

OCTOBER 2004

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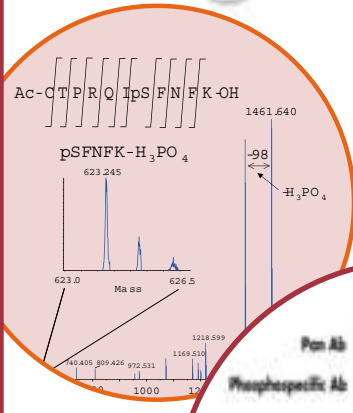
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# ASBMB *Today*

AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

OCTOBER 2004,  
Volume 3, Issue 7

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## LETTERS

# BAMBED: An Unfortunately Well-kept Secret?

**W**hen I talk with biochemical colleagues about *BAMBED*, I often get blank stares. "Wasn't that the movie about the deer fawn, back in the 1940s?" Well, no. *BAMBED* is one of five journals published by ASBMB (including *ASBMB Today*, which you are holding as you read this). *BAMBED* is *Biochemistry and Molecular Biology Education*, formerly the *Journal of Biochemical Education*, which was taken over by ASBMB several years ago.

Under the capable co-Editorship of Don and Judy Voet, *BAMBED* is, in my opinion, one of the most enjoyable biochemical journals to read. I believe that everyone who teaches biochemistry should see this journal; certainly every department that teaches biochemistry courses should have a departmental subscription, to supplement personal subscriptions among the faculty. But even biochemists not involved in teaching can find something to enjoy in this highly readable journal.

Consider the contents (partial) of the past two issues of this slim bi-monthly publication. The May-June issue contained one in a series of Metabolic Minimaps, this one covering purines and pyrimidines. Articles included "Virtual Bioinformatics Distance Learning Suite," "Oxidation-Reduction Calculations in the Biochemistry Course," and "An Interactive Introduction to Protein Structure." Laboratory Exercises included an integrated molecular biology course built about PCR and sub-cloning into a GFP-fusion plasmid vector. Two problem-based learning modules focused on "Biochemistry and Academic Abstinence," and "cAMP Regulation of the Lactose Operon." There followed several articles on multimedia and websites of

note, and the journal concluded with four sprightly book reports.

The July-August issue included articles about the microarray revolution and how to incorporate bioinformatics into undergraduate courses. The five laboratory exercises included an exercise using changes in plasmid topology, as shown by agarose gel electrophoresis, to analyze DNA strand breaks. A brave author wrote about the challenge of defining biotechnology and reaching a national or global consensus (harder than defining what "is" is?). Finally, more multimedia/website articles, and at the end, six book reviews, including a review of George Beadle, *An Uncommon Farmer: The Emergence of Genetics in the 20th Century*, by P. Berg and M. Singer. You don't have to be a biochemistry teacher to find this kind of material a good read.

My impression is that this excellent journal is not being seen by many ASBMB members and others who would enjoy it if they saw it. That might even lead to improvement in many biochemistry courses. So I am recommending first, that every department chair order and circulate a departmental subscription, and second, that individual faculty members, who may already have more personal subscriptions than they can handle, urge their libraries to take institutional subscriptions. Help this journal to reach its full potential; help us to make *BAMBED* a household word!

*Sincerely,*

Christopher K. Mathews  
Department of Biochemistry and  
Biophysics  
Oregon State University  
Corvallis, OR 97331-7305

# Introducing ...

## Peggy J. Farnham, New Secretary of the ASBMB Council

**I** obtained my Ph.D. from Yale University in 1982, which is when I began working on transcriptional regulation. This topic was also the focus on my postdoctoral work at Stanford University and became the cornerstone of my lab research when I joined the faculty at the McArdle Laboratory for Cancer Research at the University of Wisconsin in Madison, WI in 1987. While at the University of Wisconsin, I also served as Chair of the Cellular and Molecular Biology Ph.D. Degree Program from 1996-2002. Major scientific contributions that came from my research at the University of Wisconsin include the identification of the E2F and Myc families of transcription factors as key mediators of the G1/S-phase transition of the mammalian cell cycle and the development of *in vivo* DNA-protein assays to study transcription factor binding to promoter regions using living cells.

Over the last two decades, the questions addressed in my lab have evolved from a detailed analysis of the transcriptional regulation of particular genes to a desire to investigate transcriptional regulation using a more global approach. Therefore, in August, 2004 I relocated my laboratory to the Genome Center at the University of California in Davis, CA. My current studies are focused on the development of high throughput, global analyses of transcription factors using methods which com-

bine chromatin immunoprecipitation with genomic microarray hybridization.

I have been associated with ASBMB since 1996 when I was appointed to a five-year term as an Editorial Board Member for the *Journal of Biological Chemistry*. In 2001, I became an Associate Editor of the *Journal* and continue to serve in this capacity at the current time. Through my position as Secretary, I plan to expand my involvement with ASBMB by becoming an active participant in the government of the Society. I also hope to participate in discussions and actions directed towards ensuring an enduring and rewarding relationship between the Society and

its members. I find that one of the most enjoyable aspects of my scientific career is the training of young scientists. To date, 24 undergraduates have performed independent research in my lab, I have mentored 10 postdoctoral fellows, and 17 graduate students have received Ph.D.s under my guidance. As Secretary, I hope to be able to strengthen the ties between a new generation of biochemists and molecular biologists and ASBMB. ☺



*Dr. Peggy Farnham*

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by Peter Farnham, CAE, ASBMB Public Affairs Officer

## Science Policy: Many Similarities, Some Stark Differences

**I**n most election years, the choice for President is likely to turn mostly on issues far removed from science—but this year is something of an anomaly, in that one scientific issue, stem cell policy, seems to be generating some buzz on the hustings. Except for this single issue, however, there is little substantive difference between the two parties on science policy. Both parties support extension of the R&D tax credit, both support nanotechnology, both support scientific and biomedical research, and both praise modern telecommunications.

Both parties also deal with science in their party platforms in a more or less perfunctory way. They address the issue in the context of other issues presumably considered more important. For example, science is not dealt with as a good in and of itself, nor is it discussed in the context of education or academia. Rather, it is treated as an underlying way to benefit the economy through creation of new technologies and jobs, and as a way to improve the average American's health.

### **GOP Language Is a Bit More Prominent**

The Republican platform gives science a bit more space, but compared to sections on dealing with terrorism, the economy, health care, and other major issues, the treatment is still relatively minor.

The GOP language is found under the title, "Investing in Science, Technology, and Telecommunications,"

and starts with a paean to innovation and the "Information Revolution," both of which were the product of people in the private sector who "have had the freedom to innovate." The platform also acknowledges the role of government in leveling the playing field, ensuring fairness, and mitigating "possible downsides." Note the limited role of the government implied by this language—merely to set the rules, and then to get out of the way and let the private sector handle the innovating.

The language then discusses research and development, and makes a few reasonably justifiable boasts here—Federal R&D spending is up 44 percent to \$132 billion in 2005, including a 26 percent increase in basic research. The President's doubling of the NIH budget is touted, as well as the increase in the National Science Foundation budget of 30 percent (presumably since 2001). Of course, unstated here is that the NIH is slated for 2 percent increases for the rest of the Bush presidency (assuming he wins a second term) and that the President requested less than 3 percent for NSF in 2005 (and worse, the House wants to cut this undervalued agency by \$110 million).

Nanotechnology legislation, spending on "next generation energy technologies," and support for NASA and space exploration are also touted, along with making permanent the R&D tax credit.

A special section is devoted to medical research, and NIH receives particular focus. The NIH currently funds nearly

40,000 projects, "an all-time high," and the benefits of biomedical research (decreased death rates, better access to health care, and a better quality of life for all Americans) are pointed out.

Finally, stem cell research is characterized as "important," but the platform makes it clear that the President's decision to restrict funding for embryonic stem cell research is based on moral rather than scientific grounds. The platform strongly supports "the President's policy that prevents taxpayer dollars from being used to encourage the future destruction of human embryos . . .

*The President's decision to restrict funding for embryonic stem cell research is based on moral rather than scientific grounds.*

applaud the President's call for a comprehensive ban on human cloning and on the creation of human embryos solely for experimentation." The language also notes that the administration was in fact the first to provide federal funds for embryonic stem cell research (\$28 million this year). Also, it notes that there are no restrictions on private sector research in the area.





