

Minnesota State University Moorhead UAN Chapter Hosts Regional Science Meeting

BY JOSEPH PROVOST

On Friday, Oct. 17 and Saturday, Oct. 18, the UAN chapter from Minnesota State University Moorhead (MSUM) and Concordia College hosted the fourth annual Undergraduate Research in the Molecular Sciences (URMS) meeting. This meeting was attended by over 90 students and faculty from 12 different schools in Minnesota, North Dakota, and South Dakota.

Thomas Murray, Professor and Chair of the Department of Pharmacology at Creighton University School of Medicine in Omaha, presented his work on “Neuroactive Drugs from the Sea.”

Students presented their research both orally and in poster sessions and were treated to a seminar on biochemistry and microbiology in the beef processing industry by Don Morrow from Creekstone Farms.

A break-out session on how to get into medical school was given by Judy Demers, Chief Admissions Officer at the University of North Dakota School of Medicine. Other break-out sessions included how to get into grad school (by Murray), how to get a job in industry, and starting, sustaining, and funding undergraduate research.

Students also participated in an oral and poster competition. The winners of \$400 Travel Awards to attend the ASBMB annual meeting in New Orleans were:

- Alex Ritter (Concordia College),
- Jarrett Failing (North Dakota State University),
- Andrew Haak (Minnesota State University Moorhead), and
- Craig Kutz (Minnesota State University Moorhead).

Honorable Mentions were awarded to:

- Micheal Scheidt (Concordia College),
- Jenny Canine (Minnesota State University Moorhead),
- Shandon Collins (Minnesota State University Moorhead),
- Dan Fetzer (Minnesota State University Moorhead),
- Nichol Haverland (Minnesota State University Moorhead),
- Peace Enuh (Concordia College),
- Megan Getting (University of North Dakota), and
- Danielle Rastadt (Minnesota State University Moorhead). 



Travel Award Winners

Joseph Provost is Chair of the Biochemistry and Biotechnology Program Committee as well as Professor in the Department of Chemistry at Minnesota State University Moorhead.



URMS Attendees

ASBMB 2008 Graduation Survey Results

BY JAMES ZIMMERMAN

After a three-year hiatus, the annual ASBMB graduation survey is back, and the results are encouraging. While only 220 of the 831 contacted departments responded (about the same number as usual), the number of undergraduates reported receiving baccalaureate degrees was up by more than 10 percent (the highest ever reported in our survey), and the number of doctorate degrees reported increased by almost 20 percent (the second highest ever reported). However, the number of master's degrees reported was down over 40 percent (the lowest ever reported).

Especially encouraging are the reports of tremendous increases in minority graduates at both the baccalaureate and doctoral levels. This year, more Native American, Hispanic, and Black students received degrees than any other time in our nine previous surveys.

Congratulations should go to the Department of Biochemistry, Biophysics & Molecular Biology at Whitman College, the Department of Biochemistry & Biophysics at Oregon State University at the undergraduate level, and to the University of Washington at the doctorate level for the number of Native Americans receiving degrees.

The Biology & Biochemistry Department at the University of Houston, the Chemistry Department at Spelman College, and the Department of Chemistry at Tennessee State University deserve special notice for the number of Black baccalaureate degrees awarded,


while Spelman College deserves special notice for the number of awarded doctoral graduate degrees.

The Biology and Biochemistry Department at the University of Houston was by far the leading producer of Hispanic baccalaureate degrees, and the Biological Sciences Department of Louisiana State University was the major producer of Hispanic Ph.D.'s.

The Department of Chemistry and Biochemistry at Arizona State University led the way in graduating those identifying themselves as Pacific Islanders.

There has also been a change at the faculty level. While the average size of the tenured faculty reported has not changed in the five years since the data was last reported (15.8 percent in 2003 and 15.9 percent in 2008), the percentage of women in these tenured positions has increased from 22 to 35 percent.

A list of schools known to offer degrees in Biochemistry, Molecular Biology, Biotechnology, or Chemistry with a Biochemistry option can be found online at www.asbmb.org/Page.aspx?id=1702. If your school offers such a degree and is not on the list, please contact us at education@asbmb.org.

These survey results can also be found online at asbmb.org/Page.aspx?id=1702. 

James Zimmerman is an Emeritus Professor of Biochemistry at Clemson University and is a Visiting Professor of Chemistry at Colby College.

Graduation Survey Results

	Female B.A./B.S.	Male B.A./B.S.	Female M.A./M.S.	Male M.A./M.S.	Female Ph.D.	Male Ph.D.
American Indian or Alaskan Native	22	23	1	1	10	8
Asian	296	282	20	16	51	53
Black, not of Hispanic Origin	91	59	8	5	12	14
Hispanic	84	59	11	5	16	25
Pacific Islander	12	8	3	0	1	2
White, not of Hispanic Origin	773	773	54	50	125	172
International Students	71	56	34	30	102	109
Unspecified	62	51	1	6	12	19
TOTAL	1411	1311	132	113	329	402

Core of Diversity: NUCLEUS Celebrates 15 Years of Support to Under-represented Science Majors

BY JACQUELINE ALDRIDGE, DAVID USHER, AND HAL WHITE

Chinedu Nworu, a Cell Biology and Anatomy graduate student at the University of Arizona, doubts he would be in graduate school now if it hadn't been for NUCLEUS. Nicole Barkley, a graduate student in Biological Sciences at the University of Maryland Baltimore County, also praises NUCLEUS for providing the support she needed at a majority white institution. These sentiments are shared by many undergraduates who have been nurtured and encouraged by the University of Delaware's NUCLEUS program that celebrated its 15th anniversary this year.

Foundation and Focus

Initiated as part of a Howard Hughes Medical Institute (HHMI) Undergraduate Science Education Grant, the NUCLEUS program at the University of Delaware has served under-represented students in the sciences since 1993. The acronym is intended to be iconic for both biology and chemistry students and stands for Network of Undergraduate Collaborative Learning Experiences for Under-represented Scholars. NUCLEUS is designed to recruit, retain, and graduate academically talented African-American, Latino, Native-American, and Asian students majoring in science disciplines. NUCLEUS seeks to increase the ethnic representation and cultural diversity in the sciences, while providing an environment that encourages academic achievement, leadership, and service.

Phillip Gottlieb conceived the program and hired Victoria Orner as the first NUCLEUS coordinator. The HHMI has continued to support the NUCLEUS program through three additional grant cycles and subsequent coordinators Cherie Dotson (1998–2005), Zakiya Wilson (2005–2006), and Jacqueline Aldridge (2006–present)—under the direction of Hal White and David Usher. Each coordinator has provided a personal touch in encouraging and motivating students to achieve academic, professional, and personal excellence.

Student Support and Enrichment

The mission of the NUCLEUS program from the start has been to provide multi-faceted support for students majoring in a variety of basic science and health disciplines. Students

participating in NUCLEUS initiatives are provided with supplemental academic advising, monitoring, tutorial support, academic and professional development workshops, and peer and professional mentoring programs. These layers of support help students realize their potential as future scientists and cultivate their membership in a community of scholars of like-minded individuals pursuing similar academic and career pathways.

Each year 100–150 students benefit from the NUCLEUS program. Currently, the program's students are 57 percent African-American, 17 percent Latino, 16 percent Asian, 1 percent Pacific Islander, and 9 percent Caucasian. Sixty-four percent of the participants are female, and 36 percent are male. The average cumulative and semester grade point average for the participants in 2007–08 was 3.05 (B average). During the Spring and Fall 2007 calendar year, 25 percent of NUCLEUS students attained Dean's List status by earning a GPA of 3.3 or higher and were recognized for their academic achievements at the annual Dean's List Dinner in the spring.

Now in its 16th year, the NUCLEUS program continues to focus on recruiting and retaining under-represented students in the sciences at the University of Delaware by providing an array of academic enrichment activities that serve as supplemental resources in fostering academic success. Particularly successful are seminar series that address issues students commonly face as science students. Seminars entitled: "How to Thrive in the Sciences: How to Study in Groups, Preparing for Science Classes, and How to Talk with Your Professors," "Academic SWOT Analysis: Identifying Strengths, Weaknesses, Opportunities, and Threats as a Science Student", and "Recommendation Letter Etiquette and Personal Statement Workshops" are held to help students improve study skills, techniques, and habits as well as their communication skills with faculty.

Mentoring, Service, and Research

Another significant feature of NUCLEUS is its Lasting Links Peer Mentoring program. This program is led by selected students (NUCLEUS Student Program Coordinators) who match freshmen and transfer students with older



Former NUCLEUS Coordinators Cherie Dotson (left) and Victoria Orner (right), with the current coordinator, Jacqueline Aldridge (center) at the 15th anniversary NUCLEUS banquet.

and veteran students who have been in the program. Peer mentoring goes beyond assistance with course work. It is designed to foster a sense of “community scholars” among students who share common academic and career interests. These activities, along with others, have proven to be effective in improving grade point averages as well as personal and professional qualities of students.

To show NUCLEUS students that pursuing science and health care careers is highly relevant to themselves and their communities, students have been encouraged to participate in health disparity outreach activities. Since the fall of 2007, students have been asked to select a health topic and participate in a variety of discussions and community activities related to the chosen topic. Students began this initiative by participating in the AIDS Walk, co-hosting a free HIV testing and education event, and hosting a series of health disparity discussions related to breast cancer, prostate cancer, obesity, and HIV.

Finally, undergraduate research is one of the fundamental components of a student’s academic experience at the University of Delaware. An increasing number of NUCLEUS students have become involved in undergraduate research through its research apprentice initiative. Since 2003, there have been 27 research apprentices, 34 HHMI Summer Scholars, 32 McNair Scholars, 1 UNCF Merck Scholar, 1 Fogarty Research Fellow, 2 Imperial

College Research Fellows, 4 Biotechnology Institute Fellows, 7 industrial interns at DuPont and AstraZeneca, 2 National Science Foundation Research Experiences for Undergraduate Scholars, and 3 HHMI EXROP Scholars. These students have presented their work at a variety of scientific meetings, some of which include the International Bone and Cancer Conference, the American Society of Andrology Conference, the Annual Biomedical Research Conference for Minority Students, and the ASBMB Annual Meetings. Most of the students participating in research have gone on to graduate or professional school.

15 Years and Counting


In April, over 125 students, NUCLEUS alumni, faculty, and parents gathered for a banquet to celebrate 15 years

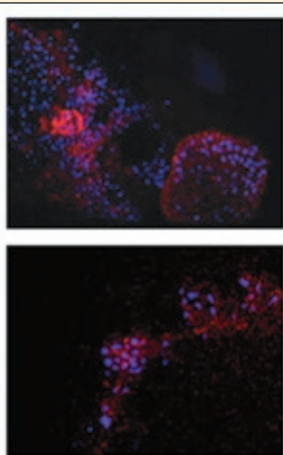
of the NUCLEUS program. Among the attendees were former coordinators Victoria Orner, now Associate Director of Admissions, Saint Michael’s College, Colchester, VT, Cherie Dotson, now Student Affairs Program Manager for Graduate Student Recruitment & Outreach for the College of Pharmacy at the University of Michigan, and featured speaker Marijka Grey, one of the early graduates of the program, who reflected on her NUCLEUS experiences and shared the lessons she had learned in her career. While maintaining its ties to the past, the NUCLEUS program continues to focus on the future and is well poised to continue its impact on diversity in science. As current NUCLEUS coordinator Jacqueline Aldridge states, “When students join NUCLEUS, they are met with a standard that has already been set for them. I want students to understand that it’s not enough just to meet someone else’s standard, but to accomplish your goals in life, you must meet the bar, surpass it, and set a new standard.”

Jacqueline Aldridge is NUCLEUS coordinator at the University of Delaware; David Usher is an Associate Professor and Associate Chairperson in the Department of Biological Sciences at the University of Delaware; and Hal White is a professor in the Department of Chemistry and Director of the University of Delaware’s Howard Hughes Medical Institute Undergraduate Science Education Program.

Going From Skin to Islet

Although islet cell transplantation has shown great promise for achieving insulin independence for patients with type I diabetes, the dearth of matched organ donors and the necessity for chronic immunosuppression makes this treatment less than ideal for the general diabetes population. Therefore, significant research efforts have been put into deriving islet cells from stem cell populations, such as this study, in which the researchers build upon the recent work in successfully reprogramming human skin cells to resemble stem cells. They found that these induced pluripotent stem (iPS) cells can differentiate into islet-like clusters that contain cells positive for pancreatic biomarkers glucagon and C-peptide. Importantly,

these clusters have the capability to respond to glucose treatment with insulin secretion. The researchers point out that the efficiency of generating functional islet-like clusters still needs to be improved, and the safety issues associated with iPS cells must be resolved before clinical application, but this study does provide evidence that insulin-producing cells might someday be easily generated from skin in a patient-specific manner. 



Islet-like cell clusters derived from human stem cells (*top*) or reprogrammed human skin cells (*bottom*) both produce insulin by-product C-peptide (*red*) upon glucose stimulation.