## between GOP, Democrats

### Democrats Call for Less Ideology, more Stem Cell Research

The Democratic Party platform is 41 pages long, and devotes a total of three paragraphs to science and technology policy. In the section dealing with the economy (page 21), the democrats promise to “invest in the technologies of the future, from renewable energy to nanotechnology to biomedicine, and will work to make permanent the research and development tax credit. We will achieve universal access to broadband services, which could add \$500 billion to our economy, generate 1.2 million jobs, and transform the way we learn and work. And we will put science ahead of ideology in research and policymaking.”

This latter sentence, of course, addresses the issue of politicization of science—stacking advisory committees, deleting inconvenient information from government websites, hiring non-scientist ideologues to fill scientific positions—of which the Bush administration has been accused and which we discussed in some detail in the June issue of *ASBMB Today*.

The next place that science and technology come up is in the section on health care (page 29). To quote the platform: “We will push the boundaries of science in search of new medical therapies and cures. The Bush Administration has put ideology over science, skewing information about everything from women’s health to

scientific research. Americans deserve access to the best evidence available about illnesses, therapies, and cures. From new therapies to prolong life for people with AIDS, to new openings in the battle to cure cancer, the possibilities of medical research fill us with hope. We will secure more funding for aggressive biomedical research seeking affordable and effective therapies based on real science.”

The Democrats’ platform strongly endorses eliminating the current restrictions on federal funding for embryonic stem cell research. “President Bush has rejected the calls from Nancy Reagan, Christopher Reeve, and Americans across the land for assistance with embryonic stem cell research. We will reverse his wrong-headed policy. Stem cell therapy offers hope to more than 100 million Americans who have serious illnesses—from Alzheimer’s to heart disease to juvenile diabetes to Parkinson’s. We will pursue this research under the strictest ethical guidelines, but we will not walk away from the chance to save lives and reduce human suffering.”

While both parties acknowledge the importance of stem cell research (albeit while also taking very different approaches) what has been lost in the discussion is that this research is, so far, nothing more than a promising approach. It is not a proven therapy, and there is great danger that it is being oversold in the debate. This has, of course, happened before—remember how Interferon was going to cure

everything from the common cold to cancer? Unfortunately, the drug was ineffective in many applications for which it had been heavily touted. Likewise, transplanting fetal tissue was going to cure Alzheimer’s and other neurological diseases—but this turned out to be another dry hole.

The point is not that embryonic stem cell research shouldn’t receive federal funding—of course it should, and far more than the current administration is spending. Rather, for the future, overselling the research’s potential as a cure-all is likely to seriously affect biomedical research’s credibility. It would have been refreshing to see such language in one or both platforms—but that is probably too much to have expected.


Both campaign websites discuss these issues in more detail than the party platforms do. The Bush website ([www.GeorgeWBush.com](http://www.GeorgeWBush.com)) has a lengthy discussion of its stem cell policy (type “stem cells” in the home page search bar). In addition, the Office of Science and Technology Policy ([www.ostp.gov](http://www.ostp.gov)) website has a number of administration science policy documents available (the advantage of being the incumbent is that you have the resources of the entire government available to you). The Kerry campaign site ([www.JohnKerry.com](http://www.JohnKerry.com)) discusses science and technology in general terms under its “Plan for America” (click on “more issues” and then on “science and technology”). ☞

## Synthetic Prion Causes Neurological Disease in Mice

**S**cientists have produced a prion protein that can trigger the development of a neurological disorder in mice that is similar to “mad cow” disease, according to a new study supported by the National Institute on Aging (NIA) of NIH. The findings demonstrate that prions, an unusual class of infectious proteins, can make copies of themselves without the presence of viral DNA or RNA, damage brain tissue, and cause neurological diseases.

The work by Nobel Laureate Stanley B. Prusiner\* and colleagues at the University of California, San Francisco, and Heinrich-Heine Universität in Germany, appeared in the July 30, 2004, issue of *Science*. For the study, Dr. Prusiner and his colleagues produced prion protein fragments in bacteria, folded them into larger protein structures called amyloid

fibrils, and then injected them into the brains of susceptible mice. The mice began exhibiting symptoms of disease in their central nervous systems between 380 and 660 days after they were given the synthetic prion proteins. The amyloid form of the prion protein, which is thought to cause prion disease, was also found in the brains of the diseased mice. The researchers then administered brain extracts from these animals to another group of mice, which subsequently developed similar symptoms 90 to 150 days later. The disorder seems to be distinct from that caused by other known strains of prions, suggesting that the synthetic prion didn't merely activate a pre-existing prion in these mice and that the synthesized prion protein itself is sufficient to make infectious and disease-causing prions.

Unlike viruses, bacteria, fungi and parasites, prions contain no DNA or RNA. Instead, they are a type of protein normally found within cells in humans and other organisms. In some cases, the structure of prions can change into a disease-causing form. These abnormal proteins appear to convert other, normal prions to the abnormal shape. Many scientists now believe this conversion process leads to several dementing diseases in humans, including Creutzfeldt-Jakob disease. Abnormal, misfolded proteins contribute to other age-related neurological diseases such as Alzheimer's and Parkinson's diseases, and so these new findings may provide insights into the cause and possible prevention of other brain disorders. 

\*ASBMB member

## NHGRI Adds 18 Organisms to Sequencing Pipeline

The National Human Genome Research Institute (NHGRI) has received the green light to begin sequencing 18 strategically selected organisms, including the orangutan, African savannah elephant and domestic cat.

In a shift from NHGRI's previous procedure of choosing sequencing targets one at a time on the basis of proposals from individuals or groups of scientists, the National Advisory Council for Human Genome Research, a federally chartered committee that advises NHGRI on program priorities and goals, recently approved a comprehensive plan that identified two groups of organisms on the basis of their collective scientific merits.

The first group consists of nine mammals selected because each repre-

sents an important position on the evolutionary tree and will contribute a sequence that will be helpful in interpreting the human genome.

The data from seven of these mammalian genomes will be used primarily in the identification of features that are similar among the genomes of humans and other mammals. The seven mammals selected are the African savannah elephant, the European common shrew, the European hedgehog, the guinea pig, the lesser hedgehog tenrec, the nine-banded armadillo, and the rabbit. An eighth, the domestic cat, was selected primarily because of its importance as a medical model for studying disease.

The ninth, the orangutan, is a primate, one of the animals that are most closely related to humans. The orang-

utan genome will be used in conjunction with the other primates selected to identify those features in the human genome that differ among primates. The ultimate goal is to better define and understand the unique DNA sequences that set primates apart from other mammals and humans apart from other primates.

The second group chosen for the new sequencing effort includes nine non-mammalian organisms, each of which represents a position on the evolutionary timeline marked by important changes in animal anatomy, physiology, development or behavior. The organisms are a slime mold, a ciliate, a choanoflagellate, a placozoan, a cnidarian, a snail, two roundworms (*Pristionchus pacificus* and *Trichinella spiralis*) and the lamprey.



## Scientists Take 'Snapshot' of Molecular Tether

**S**cientists funded by the National Institute of General Medical Sciences (NIGMS) have snapped a molecular picture of the tether that anthrax- and staph-causing bacteria use to hook onto human red blood cells. The tether, an enzyme called sortase B, allows the bacteria to rob the cells of iron, which they need to survive.

The researchers took a mere three weeks to solve the high-resolution crystal structure of the sortase B protein, a process that normally takes several months or longer to complete.


The work is part of NIGMS Protein Structure Initiative (PSI), a federal, uni-

versity, and industry effort aimed at dramatically reducing the costs and lessening the time it takes to determine a three-dimensional protein structure. The long-range goal of the PSI is to make the structures of most proteins easily obtainable from knowledge of their corresponding DNA sequences.

Structural Biologist Andrzej Joachimiak who directs the PSI's Midwest Center for Structural Genomics at Argonne National Laboratory in Illinois, led the research, which was reported in the July 2004 issue of the journal *Structure*.

"Joachimiak's findings are an example of the payoffs of the PSI's auto-

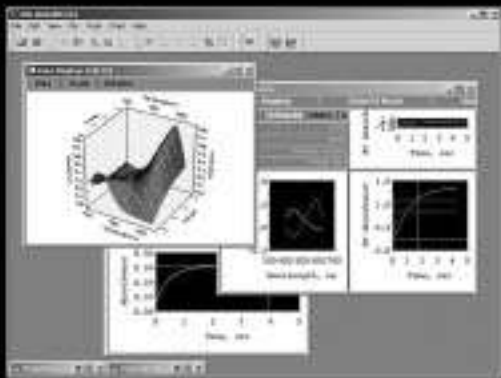
mated, high-throughput approaches to solving protein structures," said PSI Director John Norvell. "By providing access to state-of-the-art robotic devices and facilities for sample preparation, the PSI enables researchers to work very efficiently and productively."