Generation of Insulin-secreting Islet-like Clusters from Human Skin Fibroblasts

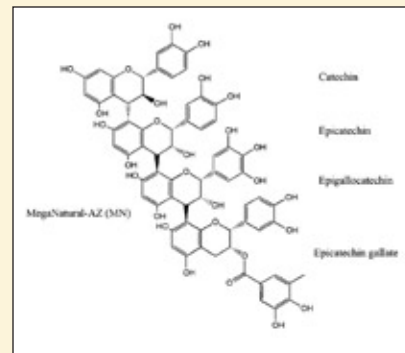
Keisuke Tateishi, Jin He, Olena Taranova, Gaoyang Liang, Ana C. D'Alessio, and Yi Zhang

J. Biol. Chem. 2008 283, 31601-31607

jbc


Why Red Wine Is Good for Your Brain

Epidemiological studies have shown that, among other health benefits, moderate consumption of red wine can decrease the incidence of Alzheimer disease (AD). The active compounds in wine that contribute to this benefit are most likely polyphenols, and in this study, the researchers describe the effects of one such grape seed polyphenolic extract (GPSE) on the assembly and dynamics of amyloid β -proteins, major culprits in



Structure of MegaNatural-AZ, a grape seed polyphenol that may protect against Alzheimer disease.

AD pathogenesis. Using a combination of approaches including CD

spectroscopy and photo-induced cross-linking, they found that this commercially available extract, called MegaNatural-AZ (MN), was a potent inhibitor of all stages of amyloid formation: protofibril formation, peptide oligomerization, and assembly into amyloid β -sheet aggregates. Cytotoxicity assays also demonstrated that MN was cell-protective when mixed in with amyloid proteins prior to either peptide assembly or addition of peptides to cells. Taken together with recent mouse studies showing that MN can attenuate AD-like cognitive defects, this work suggests that MN could be a potent therapeutic agent against AD. 


Effects of Grape Seed-derived Polyphenols on Amyloid β -Protein Self-assembly and Cytotoxicity

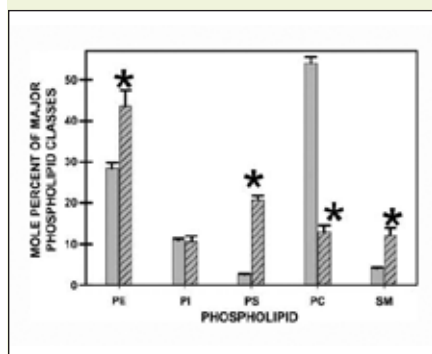
Kenjiro Ono, Margaret M. Condrón, Lap Ho, Jun Wang, Wei Zhao, Giulio M. Pasinetti, and David B. Teplow

J. Biol. Chem. 2008 283, 32176-32187


jbc

Lipid Changes During Fertilization

The fertilization of a sperm and an egg involves metabolic activation, membrane fusion events, and the production and hydrolysis of phospholipids. Until now, though, there has been no thorough quantification of the varied phospholipid changes during fertilization. In this study, researchers have combined traditional fatty acid analysis by thin-layer chromatography (TLC) and gas chromatography, along with a new measurement technique involving high pressure liquid chromatography (HPLC) separation and evaporative light-scattering detection to report on lipid levels in eggs, sperm, and during fertilization in *Xenopus*. Not surprisingly, sperm and eggs contained significant differences in their phospholipid content; for example, sperm contain more phosphatidylethanolamine but less phosphatidylcholine. And, as expected, lipid composition changed dramatically during fertilization as well, such as a decrease in phosphatidylinositol likely brought on by the increased levels of PIP2. This detailed examination of the total amount and composition of the major lipid classes during this developmental process should provide for a more comprehensive model of both gamete physiology and fertilization events. 



A comparison of *Xenopus* egg (solid bar) and sperm (hatched bar) phospholipids.

This detailed examination of the total amount and composition of the major lipid classes during this developmental process should provide for a more comprehensive model of both gamete physiology and fertilization events. 


Lipid Levels in Sperm, Eggs, and During Fertilization in *Xenopus Laevis*

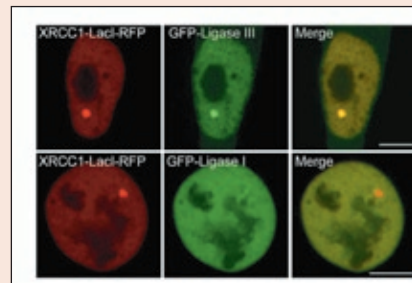
Douglas W. Petcoff, William L. Holland, and Bradley J. Stith

J. Lipid Res. 2008 49, 2365-2378




The Wonders of GFP

Advances in high-throughput genetic screening have yielded large sets of potential protein-protein interactions that now need to be verified and further investigated. In this study, the researchers developed a simple assay to accomplish just that, combining the power of a yeast two-hybrid system with fluorescence imaging of GFP to directly visualize protein-protein interactions in living cells. This fluorescent two-hybrid (F2H) assay uses a modified *lac* repressor system to tether a fluorescent bait protein at a chromosomal *lac* operator array, producing a brightly colored spot. Fusion prey proteins with a different fluorescence can then be assayed for co-localization, as revealed by a change in color. With the F2H assay, the researchers successfully investigated the interaction of proteins from multiple subcellular compartments including the nucleus, cytoplasm, and mitochondria. In combination with an S-phase marker, they could also study the cell cycle dependence of these interactions. This study indicates that F2H could be a powerful tool to investigate protein-protein interactions within their cellular environment in real-time and provides a fine example of what can be done with the recent awarding-winning GFP technology. 



The F2H assay reveals the specific interaction of DNA Ligase III, but not the homologous DNA Ligase I, with the DNA repair protein XRCC1.

This study indicates that F2H could be a powerful tool to investigate protein-protein interactions within their cellular environment in real-time and provides a fine example of what can be done with the recent awarding-winning GFP technology. 

A Fluorescent Two-hybrid (F2H) Assay for Direct Visualization of Protein Interactions in Living Cells

Kouros Zolghadr, Oliver Mortusewicz, Ulrich Rothbauer, Regina Kleinhans, Heike Goehler, Erich E. Wanker, M. Cristina Cardoso, and Heinrich Leonhardt

Mol. Cell. Proteomics 2008 7, 2279-2287



Sung-Hou Kim: Consummate Crystallographer

BY NICK ZAGORSKI

Symmetry. It's a simple concept, yet whether they occur naturally or through man-made design, symmetrical objects often evoke a sense of beauty and wonder. But symmetry is more than just an aesthetically pleasing design; it's also an underpinning component of physics, chemistry, and biology. The symmetrical properties of molecules define both their chemical and spectroscopic qualities and are a key reason the structures of proteins and other macromolecules can be deduced through x-ray crystallography.

These symmetrical properties are also a major reason that Sung-Hou Kim, professor in the Department of Chemistry at the University of California, Berkeley, became enamored with science. Kim was a bit of a late-bloomer, as he was not interested in science until his final year of high school, when the beauty and functionality of molecular shapes led him down a path of crystallography, a field in which symmetry was especially prominent.

And amongst the numerous scientists who have employed crystallography in their work, few have been more prolific than Kim. He has been dutifully solving molecular structures for over 40 years, starting at a time when using crystallography for protein structures was not even feasible. Back then, he was content looking at the level of small molecules, but as his skills and vision matured, he moved up the hierarchy; first looking at nucleic acids, then proteins, and now, grand projects aimed at obtaining structural information of all proteins in a mini-

mal organism and subsequently "mapping" all known architectural motifs in the protein universe.

Opportunities and Luck

Unfortunately, though, while the world of atoms and molecules featured an abundance of symmetry and balance, the real world in South Korea was anything but when Kim was studying chemistry at Seoul National University in the late 1950s. In the years since the end of the Korean War, Kim's homeland had been experiencing a near-continuous period of political and economic instability. "It was at the point where you really couldn't plan your life more than a few months in advance," Kim says, who, after completing his Masters in Chemistry in 1962, realized that if he wanted to continue his academic progress, it would be best to do so abroad. At the time, crystallography was popular in Europe, but Kim preferred to find a place in the U.S., as many of his friends had emigrated there.

Of the schools Kim applied to, the University of Pittsburgh was the first to respond with an acceptance, which was enough for Kim to make his decision. It proved to be a good one, as he ended up joining the lab of George Jeffrey, an English crystallographer renowned for his work on hydrogen bonds, who had been recruited to Pittsburgh in 1953 and had since set up one of the strongest crystallography labs in the States; in fact, Jeffrey was responsible for creating the first graduate department



of crystallography in the entire U.S. "I ended up being extremely well-trained in this field," Kim notes. "In fact, in the last year of my graduate studies, I was even helping other faculties with the latest techniques in crystallography, which was an unusual experience for a foreign graduate student."

While completing his doctorate, in which he determined the structures of small organic molecules like sugars and sugar derivatives, which was considered very challenging because of the absence of heavy atoms, Kim became interested in the emerging field of "new biology," referring to the birth of modern molecular biology in the 1960s following the discoveries of DNA structure, gene expression, and the genetic code. "So, I decided to switch over from chemistry to biology for my postdoc, even though most of my colleagues warned me not to do that, because it was too big a change." Kim was steadfast, though, and when Jeffrey came to him one day and mentioned that a colleague of his in the Massachusetts Institute of Technology Biology Department was looking for a postdoc, Kim exclaimed, "I'll take it," before even asking who it was.

A Rich Endeavor

The mystery professor turned out to be Alex Rich, who has become quite well-known for his work elucidating DNA and RNA structure. When Kim joined, one of Rich's lab projects was studying abnormal base pairing, though this area had been struggling due to an inability to get structural data. "Alex knew I had a strong crystallography background and put me on the project," Kim says, "and when I first looked at it, I knew I had been well-trained, because I said to myself, 'Okay, this should be easy.'"

Sometimes those can be famous last words, but Kim's expertise prevailed, and he solved the problem in a short time, generating structures of non-standard cytosine-uracil and phenobarbital (a uracil derivative)-adenine pairs. "And that was great for me because it gave me a great deal of credibility in the lab, which I needed because I wasn't familiar with this new biology." (Though Kim made sure to attend numerous molecular biology lectures during his postdoc to learn as much as possible.)

That crystallographic cachet helped Kim tackle his next endeavor, which was determining the structure of a transfer RNA molecule, a hot commodity in molecular biology circles. "The size of the molecule was on a scale far beyond what I was used

to working with," Kim says, "but fortunately Rich had enough confidence in my abilities that he let me try." Kim notes this project got started partially from his ignorance of two well-known facts: one, several labs in Europe and the United States tried to crystallize tRNAs without success—"Alex wisely did not tell me about this"—and two, a prevailing wisdom then was that biological macromolecules such as

proteins crystallize by the contacts between hydrophobic surface patches, thus making the charged and hydrophilic surfaces of tRNAs non-crystallizable.

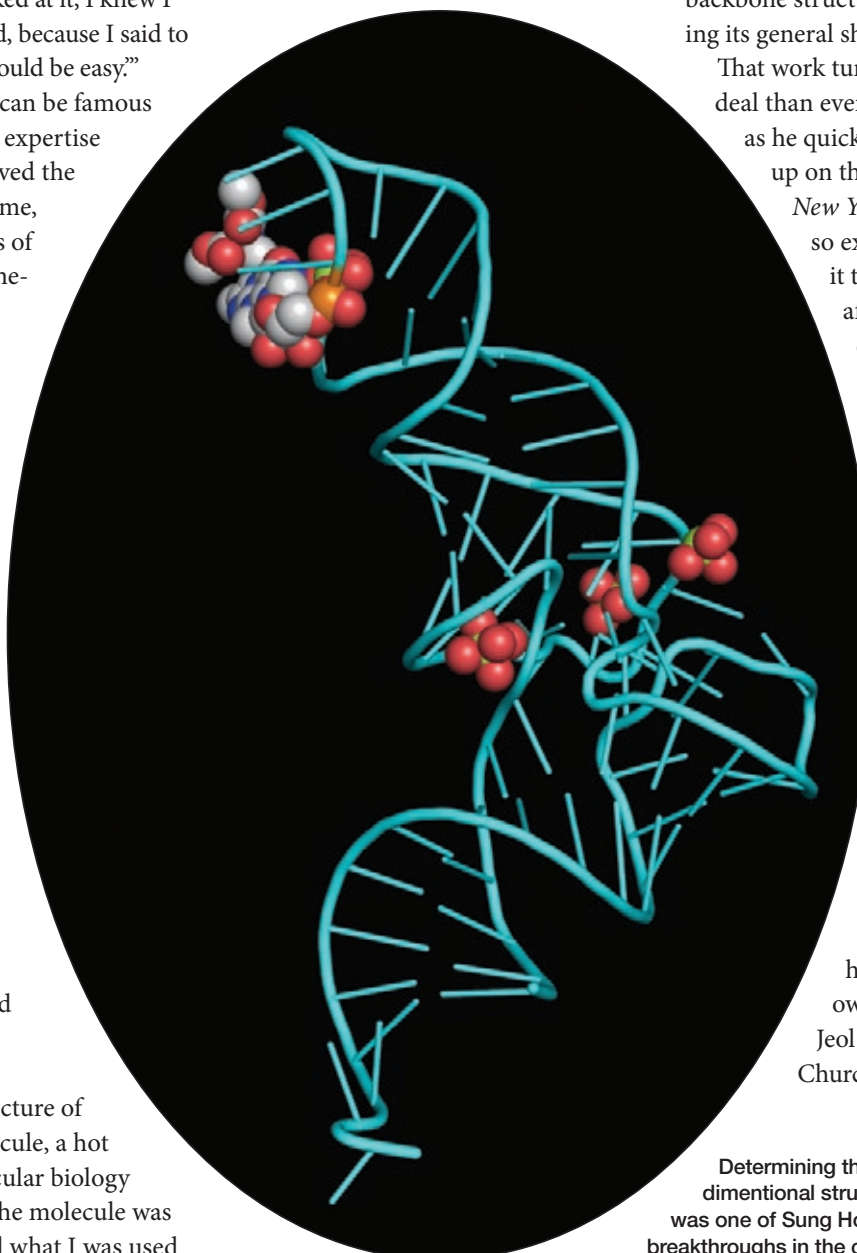
This project took longer, but after five years of collaboration with skilled colleagues of the structural group in Rich's lab (initially with Bud Suddath and Gary Quigley) and a little luck, Kim managed to solve the complete backbone structure of a tRNA, revealing its general shape for the first time.