The scientists hope to use their knowledge of sortase B's structure to rationally design new antibiotics that would nip dangerous bacteria in the bud, before they have a chance to cause infections. Staph is responsible for a range of health problems including skin infections and food poisoning, and anthrax infection can be life-threatening. 

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# LARGE Protein Can Overcome Defects

**M**uscular dystrophy is a group of genetic diseases characterized by progressive muscle degeneration. Working with mice with a type of the disease, researchers have found that by expressing an enzyme that attaches sugar molecules to a protein essential for proper muscle structure, they can restore normal muscle function.

Interestingly, the scientists found evidence of similar benefits when they expressed the protein, known as LARGE, in cells from patients with similar types of muscular dystrophies with distinct gene defects, suggesting that this approach may have clinical benefits for patients with the debilitating disease.

The study, led by Howard Hughes Medical Institute investigator Kevin P. Campbell\* at the University of Iowa College of Medicine, was published online in the journal *Nature Medicine* on June 6, 2004. The study complements additional work by Campbell and colleagues which elucidated the critical role of LARGE in the processing of a protein required to link muscle cells to their surrounding matrix. This work was published in an advance online publication of *Cell* on June 3, 2004.

A subset of muscular dystrophies have recently been linked to mutations in a group of enzymes involved in adding sugars to the muscle protein alpha-dystroglycan, in a process known as glycosylation. Without the attached sugars, alpha-dystroglycan is unable to carry out its function of linking the internal structural proteins of muscle cells to the surrounding extracellular matrix, providing essential structural support that protects the muscle membrane from contraction-induced damage.

Intense muscle activity, particularly when combined with stretching as in running downhill or walking down stairs, places stress on a muscle cell. In normal muscle, the link between alpha-dystroglycan and the surround-

ing matrix protects against this stress. According to Dr. Campbell, for patients with muscular dystrophy the absence of this link makes the muscle much more susceptible to damage.

"In most cases, if a normal person went out and ran 20 miles, the muscle is going to be damaged. But the muscle is actually able to repair itself," he explained. "However, patients with muscular dystrophy undergo this process much more quickly, and they eventually lose the ability to repair. That's when they get weak."

Defects in enzymes that transfer sugar molecules, known as glycosyltransferases, have been implicated in at least six different types of muscular dystrophy, according to Campbell. Therefore, the researchers wondered whether restoring glycosyltransferase activity would correct the defects in the muscle. To test this idea, they used mice in which the gene for a particular glycosyltransferase known as LARGE is mutated.

Mice without functional LARGE have a type of muscular dystrophy similar to that seen in a subset of patients, and are commonly used as a model for the disease. In these animals, alpha-dystroglycan lacks its attached sugars and cannot bind to the extracellular matrix.

Dr. Campbell and colleagues identified LARGE as the critical enzyme for initiation of alpha-dystroglycan processing. They found a LARGE recognition motif in alpha-dystroglycan, and subsequently showed that without this recognition, alpha-dystroglycan is not functional in muscle. They propose that the interaction between LARGE and alpha-dystroglycan is a key determinant to maintain healthy muscle.

To increase the levels of LARGE in the mice, the researchers engineered a virus expressing the LARGE gene. When they injected the virus directly into the muscle of mice that were a



*Dr. Kevin P. Campbell*

few days old, the muscle cells produced functional LARGE protein.

Once LARGE was expressed in the muscle cells of the mice, the group investigated the effect this had on muscle structure and function. Examining alpha-dystroglycan, they found that it had been glycosylated and was able to bind to the extracellular matrix, restoring the proper link between the muscle cell and its surroundings. When viewed under a microscope, the muscle lacked the features associated with dystrophic muscle and instead had the appearance of healthy tissue. Importantly, the researchers also found that expression of LARGE did not have any pathological effects on normal muscle tissue when injected into healthy mice.

The researchers next tested the mice to determine whether the structural changes seen with LARGE expression conferred functional benefits. Mice with and without the transferred gene were exercised by running downhill on a treadmill, and the researchers found that the muscular dystrophy mice who had the LARGE gene had significantly less muscle damage.

# In Some Types of Muscular Dystrophy

With the encouraging results from the mouse experiments, the researchers moved on to test whether addition of LARGE would have similar effects in the cells of patients with muscular dystrophy. Cells from patients with three different types of muscular dystrophy—Fukuyama congenital muscular dystrophy, muscle-eye-brain disease, and Walker-Warburg syndrome—were treated with the virus carrying the LARGE gene.

Indeed, the addition of the LARGE gene had an effect in the human cells similar to that seen in mice. Prior to the treatment, alpha-dystroglycan in the cells had lacked the normal sugar groups, but glycosylation was restored when the LARGE gene was expressed.


“What’s nice about this is that cells from patients, which we can grow up

in the laboratory, actually showed that we can correct the defect in their cells with LARGE,” Dr. Campbell said. Furthermore, although each of the cell types had a mutation in a different enzyme, glycosylation was similarly increased in all three, suggesting that increasing LARGE levels could be helpful regardless of the type of glycosyltransferase mutated in patients’ cells.

“At least for all the glycosylation-related muscular dystrophies, we think that LARGE may be able to restore the function of alpha-dystroglycan. This has potential for developing therapy for a group of muscular dystrophies. If we could come up with a drug that would stimulate LARGE activity, then we could possibly bypass the defect that’s seen in these different forms of

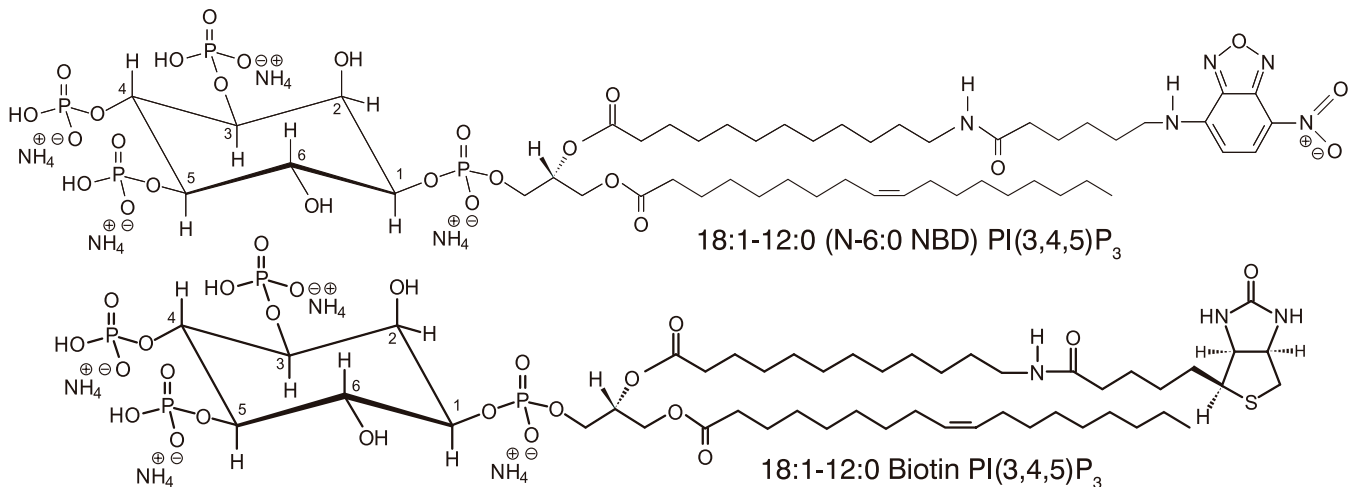
muscular dystrophy,” the HHMI investigator noted.

He added that although it might also be possible to utilize gene therapy to introduce the LARGE gene into patients similar to what was done in the mice, there are still many challenges to be overcome in the administration of gene therapy, and a pharmaceutical approach may be more appropriate.

Dr. Campbell noted that the researchers had observed that even in normal tissue, LARGE increased the binding of alpha-dystroglycan to the extracellular matrix. This suggests that LARGE may be able to improve the link between muscle cells and their surrounding matrix even in muscular dystrophies that are not caused by glycosylation defects. 

\*ASBMB member.

## FLUORESCENT PIP<sub>3</sub>, BIOTINYLATED PIP<sub>3</sub>, SHORT PIP'S, LONG PIP'S & PUFA PIP'S



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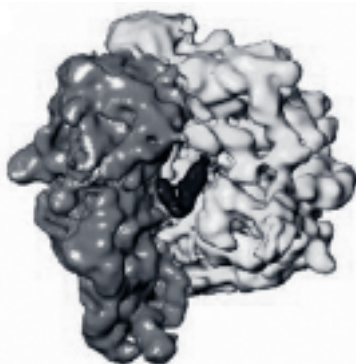


# Bacterial Protein Recycling Factor Could Be Key to New Class of Antibiotics

**U**nderstanding the last step of protein synthesis – the basic process of translating messenger RNA into its final protein product – just became more clear both literally and figuratively. This final phase, called recycling, is essential for the proper function of all cells. Using a three-dimensional cryo-electron microscope to directly observe protein structure, investigators at the University of Pennsylvania School of Medicine and the State University of New York, Albany can now visualize the exact configuration of a molecule called ribosome recycling factor (RRF) in the common bacteria *Escherichia coli*. This image, reported in the June 15, 2004 issue of the *Proceedings of the National Academy of Sciences*, may help guide the design of new antibiotics aimed at inhibiting RRF-related steps of protein synthesis.

“Every living organism has to have this last step, the recycling of spent protein synthesis machinery for the next round of translation,” says Akira Kaji,\* Professor of Microbiology at Penn. “Strangely, at this day and age, this most fundamental process remained vague until we launched our studies of RRF.”

Most antibiotics influencing protein synthesis act by stopping its molecular machinery. However, none as yet target the recycling step. “We believe RRF is one of the best candidates for a new antibiotics target because the mechanism involved in recycling of the protein-making machinery is different in eukaryotes versus prokaryotes, that is in humans versus bacteria,” says Dr. Kaji. “With the emergence of antibiotic-



resistant pathogens, this will be the best avenue of devising new antibiotics.”

In an earlier paper by he and colleagues from Sweden, the crystal structure of RRF showed that RRF mimics the L-shape and dimension of transfer RNA. Chemical probing by Kaji and colleagues at the University of California, Santa Cruz showed the approximate ribosomal binding site of RRF. In the current PNAS paper, direct observation of the RRF-ribosome structure revealed the exact ribosomal position of bound RRF. It further showed that part of the ribosome contorts by a significant amount—molecularly speaking—when RRF binds to it.

More precisely, the position of the key helices of the ribosomal small and large subunits that hold messenger RNA move inward, suggesting that this movement may be essential for the release of messenger RNA from the ribosome. In addition, the RRF binding sites are very close to where the two ribosomal subunits are held together, which explains an earlier observation that the disassembly reaction by RRF may be followed by dissociation of the two subunits.

In the recycling process, RRF along with EF-G (elongation factor G) binds to

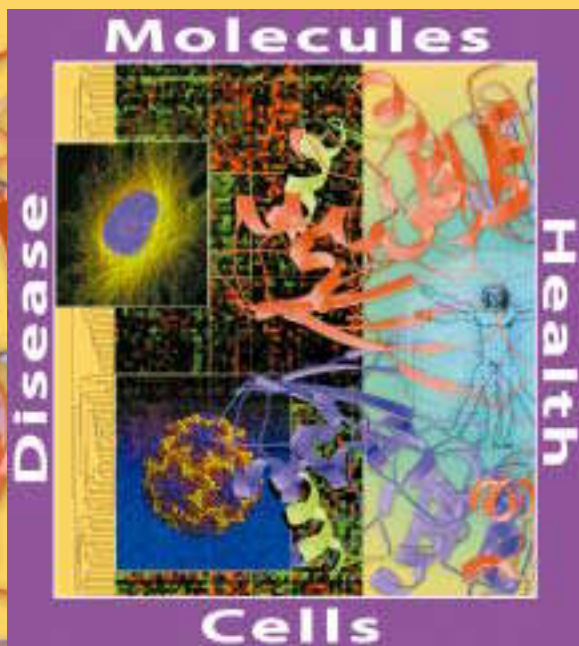
the ribosome. This promotes the release of transfer RNAs by the movement of RRF, similar to transfer RNA movement. “This is the first example of a functional mimic of transfer RNA by a protein,” noted Dr. Kaji. After the transfer RNAs leave, RRF, EF-G, and messenger RNA also detach from the ribosome. The released ribosome is now empty and free to start a new session of translating messenger RNA into protein. Where RRF binds is near the key ribosomal spot holding messenger RNA.

Humans have an RRF analogue in the mitochondria, the respiratory organelle within cells. “One may argue that proposed antibiotics against RRF may influence mitochondrial protein synthesis,” notes Kaji. However, commonly used antibiotics such as erythromycin and tetracycline kill bacteria but are virtually harmless to humans, showing little side effect despite their influence on mitochondrial protein synthesis. “With rational drug design it is even possible to design anti-RRF which would only influence bacterial RRF,” says Dr. Kaji.

His lab is currently working to identify the ribosomal site to which RRF is moved from the currently identified position. “It is from this position where RRF performs the final and the most important act—release of messenger RNA,” he explained. “The fourth step of protein synthesis within human cells is shrouded in complete mystery and nothing is known. This fundamental step must be elucidated before we can take advantage of the fact that the same step is catalyzed by RRF in bacteria.”

\*ASBMB member

# See You Next Year in San Diego!



## 2005 ASBMB Annual Meeting

Held in conjunction with EB 2005

April 2-6, 2005

San Diego, CA

### Meeting Organizers

Dennis R. Voelker, National Jewish Medical Research Center

Cecile Rochette-Egly, IGBMC, Strasbourg

and the 2005 ASBMB Program Planning Committee

### Meeting Themes

#### Dynamics of Protein—

#### Protein Interactions (Bumping in the Night)

Chair: Ben Margolis, HHMI, Univ. of Michigan

#### DNA Replication and Interactive Repair and Recombinational Processes

Chair: Charles S. McHenry, Univ. of Colorado Health Sciences  
Center

#### Coordinate Regulation of Transcription

Chair: Cecile Rochette-Egly, IGBMC, Strasbourg

#### Interactions and Functions of Glycoconjugates

Chair: Mark A. Lehrman, Univ. of Texas Southwestern  
Medical Center

#### Integration and Organization of Signaling Pathways

Chair: Alex Tokor, Beth Israel Deaconess Medical Center

#### Minority Affairs Committee Symposia

Chair: Phillip A. Ortiz, Empire State College

#### Biochemistry and Molecular Biology of Lipids

Chair: Charles O. Rock, St. Jude Children's Research Hospital

#### Organelle Biogenesis and Dynamics

Co-Chairs: Carla Koehler, UCLA and Danny Schnell, Univ. of  
Massachusetts, Amherst

#### Proteolysis and Disease

Chair: Charles Craik, Univ. of California, San Francisco

#### Catalysis: Structure, Function, and Evolution

Chair: John A. Gerlt, Univ. of Illinois, Urbana-Champaign

#### Metabolic Regulatory Circuits

Chair: M. Daniel Lane, Johns Hopkins Univ. School of Medicine

#### Genomes and Proteomes

Chair: Andrew J. Link, Vanderbilt Univ.

#### Education in the Biomolecular Sciences:

#### The Next Generation

Co-Chairs: Judith G. Voet, Swarthmore College and Marion O'Leary,  
California State Univ. at Sacramento

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# San Diego 2005

## Christopher T. Walsh to Receive Fritz Lipmann Lectureship

**C**hristopher T. Walsh, Hamilton Kuhn Professor of Biological Chemistry and Molecular Pharmacology at Harvard Medical School, has been chosen for the Fritz Lipmann Lectureship by the Program Planning Committee for the 2005 ASBMB Meeting.

The Fritz Lipmann Lectureship was established by friends and colleagues of Fritz Lipmann. Previous awardees include Roddrick MacKinnon, Ulrich Hartl, James E. Rothman, Helmut Beinert, Wayne A. Hendrickson, Joan A. Steitz, Steven Fesik, and Heidi Hamm. The recipient will receive a stipend and a plaque. In addition, he or she will be reimbursed for all travel, hotel accommodations, meals, and expenses to attend the meeting, where he will deliver the Fritz Lipmann Lecture.