That work turned out to be a bigger deal than even Kim had imagined, as he quickly saw his work pop up on the front page of *The New York Times*. "That was so exciting," he says, "and it taught me not to be afraid to tackle some of the big problems of biology, and to take 'known' facts and prevailing wisdoms with a grain of salt."

Proteins of Interest

After completing his post-doctoral training, Kim moved on to a professorship in the biochemistry department at Duke University School of Medicine, where he continued his tRNA work with his own group (started with Jeol Sussman and George Church) and, with the help

Determining the L-shaped three-dimensional structure of transfer RNA was one of Sung Hou Kim's first major breakthroughs in the crystallographic arena.

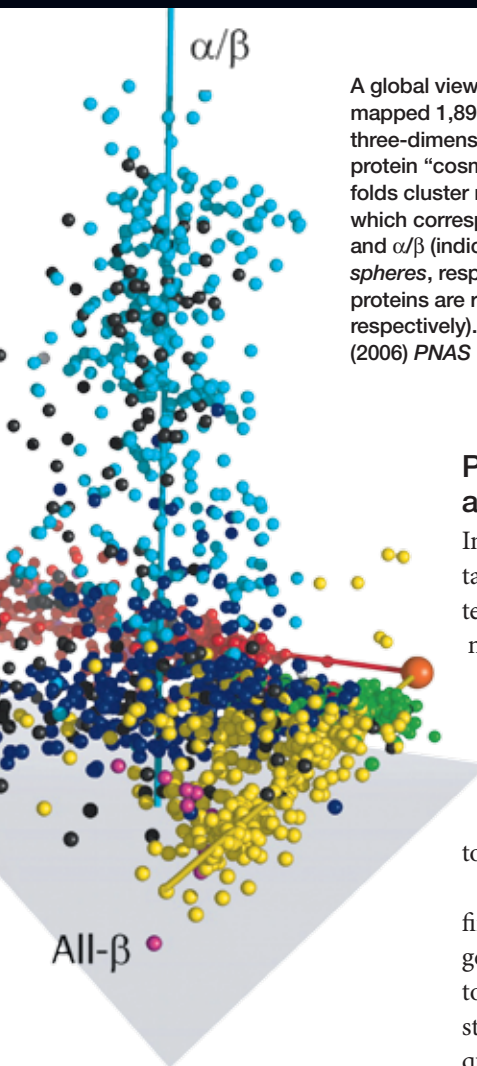


of his colleagues back at MIT, managed to piece together the complete atomic structure. At Duke, recognizing the staggering diversity of proteins, he also took his first forays into protein crystallography, initiating the structural studies of a pair of recently discovered unusual proteins, monellin and thaumatin, that produced an intensely sweet sensation (over 1000 times more potent than sugar).

In 1978, Kim relocated to Berkeley after being recruited by the school. "Initially, I wasn't very keen on the idea of moving," he says. "But I realized that some of the projects I was becoming interested in required not only a knowledge of biology, but also chemistry, physics, and mathematics. I decided that Berkeley would give me a better chance to interact with people of different backgrounds."

It wouldn't take long for Kim to interact with one such individual who exposed him to new concepts. One day, while he was working in his office, he was paid a visit by his Berkeley colleague Daniel Koshland, who started explaining chemotaxis (Koshland's area of expertise) to a very intrigued Kim. "I said, 'Wow, that's a really neat system. How does the signal get from the outside to the inside of the cell?'" Koshland replied that he was unsure, because he had no idea what the chemotaxis receptor looked like. So I said 'Oh, really? Well, let's get on it.'"

Get on it they did, and soon they had solved the first structures of a chemotaxis receptor, initially getting the external ligand binding domain and later the internal signaling domain, work which helped explain how weak chemotaxis signals can be readily amplified. Over the years, he tackled other proteins of interest and



A global view of protein structure space. Kim has mapped 1,898 non-redundant protein structures in three-dimensions, revealing a sparsely populated protein "cosmos" in which all of the known protein folds cluster mostly into four elongated regions, which correspond to four classes: all- α , all- β , $\alpha+\beta$, and α/β (indicated by red, yellow, purple, and cyan spheres, respectively; small proteins and multidomain proteins are represented by green and black spheres, respectively). Reprinted from Choi, I.G. and Kim, S.-H. (2006) *PNAS* **103**, 14056-14061.

continued his penchant for structural "firsts," such as: first proto-oncogene product (c-H-Ras) (in collaboration with the groups of Susumu Nishimura and Eiko Ohtsuka), the first human cyclin, CDK2 (in collaboration with David Morgan's group), and cyclin-dependent kinase, and the first small heat shock protein.

The collaboration with Koshland also brought about a second major epiphany for Kim. "Our structural data was actually not consistent with some of the results Koshland's group obtained through biochemistry," he says, "but now they could reinterpret their data based on the structure. Right then, I realized how important structural information is, in order to unify all the other data about a biological molecule."

Protein Space, a Final Frontier?

In the past decade, Kim has begun taking a larger view of the world of proteins. "When I first started my research, not many people were doing structural biology," he says. "But then, not long ago, I looked around me and saw all these bright young people solving complex protein structures, so I thought, 'Okay, maybe I don't have to do this anymore.'"