The Committee identified Dr. Walsh as an outstanding and highly productive researcher who uses a broad integrated approach that includes genetics, protein and carbohydrate chemistry, mechanistic enzymology, molecular biology and X-ray crystallography to elucidate and exploit the pathways for natural antibiotic synthesis. This body of work not only defines pathways for antibiotic synthesis, and the molecular targets of antibiotic action, and the mechanisms of antibiotic resistance, but also serves as a platform for the synthesis of novel antibiotics.

The Committee also identified Dr. Walsh as an accomplished mentor who has provided rigorous and insightful training for many younger scientists. During his illustrious career Dr. Lipmann was widely recognized for seminal work identifying the structure of Coenzyme A, elucidating important steps in protein synthesis and describing critical aspects of protein phospho-

rylation and dephosphorylation. However, many biochemists may not be aware of Dr. Lipmann's keen interest and research into the RNA-independent synthesis of polypeptides that function as antibiotics. It is quite fitting that Dr. Walsh is now being recognized for a large body of work whose fundamental biochemistry also captivated Dr. Lipmann.

The broad area of interest to the Walsh Laboratory is the molecular basis of biological catalysis with focus on the structure and function of enzymes. Much of the current focus is on the biosynthesis and mechanism of action of antibiotics and bacterial siderophores. Several ongoing projects in the laboratory illustrate their approaches.

### Vancomycin Biosynthesis

The Walsh Lab is currently investigating the enzymatic pathway for biosynthesis of the vancomycin family of glycopeptide antibiotics. Vancomycin is a front line antibiotic for treatment of life-threatening gram-positive bacterial infections and many clinical isolates have become resistant to it, focussing interest on successors to vancomycin. The enzymatic pathway involves about two dozen enzymatic steps, including provision of nonproteinogenic amino acid monomers that get incorporated into the heptapeptide scaffold of the antibiotic, the assembly line for fashioning the heptapeptide as a series of elongating acyl-S-enzyme intermediates, cytochrome P450 oxidases that crosslink the scaffold, glycosyl transferases to add the sugar residues, and enzyme dedicated to the construction of the unusual aminodeoxy hexose vancosamine. They are

studying all these different enzymatic steps with an eye to potential reprogramming of one or more steps for combinatorial biosynthesis.



*Dr. Christopher T. Walsh*

### Microcin B17

Certain strains of *E. coli* produce a peptide antibiotic Microcin B17 from an operon that encodes the 69 amino acid Microcin A orf that is the antibiotic precursor, orfs B-D that carry out posttranslational modification of A, orfs E and F for export of mature MccB17, and the immunity protein orf G. They are studying how orfs B,C,D carry out the posttranslational modification of 14 residues of orf A to produce four thiazoles and four oxazoles, heteroaromatic rings that are the key determinants of antibiotic activity. They are also studying how mature microcin interacts with its intracellular target DNA Gyrase to cause accumulation of double strand breaks in DNA.

### Bacterial Siderophore Biogenesis

When bacteria are starved for iron, as occurs when they infect vertebrates, they turn on genes for biosynthesis of nonribosomal peptides, siderophores, that scavenge iron and then are taken back up by the bacteria. Siderophores are virulence factors by enabling pathogenic bacteria to multiply in hosts. They are examining the enzymatic assembly lines that make enterobactin, the *E. coli* siderophore, pyochelin from *Pseudomonas aeruginosa*, vibriobactin from *Vibrio cholerae*, and Yersini-

*Continued on page 18*



## Molecular Discovery and the Foundations of Human Health and Disease

By Dennis R. Voelker, co-organizer with Cecile Rochette-Egly of 2005 ASBMB

The major goal of the 2005 ASBMB Meeting is to provide a forum for the dissemination of the latest and most important scientific advances in biochemistry. Implicit in this objective is the appreciation that the elucidation of molecular structures and mechanisms of molecular interactions constitute the most important foundations of understanding how biological systems work and how they are compromised in disease processes. The ASBMB Meeting is focused upon elucidating the biochemical features of all aspects of living systems and understanding how they are integrated from the level of individual reactions to organelles to single cells and finally to intact organisms. No single class of biological molecule has a monopoly on governing biological homeostasis or disease pathogenesis, and the national meeting will provide a showcase of how different classes of molecules contribute in varied and important ways to diverse life processes.

The preliminary program of the 2005 ASBMB Meeting that will be held in San Diego, April 2-6, in conjunction with FASEB, has been drafted and will continue an aspect of organization that has been successfully employed in the last two annual meetings. This approach emphasizes the rich intellectual diversity within the biochemical community. The meeting will consist of 13 themes that cover much of the breadth of biochemistry. The themes scheduled for the meeting include: 1) Coordinate

Regulation of Transcription, 2) Proteolysis and Disease, 3) Catalysis: Structure, Function and Evolution, 4) Regulatory Circuits in Metabolism, 5) Organelle Biogenesis and Dynamics, 6) Interactions and Functions of Glycoconjugates, 7) Genomes and Proteomes, 8) Dynamics of Protein-Protein Interactions, 9) DNA Replication and Associated Processes/Recombination and

*A forum for the dissemination of the latest and most important scientific advances in biochemistry.*

Repair, 10) Biochemistry and Molecular Biology of Lipids, 11) Integration and Organization of Signaling Pathways, 12) Education in Biomolecular Sciences and 13) Minority Affairs Sponsored Symposia. This multi-theme approach was instituted to provide a core of symposia that highlight important new findings within many of the varied sub-disciplines of biochemistry. With this organization, conference attendees specializing in a specific discipline will have a core of symposia and poster sessions for their respective discipline that they can attend every day. The scheduling for the meeting has been planned so that these core symposia and accompanying posters will occupy about 50% of the time of a typical conference attendee. The remaining 50% of the

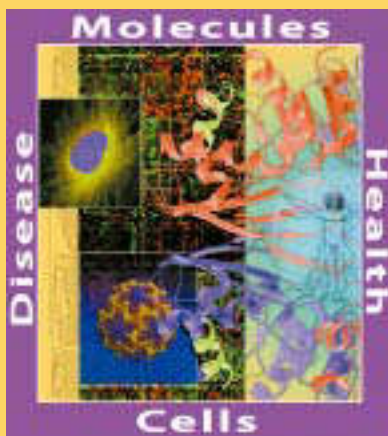
time will be available for attending core symposia offered by other disciplines, or exhibits, or scientific sessions from other FASEB societies.

During the 2005 Meeting the organizers and the society will also work to highlight the research efforts of younger scientists, especially postdoctoral fellows, graduate students and undergraduate biochemistry majors. Over the last 3 years the society has made a strong effort to provide increasing numbers of Travel Awards to these young scientists. Symposia organizers have scheduled specific slots in their programs for short presentations by these individuals that will be selected from submitted abstracts. In addition special sessions with short presentations and posters by Travel Award winners will serve to further publicize the accomplishments of young scientists

Finally, the organizers wish to emphasize that one of the most important goals of the national meeting and ASBMB itself, is to serve the needs of the membership. We are open to your concerns, comments and participation for planning future meetings. We believe that in the long-term we should work to continually improve the national meeting so that it serves the largest number of ASBMB members in the best possible way. ☺



*Dr. Dennis R. Voelker*



# Biochemistry and Molecular Biology of Lipids

Organizer: Charles Rock, St. Jude Children's Research Hospital

2005 ASBMB Annual Meeting

Held in conjunction with EB 2005

April 2-6, 2005, San Diego, CA

Additional Speakers will be chosen from the abstracts submitted.

**Abstract Deadline:**  
**November 3, 2004**

Travel Awards Available for Undergraduates, Graduates, Postdoctoral Fellows, and Undergraduate Faculty.

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## Intracellular Lipid Dynamics

Non-vesicular ER-to-Golgi trafficking of ceramide by CERT

**Chair, Masahiro Nishijima**, National Inst. of Infectious Diseases, Tokyo

Roles for phospholipase D in vesicular trafficking and plasma membrane fusion during regulated exocytosis

**Michael A. Frohman**, SUNY-Stony Brook

StAR-related lipid transfer proteins in intracellular cholesterol metabolism

**Jan L. Breslow**, Rockefeller Univ.

## Control of Lipid Metabolism

LXR and FXR, nuclear receptors that control lipid homeostasis

**Chair, Peter A. Edwards**, UCLA School of Medicine

Genomic analysis of *C. elegans* fat regulation

**Kaveh Ashrafi**, Univ. of California, San Francisco

Curious evolution: S1P receptor control of immune and cardiovascular function

**Hugh Rosen**, Scripps Research Inst.

## Compartmentation of Lipid Metabolism

Does acyl-CoA synthetase compartmentation control the metabolic fate of fatty acids?

**Chair, Paul A. Watkins**, Kennedy Krieger Inst., Johns Hopkins Univ.

Fatty acid synthesis in mitochondria: new insights

**Kalervo J. Hiltunen**, Univ. of Dulu, Center for Biomembranes and Lipids

Sphingomyelin synthases: localization, regulation and functions

**Joost Holthuis**, Center for Biomembranes and Lipid Enzymology, The Netherlands

## Structural Insights into Lipid Metabolism

Role of structural lipidomics in genome annotation

**Chair, Christian R. Raetz**, Duke Univ.

The enzymatic regulation of the fatty acid amide family of endogenous signaling lipids

**Benjamin F. Cravatt**, Scripps Research Inst.

A hydrocarbon ruler measures palmitate in the acylation of endotoxin by the integral membrane enzyme PagP

**Russell E. Bishop**, Univ. of Toronto



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## Biochemistry and Molecular Biology of Lipids

By Organizer, Charles O. Rock, Department of Infectious Diseases,  
St. Jude Children's Research Hospital, Memphis, TN.

**T**he investigation of the biochemistry of lipid metabolism has entered a dynamic stage of development. The fields of lipodomics, structural, cell and chemical biology are being integrated into our existing experimental repertoire to drive new discoveries about the role of lipid metabolism in health and disease. The four symposia that form the focus of the Biochemistry and Molecular Biology of Lipids section of the 2005 ASBMB meeting highlight areas where these contemporary technologies are applied. Selected presentations from the submitted abstracts will fill out the symposium and complement the plenary presentations.

### Intracellular Lipid Dynamics

**Chair:** Masahiro Nishijima

Cells are composed of multiple organelles and their membrane lipids constituents must be distributed from their sites of synthesis to manufacture the various organelles. The mechanisms that control the intracellular movement, sorting and distribution of lipid molecular species will be the focus of this symposium. Plenary talks by Masahiro Nishijima and Jan Breslow will focus on the biochemistry of the key proteins required for the trafficking of ceramide and cholesterol. Phospholipid turnover is a key facet of organelle trafficking and Michael Frohman will discuss the regulation of one of the key enzymes in this process.

Non-vesicular ER-to-Golgi trafficking of ceramide by CERT, Masahiro Nishijima, National Institute of Infectious Diseases, Tokyo; Roles for phos-

pholipase D in vesicular trafficking and plasma membrane fusion during regulated exocytosis, Michael A. Frohman, SUNY-Stony Brook; StAR-related lipid transfer proteins in intracellular cholesterol metabolism, Jan L. Breslow, Rockefeller University.



*Dr. Charles O. Rock*

### Control of Lipid Metabolism

**Chair:** Peter A. Edwards

Lipid metabolism is a highly regulated process and imbalances in the control of lipid synthesis, catabolism and transport are major causes for disease. The transcriptional regulation of lipid metabolism is central to lipid homeostasis and the plenary talk by Peter Edwards will highlight the recent advances in understanding the role of nuclear hormone receptors. The presentation by Kaveh Ashrafi will explore the application of contemporary genomic approaches to identify new players in fat regulation using a model organism. Lipids are also signally molecules that control central bodily functions and Hugh Rosen will describe the role of the sphingosine 1-phosphate signaling receptor on animal physiology.

LXR and FXR; nuclear receptors that control lipid homeostasis, Peter A. Edwards, UCLA School of Medicine; Genomic analysis of *C. elegans* fat regulation, Kaveh Ashrafi, University of California, San Francisco; Curious evolution: S1P receptor control of immune

and cardiovascular function, Hugh Rosen, Scripps Research Institute.

### Compartmentation of Lipid Metabolism

**Chair:** Paul A. Watkins

Eukaryotic cells are composed of an array of different cellular compartments designed for specific biochemical functions. The processes of lipid metabolism are highly compartmentalized and the appreciation of the roles these different compartments play in the synthesis and degradation of lipids is key to understanding normal cell function and disease. The peroxisomes are dynamic lipid metabolic organelles and Paul Watkins will focus on an important enzyme that modulates the distribution of fatty acids between the cellular compartments. The emerging area of the function of mitochondria in de novo fatty acid synthesis will be discussed by Kalervo Hiltunen. Some compartments are not as clearly delineated as those of the peroxisomes and mitochondria, but nonetheless it is critical to understanding metabolism to define the precise locations of biosynthetic proteins and metabolic channeling. Joost Holtluis will discuss one clear example of this type of compartmentation in the synthesis of sphingomyelin.

Does acyl-CoA synthetase compartmentation control the metabolic fate of fatty acids? Paul A. Watkins, Kennedy Krieger Institute, Johns Hopkins University; Fatty acid synthesis in mitochondria: new insights, Kalervo J. Hiltunen, University of Oulu, Center for Biomembranes and Lipids; Sphin-

*Continued on page 18*





# San Diego 2005

## Integration and Organization of Signaling Pathways

By Organizer: Alex Toker, Department of Pathology,  
Beth Israel Deaconess Medical Center, Harvard Medical School.

**S**ignaling molecules control nearly every aspect of cellular behavior, ranging from cell growth and cell death, to cell motility and differentiation. It is therefore not surprising that an increasing number of human diseases are directly attributed to perturbations in signaling proteins or pathways. The explosion in signaling research in the last two decades has intensified with the deciphering of the human genome, and the task at hand for scientists in this field is to unravel the complexities underlying virtually all known signal relay pathways. This symposium will focus on how proteins and lipids integrate signaling in a spatially confined manner to achieve specific and ordered cellular responses. Four concurrent symposia will highlight new technologies and emerging areas in this intense field of biology.

### Specificity in Signaling Networks

**Chair:** Tony Hunter, The Salk Institute: Protein Phosphorylation and Signaling Networks

**Speakers:** Kavitha Shah, Purdue University: Chemical Genetic Dissection of Signaling Pathways; Alex Toker, Beth Israel Deaconess Medical Center, HMS: Regulation and Function of Protein Kinase D in Oxidative Stress Signaling.

The complexities of signaling pathways are typified by the protein kinases, a family of enzymes that comprise almost two percent of the entire human genome. In this symposium, the specificity in signaling pathways achieved by protein kinases will be highlighted. Recently, the deciphering

of the human Kinome, the protein kinase complement of the human genome, has given researchers a glimpse into the future and the tasks which lie ahead. Considering that almost one third of all proteins encoded by the human genome contain bound phosphate, Dr. Hunter, who will chair the symposium, will discuss new advances in this intense field of research and highlight mechanisms by which protein kinases achieve specificity in signaling. Dr. Shah will focus on exciting new developments in the field, by combining chemical modifications of phosphate donors along with genetic mutagenesis of enzymes. An emerging field in cellular signaling is the regulation of signaling pathways by oxidative stress, which can occur during normal cellular metabolism, and also in human diseases. Dr. Toker will discuss one such pathway which is necessary for cellular survival when cells are exposed to reactive oxygen species.

### Imaging Signaling Pathways

**Chair:** Tobias Meyer, Stanford University Medical Center: Spatial and Temporal Control in Cell Signaling Networks.

**Speakers:** Daniel Jay, Tufts University School of Medicine: Light-Based Inactivation Strategies to Dissect Signaling Pathways; Philippe Bastiaens, EMBL Heidelberg: Imaging Protein Reaction States in Cellular Signaling and Morphogenesis.

This symposium will focus on the remarkable advances in the understanding of the spatial and temporal

control of signaling pathways which have been possible because of new cellular imaging technologies.

The advent of fluorescent-based reporters of protein localization and activity which can be performed in intact cells and in real time has added a much needed weapon in the arsenal of molecular genetic techniques which investigators can use to unravel the complexities of signal relay pathways. The symposium will be chaired by Dr. Meyer who will discuss emerging technologies to investigate the spatial and temporal control of signaling. Dr. Jay will present on a new and powerful tool, light-based inactivation of signaling molecules, which his lab has been using to interrogate specific pathways. Dr. Bastiaens will discuss the second and third generation FRET-based technologies currently used to visualize signaling in real-time.