With that, Kim became one of the first to enter the field of structural genomics. "We had figured out how to solve large numbers of protein structures from hyperthermophiles quickly," he says, "And I had an idea that we could use these tools to get global views of relative usage of architectural motifs (fold patterns) by proteins in one single organism and, then, in all organisms." This idea, Kim notes, arose after he heard about a project in Lawrence Berkeley Lab aimed at creating a three-dimensional map of the cosmic universe. His proposal, initially funded as a Department of Energy project, was taken up by NIH in 2000 as part of the Protein Structure Initiative (PSI).

After accomplishing the first goal and obtaining protein fold information of over 92 percent of all soluble proteins in the minimal organism *Mycoplasma*, Kim's group developed a computational approach that took about 2,000 unique protein structures containing all the known architectural motifs and mapped them in space,

based on how closely related the folds were. “I had some thoughts as to how it would turn out, but much of my initial intuition turned out to be wrong. The results were full of surprises.”

For one, Kim was confident that the abundance and diversity of folds would fill up the protein fold space uniformly (like the cosmic universe) as nature had billions of years to maximize all the potential conformations. However, the demography of protein structures concentrated in only four areas in the map, comprising alpha helices, beta sheets, a random mix of the two, and an alternating alpha-beta mix (the most populated area); this mathematically derived demographic grouping ended up being remarkably similar to the Structural Classification System of Proteins (SCOP), based on visual comparisons. Kim could also use his model to figure out the age of certain motifs and found that the alternating alpha/beta fold was the longest evolving protein family.

Borrowing a Page from the Plagiarists

Encouraged by the mapping of the protein structure universe, Kim is currently excited about organizing the whole genome/chromosome universe, another project that stemmed from an external lecture Kim listened in on. This one came from the computer science department, in a talk about the computer programs used to detect plagiarism in written texts (incidentally, these programs were originally developed as a means to detect plagiarism in computer coding, as people would cheat by using someone else’s code, just rearranged, in their own programs).

“Normally, when scientists compare organisms, they pick a set of common genes and align them to examine similarity,” Kim says. “Now, depending what genes you pick, you may get different results. However, it’s still the only method because we have no way

of accurately comparing genome/chromosomal sequences.” As Kim listened to this talk, though, he wondered if he could modify this program for biology. If one considers each organism’s genome as a book and their DNA as the text—granted it’s text without spaces, thus making each chromosome essentially one big word—then maybe he could determine how much genetic plagiarism two organisms share.

“I’m convinced this method could be a much more general way to characterize species from bacteria to humans,” he notes. Of course, he will tread carefully as evolution is not his specialty, but he’s tackled areas outside his expertise before and thinks an outsider’s view sometimes can be very revealing.

For all the growth Kim has been doing as a scientist—going from the structures of simple sugars to entire

Out of Focus: Making a List, Checking It Twice...

Picking the right graduate school is always a challenge, and for Sung-Hou Kim, who knew precious little about American universities, it was a particularly big one. He admittedly had no idea which U.S. schools—if any—had strong crystallography programs, so he decided the best bet was to let the journals decide. “I just went to the library, picked out one of the current crystallography journals, and made a short table ranking universities by the number of publications they had.” When he was done, he sent off his applications to the three most “prolific” institutions on his list, which happened to be Pennsylvania State University, the University of Pittsburgh, and the University of Connecticut.

chromosomes is no easy feat—he’s equally impressed with how his home country has grown since he left over 40 years ago. Over the past several years, he has taken numerous trips back to Korea, either to help set up new research institutes or act as an advisor for different governmental offices, research and educational institutes, “I can barely recognize it sometimes, even in contrast to as recently as 15 years ago.”

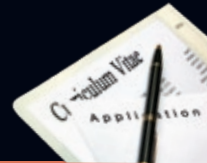
Kim notes that the Korean government has been spending money on science and technology programs, and combined with an influx of bright young scientists, many of whom trained in the U.S. and have returned home, has spurred a new boom in research. “The only thing Korean research needs now is a stronger presence on the managerial level, getting in those scientists who have a good scientific vision and a practical sense of how to realize the vision. But, I think within the next generation, they should be there.”

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

REFERENCES

- Kim, S.-H., Quigley, G. J., Suddath, F. L., McPherson, A., Sneden, D., Kim, J. J., Weinzierl, J., and Rich, A. (1973) Three-dimensional Structure of Yeast Phenylalanine Transfer RNA: Folding of the Polynucleotide Chain. *Science* **179**, 285-288.
- De Vos, A. M., Tong, L., Milburn, M. V., Matias, P. M., Jancarik, J., Noguchi, S., Nishimura, S., Miura, K., Ohtsuka, E., and Kim, S.-H. (1988) Three-dimensional Structure of an Oncogene Protein: Catalytic Domain of Human c-H-Ras p21. *Science* **239**, 888-893; Correction: *Science* (1989) **245**, 244.
- Yeh, J. I., Biemann, H. P., Pandit, J., Koshland, D. E., and Kim, S.-H. (1993) The Three-dimensional Structure of the Ligand-binding Domain of a Wild-type Bacterial Chemotaxis Receptor. Structural Comparison to the Cross-linked Mutant Forms and Conformational Changes upon Ligand Binding. *J. Biol. Chem.* **268**, 9787-9792.
- Kim, K. K., Yokota, H., and Kim, S.-H. (1999) Four-helical-bundle Structure of the Cytoplasmic Domain of a Serine Chemotaxis Receptor. *Nature* **400**, 787-792.
- Hou, J., Jun, S.-R., Zhang, C., and Kim, S.-H. (2005) Global Mapping of the Protein Structure Space and Application in Structure-based Inference of Protein Function. *Proc. Natl. Acad. Sci. U. S. A.* **102**, 3651-3656.

career opportunities



Mississippi State University **ASSISTANT PROFESSOR** **DEPARTMENT OF BIOCHEMISTRY** **AND MOLECULAR BIOLOGY**

Mississippi State University (MSU) invites applications and nominations for the position of Assistant Professor with a cross-disciplinary approach to the biochemical and/or molecular sciences with potential agricultural research applications consistent with the mission of a Land Grant University in the Department of Biochemistry and Molecular Biology. This 9-month tenure track position has an anticipated 50% teaching and 50% research appointment. The successful candidate will be expected to develop a nationally recognized teaching and research program in their subject discipline, develop new and/or modify existing courses (including technology-based course development), pursue extramural funds in support of research aims, and publish results in peer reviewed research journals. Applicants should have a Ph.D. in Biochemistry, Molecular Biology, or related field. Preference will be given to candidates with postdoctoral experience

and a clear potential for, or demonstrated, excellence in teaching, advising, research, service and/or grantsmanship. Review of applicants will begin October 24, 2008, and will continue until a suitable candidate is identified.

Applicants are required to complete the Personal Data Information Form on-line at www.jobs.msstate.edu. Please submit either on-line, at www.hrm.msstate.edu/employment/postings.htm, or to the address below a letter of application outlining career goals, a curriculum vitae, transcripts and three letters of reference to:

Scott T. Willard, Ph.D.
Department of Biochemistry
and Molecular Biology
Box 9650
Mississippi State, MS 39762
Email: swillard@ads.msstate.edu,
telephone: 662-325-7736.

Mississippi State University is an Affirmative Action/Equal Opportunity Employer.



TWO TENURE-TRACK POSITIONS **Departmental Chair of Chemistry and Biochemistry** **and tenure-track position in Biochemistry**

The Department of Chemistry and Biochemistry invites applications and nominations for the position of Chair at the rank of Professor. Applications are also sought for a tenure-track faculty position in the area of biochemistry. Both positions have a start date of July 1, 2009. The Information regarding our Department, description of these positions, and procedure for application can be found at www.science.duq.edu/chemistry.

For the **Chair** position, we seek an accomplished scientist with imagination and energy, as well as leadership to strengthen our educational and research programs to a new level of international recognition and accomplishment. The preferred candidate will have an excellent record of publication and extramural support, a commitment to education, and strong leadership skills.

For the **Biochemist** position, we anticipate that the appointment will be at the assistant professor rank, but exceptional candidates at a higher rank will be considered. Candidates must have a Ph.D. in biochemistry or related field, the potential to develop an externally funded, internationally recognized research program, and the commitment to excellence in teaching at the undergraduate and graduate levels.

The Department of Chemistry and Biochemistry encourages quality candidates from diverse backgrounds to apply. Salary will be commensurate with qualifications and experience. Review of applications will begin **December 8, 2008** and will continue until the positions are filled.

Applicants must be willing to contribute actively to the University Mission and to respect the Spiritan Catholic identity of Duquesne University. The Mission is implemented through a commitment to academic excellence, a spirit of service, moral and spiritual values, sensitivity to world concerns, and an ecumenical campus community.

Duquesne University was founded in 1878 by its sponsoring religious community, the Congregation of the Holy Spirit. Duquesne University is Catholic in mission and ecumenical in spirit. Motivated by its Catholic identity, Duquesne values equality of opportunity both as an educational institution and as an employer.



June 6-11
2010

Hyaluronan 2010

International Society for Hyaluronan Sciences
8th International Conference, Kyoto, Japan

Conference organizers

Koji Kimata (Aichi Medical University)
Masaki Yanagishita (Tokyo Medical & Dental University)
Bryan Toole (Medical University of South Carolina)

Venue

Kyoto Brighton Hotel, KYOTO, JAPAN
(<http://www.kyotobrighton.com/>)

SCIENTIFIC SESSIONS

- Structure and Biophysics
- Synthesis and Degradation
- Development and Aging
- Musculoskeletal Systems
- Neural Tissues
- Tumors
- Cardiovascular and Lymphomyeloid Systems
- Organs (kidney, lung, liver, glands)
- Inflammation and Regeneration
- Skin and Reproductive Systems
- Therapeutic Applications (4 sessions)

For more information on the Conference please contact the Society at : www.ISHAS.org

International Society for Hyaluronan Sciences

<http://www.ishas.org>

Tel:843-388-2678 Fax:843-971-9132

scientific meeting calendar

DECEMBER 2008

Exploring Modular Protein Architecture

DECEMBER 3-5, 2008

HEIDELBERG, GERMANY

www-db.embl.de/jss/EmblGroupsOrg/conf_110

The Annual Meeting of the American Society for Matrix Biology (ASMB)

DECEMBER 7-11, 2008

SAN DIEGO, CA

www.asmb.net

The 48th American Society for Cell Biology Annual Meeting

DECEMBER 13-17, 2008

SAN FRANCISCO, CA

www.ascb.org/meetings

The Science of Eliminating Health Disparities

DECEMBER 16-18, 2008

NATIONAL HARBOR, MD

www.blsm meetings.net/2008healthdisparities/submit/

JANUARY 2009

Gordon Research Conference: Glycobiology

JANUARY 18-23, 2009

VENTURA, CA

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

Keystone Symposium—Obesity: Novel Aspects of the Regulation of Body Weight

JANUARY 20-25, 2009

BANFF, ALBERTA, CANADA

www.keystonesymposia.org/Meetings/ViewMeetings.cfm?MeetingID=997

Sanibel Conference on Mass Spectrometry: Lipidomics and Lipids in Mass Spectrometry

JANUARY 23-26, 2009

ST. PETERSBURG BEACH, FL

www.asms.org/Default.aspx?tabid=70

The 22nd Biennial Conference of the Australian & New Zealand Society for Mass Spectrometry

JANUARY 27-30, 2009

SYDNEY, AUSTRALIA

www.mmb.usyd.edu.au/ANZSMS22

FEBRUARY 2009

Gordon Research Conference—Plant Lipids: Structure, Metabolism, & Function

FEBRUARY 1-6, 2009

GALVESTON, TX

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

Molecular Targets for Cancer Prevention Conference

FEBRUARY 4-5, 2009

BETHESDA, MD

<http://web.ncifcrf.gov/events/cancerprevention/2009/default.asp>

The 14th Annual Proteomics Symposium

FEBRUARY 6-8, 2009

LORNE, AUSTRALIA

www.australasianproteomics.org

Pacific Lipid Association 3rd Annual Scientific Forum

FEBRUARY 20-22, 2009

SALT LAKE CITY, UT

www.lipid.org

US HUPO 5th Annual Conference

FEBRUARY 22-25, 2009

SAN DIEGO, CA

www.ushupo.org

E-mail: ushupo@ushupo.org

Tel.: 505-989-4876

Keystone Symposium—Complications of Diabetes and Obesity

FEBRUARY 24-MARCH 1, 2009

VANCOUVER, BRITISH COLUMBIA

www.keystonesymposia.org/Meetings/ViewMeetings.cfm?MeetingID=998

2nd International Conference on Advanced Technologies & Treatments for Diabetes (ATTD)

FEBRUARY 25-28, 2009

ATHENS, GREECE

www.2.kenes.com/attd/Pages/home.aspx

Biophysical Society 53rd Annual Meeting

FEBRUARY 28-MARCH 4, 2009

BOSTON, MA

www.biophysics.org/2009meeting

MARCH 2009

Deuel Lipid Conference

MARCH 3-6, 2009

BORREGO SPRINGS, CA

www.deuelconference.org

Gordon Conference on Oxidative Stress & Disease

MARCH 8-13, 2009

TUSCANY, ITALY

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

ACS Spring National Meeting & Exposition

MARCH 22-26, 2009

SALT LAKE CITY, UT

www.acs.org/meetings

APRIL 2009

3rd International Congress on Prediabetes and the Metabolic Syndrome—Epidemiology, Management, and Prevention of Diabetes and Cardiovascular Disease