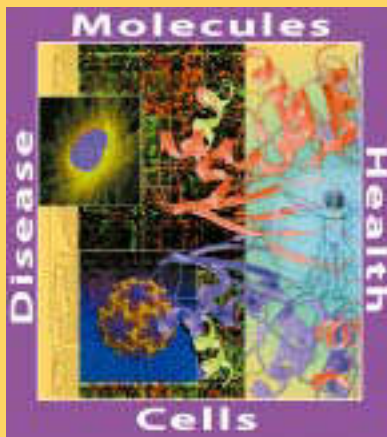
*Dr. Alex Toker*

### Vesicular Trafficking

**Chair:** Scott Emr, University of California, San Diego: Phosphoinositide Signaling in Membrane Traffic.

**Speakers:** Vivek Malhotra, University of California, San Diego: Protein Kinase D Dependent Generation of Transport Carriers from the Trans Golgi Network; Vytas Bankaitis, University of North Carolina, Chapel Hill: Phosphatidylinositol transfer proteins and regulation of membrane traffic.

*Continued on page 22*



# Integration and Organization of Signaling Pathways

Organizer: Alex Toker, Harvard Medical School

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## Specificity in Signaling Networks

Protein phosphorylation and signaling networks  
**Chair, Tony Hunter, The Salk Inst.**

Chemical genetic dissection of signaling pathways  
**Kavita Shah, Purdue Univ.**

Regulation and function of protein kinase D in oxidative stress signaling  
**Alex Toker, Harvard Medical School**

## Imaging Signaling Pathways

Spatial and temporal control in cell signaling networks  
**Chair, Tobias Meyer, Stanford Univ. Medical Center**

Imaging protein reaction states in cellular signaling and morphogenesis  
**Philippe Bastiaens, EMBL Heidelberg**

Light-based inactivation strategies to dissect signaling pathways  
**Daniel G. Jay, Tufts Univ. School of Medicine**

## Vesicular Trafficking

Phosphoinositide signaling in membrane traffic  
**Chair, Scott Emr, Univ. of California, San Diego**

Protein kinase D dependent generation of transport carriers from the trans Golgi network  
**Vivek Malhotra, Univ. of California, San Diego**

Phosphatidylinositol transfer proteins and regulation of membrane traffic  
**Vytas Bankaitis, Univ. of North Carolina at Chapel Hill**

## Structural Basis of Signaling

Structural basis for regulation of protein kinases and phosphatases  
**Chair, David Barford, Inst. of Cancer Research, Chester Beatty Laboratories**

Activation and inhibition of EGF receptor signaling  
**Mark Lemmon, Univ. of Pennsylvania School of Medicine**

Substrate recognition and presentation by the SCFCdc4 Ubiquitin Ligase  
**Frank Sicheri, Samuel Lunenfeld Research Inst., Mount Sinai Hospital**



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## Fritz Lipmann Lectureship continued ...

*Continued from page 12*

abactin from *Yersinia pestis*. They are studying the enzymatic steps in the siderophore synthetase assembly lines and the modifications to the peptide backbones that create functional-groups with high affinity for chelating iron, including hetrocycle formation and N- and C-methylations.


### Macrocyclization of Nonribosomal Peptides

A variety of peptide antibiotics are cyclic peptides (gramicidin, tyrocidine, bacitracin) or cyclic lipopeptides (surfactin, daptomycin). These are made on nonribosomal peptide

synthetase assembly lines and cyclized by the last domain, a Thioesterase (TE) domain of the multimodular enzymatic assembly line. The lab is studying mechanism and structure of cyclizing TE domains and trying to use them in combinatorial biosynthesis.

### Hybrid Polyketide/Nonribosomal Peptide Natural Products

Some antibiotics and siderophores are hybrids of polyketide and nonribosomal peptide constituents and are elongated on hybrid polyketide synthase/nonribosomal peptide synthetase (PKS/NRPS) assembly lines.

They are studying three such assembly lines to decipher the rules for switching between PKS and NRPS modules in the biogenesis of epothilone (antitumor agent), rifamycin (antitubercular drug), and yersiniabactin .

## Biology of Lipids continued ...

*Continued from page 15*


gomyelin synthases: localization, regulation and functions, Joost Holthuis, Center for Biomembranes and Lipid Enzymology, The Netherlands

### Structural Insights into Lipid Metabolism

**Chair:** Christian R. H. Raetz

Defining structure is a key to understanding function at the biochemical level. Particularly exciting is the recent launch of the "lipid maps" project that aims to characterize the precise structures of the myriad of lipids found in cells and the contribution of this approach to our understanding of lipid metabolism will be presented by Christian Raetz. Of particular importance are the routes to the biosynthesis of the minor lipid species that act as signaling molecules and Benjamin Cravatt will discuss recent advances in the regulation of fatty acid amide synthe-

sis. Structural biology of lipid enzymes is advancing rapidly and providing important insights into the detailed mechanism and regulation of the enzymes of lipid metabolism. The biological membrane is the reaction milieu for many of the enzymes in lipid metabolism, which are imbedded in bilayer. Russell Bishop will discuss approaches for solving their 3-dimensional architecture for a group of proteins that have traditionally resisted structural characterization.

Role of structural lipidomics in genome annotation, Christian R. Raetz, Duke University; The enzymatic regulation of the fatty acid amide family of endogenous signaling lipids, Benjamin F. Cravatt, Scripps Research Institute; A hydrocarbon ruler measures palmitate in the acylation of endotoxin by the integral membrane enzyme PagP, Russell E. Bishop, University of Toronto. .

## ASBMB Welcomes New Ph.D.s

ASBMB extends its congratulations to these individuals who recently received their Ph.D. degrees. In recognition of their achievement, ASBMB is presenting them with a free one-year membership in the Society. The new Ph.D.s are listed below with the institution from which they received their degree.

**Brandon L. Ason**

University of Wisconsin

**Christopher D. Carvin**

Texas A&M University

**Daniel J. Felitsky**

University of Wisconsin

**Maricela Haghiac**

Clemson University

**Brooke Heidenfelder**

University of North Carolina – Chapel Hill

**David W. Karnak**

University of Michigan

**Christopher T. Knoell\***

Brandeis University

**Patricia Mowery**

University of Wisconsin

**Stephanie Parsons**

Cincinnati Children's Medical Center

\* Candidates with an asterisk were previous Associate members who met the requirements for a free one-year membership.



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| ART 222        | Glycerophosphoinositol [myo-inositol-2- <sup>3</sup> H]   | 5 µCi           | \$999      |
| ART-473        | Glycerophosphoinositol [myo-inositol-2- <sup>3</sup> H] 4,5 bisphosphate                                    | 5 µCi           | \$1199     |
| ART-472        | Glycerophosphoinositol [myo-inositol-2- <sup>3</sup> H] 4 phosphate   | 5 µCi           | \$1199     |
| ARC-232        | Inositol, myo, [ <sup>14</sup> C(U)]  | 5 µCi           | \$479      |
| ART-261        | Inositol, myo, [1,2- <sup>3</sup> H(N)]   | 1mCi            | \$729      |
| ART-116        | Inositol, myo, [2- <sup>3</sup> H(N)]   | 1mCi            | \$649      |
| ART-171        | Inositol-1-phosphate, D-[inositol-2- <sup>3</sup> H] (1-IP)   | 5 µCi           | \$299      |
| ARC-233        | Inositol-1-phosphate, D-[inositol-2- <sup>14</sup> C(U)]  | 5 µCi           | \$299      |
| ART-268        | Inositol-3-phosphate, D-[inositol-2- <sup>3</sup> H]  | 5 µCi           | \$359      |
| ARCD-166       | D-myo-Inositol 1-phosphate dipotassium salt, "Cold"   | 1 mg            | \$179      |
| ART-264        | Inositol, scyallo, [2- <sup>3</sup> H(N)]   | 250 µCi         | \$749      |
| ART-872        | Inositol 1,3,4,5 tetrakisphosphate D-[inositol-1- <sup>3</sup> H(N)]  | 5 µCi           | \$629      |
| ARCD-108       | Inositol, myo D-1,4,5 triphosphate, "Cold"  | 1 mg            | \$209      |
| ARCD-109       | Inositol, myo L-1,4,5 triphosphate, "Cold"  | 1 mg            | \$199      |
| ART-270        | Inositol, 1,4,5-triphosphate, D-[inositol-2- <sup>3</sup> H(N)] (1,4,5-IP3)                                 | 5 µCi           | \$579      |
| ART-487        | Phorbol-12,13-diacetate, [20- <sup>3</sup> H(N)]  | 50 µCi          | \$309      |
| ART-485        | Phorbol-12,13-dibutyrate, [20- <sup>3</sup> H(N)]   | 50 µCi          | \$299      |
| ART-486        | Phorbol-12-myristate-13-acetate [20- <sup>3</sup> H(N)]   | 50 µCi          | \$319      |
| ART-184        | Phosphatidylinositol, L-α-[myo-inositol-2- <sup>3</sup> H(N)] PI [ <sup>3</sup> H]                          | 10 µCi          | \$599      |
| ART-183        | Phosphatidylinositol 4,5-biphosphate [myo-inositol-2- <sup>3</sup> H(N)] PIP <sub>2</sub> [ <sup>3</sup> H] | 5 µCi           | \$559      |
| ARCD-131       | Phosphatidylinositol 4,5-biphosphate (PIP <sub>2</sub> ), "Cold"  | 1 mg            | \$209      |
| ARE-100        | Phosphatidylinositol specific phospholipase C (PI-PLC)  | 5 units         | \$339      |
| ART-185        | Phosphatidylinositol 4-phosphate, [myo-inositol-2- <sup>3</sup> H]  | 5 µCi           | \$649      |
| ART-1297       | Prostatin [20- <sup>3</sup> H] [dPAC]   | 50µCi           | \$999      |