APRIL 1-4, 2009

NICE, FRANCE

www.kenes.com/prediabetes

ASBMB Annual Meeting

APRIL 18-22, 2009

NEW ORLEANS, LA

www.asbmb.org/meetings.aspx



**Keystone Symposium—
Complex Lipids in
Biology: Signaling,
Compartmentalization,
and Disease**

APRIL 22–27, 2009

OLYMPIC VALLEY, CA
[www.keystonesymposia.org/Meetings/
ViewMeetings.cfm?MeetingID=961](http://www.keystonesymposia.org/Meetings/ViewMeetings.cfm?MeetingID=961)

**Arteriosclerosis, Thrombosis,
and Vascular Biology Annual
Conference**

APRIL 29–MAY 1, 2009

WASHINGTON, D.C.
[www.americanheart.org/presenter.
jhtml?identifier=3057022](http://www.americanheart.org/presenter.jhtml?identifier=3057022)

2009 NLA Scientific Sessions

APRIL 30–MAY 3, 2009

MIAMI, FL
www.lipid.org

MAY 2009

**57th ASMS Conference
on Mass Spectrometry**

MAY 31–JUNE 4, 2009

PHILADELPHIA, PA
www.asms.org
E-mail: office@asms.org
Tel.: 505-989-4517

JUNE 2009

**VIII European Symposium
of the Protein Society**

JUNE 7–11, 2009

ZURICH, SWITZERLAND
Organizer: Andreas Plückthun
(University of Zurich)
www.proteinsociety.org

**21st American Peptide
Society Symposium**

JUNE 7–12, 2009

BLOOMINGTON, IN
www.21staps.org

Cancer Proteomics 2009

JUNE 8–12, 2009

DUBLIN, IRELAND
[www.selectbiosciencics.com/conferences/
files/Agendas2009/CP2009_Agenda.pdf](http://www.selectbiosciencics.com/conferences/files/Agendas2009/CP2009_Agenda.pdf)

**3rd EuPA Meeting—
Clinical Proteomics**

JUNE 14–17, 2009

STOCKHOLM, SWEDEN
[www.lakemedelsakademin.se/templates/
LMAstandard.aspx?id=2529](http://www.lakemedelsakademin.se/templates/LMAstandard.aspx?id=2529)

**VII European Symposium
of the Protein Society**

JUNE 14–18, 2009

ZURICH, SWITZERLAND
www.proteinsociety.org

**XV International
Symposium on
Atherosclerosis**

JUNE 14–18, 2009

BOSTON, MA
www.isa2009.org

**Gordon Research Conference:
Atherosclerosis**

JUNE 21–26, 2009

TILTON, NH
[www.grc.org/programs.
aspx?year=2009&program=athero](http://www.grc.org/programs.aspx?year=2009&program=athero)

SEB at Glasgow 2009

JUNE 28–JULY 1, 2009

GLASGOW, SCOTLAND
[www.sebiology.org/meetings/Glasgow/
glasgow.html](http://www.sebiology.org/meetings/Glasgow/glasgow.html)

JULY 2009

**Gordon Research
Conference: Molecular &
Cellular Biology of Lipids**

JULY 19–24, 2009

WATERVILLE VALLEY, NH
[www.grc.org/programs.
aspx?year=2009&program=lipids](http://www.grc.org/programs.aspx?year=2009&program=lipids)

**23rd Annual Symposium
of the Protein Society**

JULY 25–29, 2009

BOSTON, MA
www.proteinsociety.org

**Protein Lipidation,
Signaling, and
Membrane Domains**

JULY 26–31, 2009

SAXTONS RIVER, VT
src.faseb.org

AUGUST 2009

**ACS Fall 2009 National
Meeting & Exposition**

AUGUST 16–20, 2009

WASHINGTON, D.C.
www.acs.org/meetings

**18th International Mass
Spectrometry Conference**

AUGUST 30–SEPTEMBER 4, 2009

BREMEN, GERMANY
www.imsc-bremen-2009.de

SEPTEMBER 2009

**World Congress on Oils and
Fats and 28th ISF Congress**

SEPTEMBER 27–30, 2009

SYDNEY, AUSTRALIA
www.isfsydney2009.com

OCTOBER 2009

**3rd ESF Functional Genomics
Conference**

OCTOBER 1–4, 2009

INNSBRUCK, AUSTRIA
www.esffg2008.org

**Bioactive Lipids in
Cancer, Inflammation,
and Related Diseases
(11th International
Conference)**

OCTOBER 25–28, 2009

CANCUN, MEXICO
www.bioactivelipidsconf.wayne.edu

APRIL 2010

ASBMB Annual Meeting

APRIL 24–28, 2010

ANAHEIM, CA
www.asbmb.org/meetings.aspx

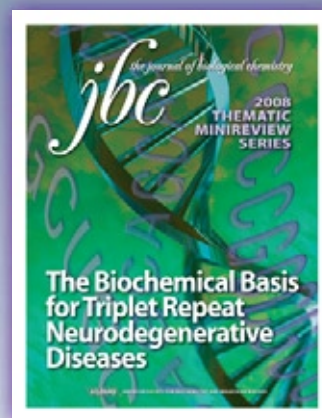
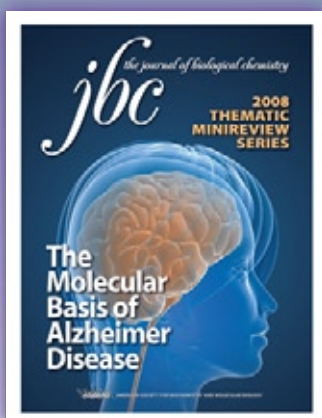
AUGUST 2010

**14th International
Congress of Immunology**

AUGUST 22–27, 2010

KOBE, JAPAN
www.ici2010.org

the journal of biological chemistry jbc



THEMATIC MINIREVIEW SERIES

With the rapid rate of today's scientific advancements, it can be difficult enough to keep up with one's own research speciality, let alone the numerous other disciplines covered under the biochemistry umbrella.

JBC Minireviews Allow You To:

- *Keep abreast of the advances and trends in biochemical research outside your own area of expertise.*
 - *Digest a concise summary of a particular field in a manner understandable to biochemists working in any area.*

www.jbc.org/thematics