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# Molecular Link that Drives Spread of Skin Cancer Identified

**A**n international team of scientists has identified an important molecular interaction involved in the metastasis of melanoma to other organs such as the lungs. The results, published in the July issue of the journal *Cancer Research*, open the door to the prospect of targeted therapeutics capable of preventing or limiting the metastasis of skin cancer.

By synthesizing a peptide that mimics one of the molecules involved in the interaction between malignant cells and the extracellular matrix, the researchers were able to block the interaction, significantly deterring the migration of cancer cells beyond the original tumor site. Blocking the binding also inhibited angiogenesis and spurred apoptosis.

"Our data show that a small synthetic peptide sequence that is based on a part of an authentic protein can bind to the same tumor cell surface molecule as the intact large protein. When the small peptide binds to this tumor cell surface protein, it blocks the tumor cells from spreading and growing," said Hynda Kleinman,\* Chief, Cell Biology Section, National Institute of Dental and Craniofacial Research, NIH.

The spread of melanoma cancer cells requires the interaction of two proteins: a cell surface matrix receptor on the malignant cell called CD44 and an extracellular matrix protein known as laminin  $\alpha 5$ .

CD44 is cell a surface protein that is often over-expressed in cancer cells. It is covered in lengthy chains of carbohydrates called glycosaminoglycans (GAGs) which can interact with other

molecules outside of the cell. Dr. Kleinman and her associates determined that laminin  $\alpha 5$  binds to CD44 via these GAG side chains.

The research team, which includes scientists from Tokyo Metropolitan Komagome Hospital and Hokkaido University in Japan, tested a library of 113 synthetic peptides from laminin  $\alpha 5$  for their ability to attach to melanoma cells and for their effect on the colonization of melanoma cells in the lung. Four of the 113 peptides were able to bind to the melanoma cells and inhibit tumor metastasis and growth. The investigators discovered that one of these peptides, A5G27, binds to CD44 on the melanoma cells. The peptide consists of 13 amino acids that correspond to residues 2893 through 2904 in laminin  $\alpha 5$ .

Dr. Kleinman's colleagues documented the ability of A5G27 to inhibit metastasis of skin cancer cells to the lungs of mice. Furthermore, when melanoma cells were placed under the skin of mice treated with A5G27 synthetic peptides, the cells formed a tumor that was smaller in size and lacking in ample growth of novel blood vessels as compared to tumors that developed in mice who received no synthetic peptide treatment.


By identifying a peptide that prevents the laminin  $\alpha 5$ -CD44 interaction from occurring and thereby preventing cancer cell migration, invasion and angiogenesis, the research team uncovered a potentially key target for molecular therapy.

"Potential therapeutics could be based on the actual peptide itself but it is likely that the peptide will need to be modified to increase its time in the



Dr. Hynda Kleinman

circulation," said Dr. Kleinman. This could be done by making the peptide into a dimer or trimer or coupling it to another molecule such as albumen or polyethylene glycol. Alternatively, some of the amino acids in the peptide could be modified to increase stability and circulation time.

"A major advantage of a peptide therapy would be that it would likely not have the side effects observed with the antimetabolites generally used to treat cancers," said Dr. Kleinman. "This peptide is not toxic to cells and its interaction with CD44 is highly specific. Since CD44 is elevated in many types of malignancies, a peptide based therapy would likely be effective against different types of cancers." 

\*ASBMB member

# UCSD Finds Genetic Time Bomb That Leads to Heart Failure in Some Patients

**A**pproximately one in every 125 babies is born with a structural defect in the heart. Each year, thousands of these children undergo corrective surgery to repair their abnormalities. However, in about ten percent of the cases, surgical correction may not fix the underlying molecular trigger that drives progressive heart failure and sudden death later in life, according to new research from the University of California, San Diego (UCSD) School of Medicine. Over time, a genetic time bomb that causes structural abnormalities at birth, continues to degrade vital heart systems, eventually disrupting the electrical impulses that control the heartbeat.

In a study published in the April 30 edition of the journal *Cell*, the investigators used mouse and human subjects to determine that genetic defects in a gene called *Nkx2-5*, which is critical for embryonic heart formation, exert detrimental effects by degrading the heart's atrioventricular (AV) node and by encouraging excessive overgrowth of heart tissue.

"People have thought that congenital heart disease is cured by surgery, which is true for the short term," said the study's senior author, Kenneth Chien,\* Professor of Medicine and Director of the Institute of Molecular Medicine at UCSD. "If a child is born with a hole in the heart, it can be patched. However, as these patients survive, it is now clear that there is an intrinsic, progressive problem with the heart that makes them get late stage heart failure and in certain cases, sudden death due to cardiac electrical problems." One of these patients was born with an atrial septal defect in 1970. Although surgery at age 5

repaired the structural defect, he experienced irregular heartbeats in his 20s and had a pacemaker implanted when he was 22. However, he died unexpectedly in 2001, at the age of 31.

The patient was a member of a large family where multiple generations had inherited atrial septal defects, causing advanced AV node malfunction, and in some cases, death. Heart tissue samples from affected family members who had a known defect in the *Nkx2-5* gene were studied by researchers at Oregon Health & Science University (OHSU) in Portland and the Imperial College and Royal Brompton Hospital in England, in conjunction with the UCSD research team. A characteristic pattern of disease in the electrical system of the heart was found.

"This family almost uniformly had surgeries to correct the structural defects," said Dr. Michael Silberbach, an OHSU cardiologist and one of the authors of the paper in *Cell*. "Then, over a period of several years, they developed problems with the conduction system – the electrical system in the heart."

Silberbach and co-author Dr. Siew Yen Ho were able to compare the human-patient results with the studies in mice by Chien and his team. The

*Over time, a genetic time bomb that causes structural abnormalities at birth eventually disrupts the electrical impulses that control the heartbeat.*

UCSD mice, which lacked *Nkx2-5* in heart ventricle cells, were shown to have significant deterioration of their AV nodes. This included an underformed AV node and disorganized cellular tissue, as compared to normal mice. Similar AV node deterioration was seen in the human patients. Also similar in both mice and humans was a progressive, massive overgrowth of cardiac muscle as they aged.

"With these studies, we learned that *Nkx2-5* is critical not only for heart formation, but also for maintenance of heart function," Chien said. "It also



*Dr. Kenneth Chien explains, "If a child is born with a hole in the heart, it can be patched. However, as these patients survive, it is now clear that there is an intrinsic, progressive problem with the heart that makes them get late stage heart failure and in certain cases, sudden death due to cardiac electrical problems."*

showed us that our mouse model closely resembled the human disease and therefore was an ideal experimental animal model for studies of this form of congenital heart disease caused by the *Nkx2-5* mutation."

To determine what was causing the excessive overgrowth in the hearts of *Nkx2-5*-deficient humans and mice, the UCSD researchers utilized DNA

*Continued on next page*



## Signaling Pathways continued ...

*Continued from page 16*

The location of signaling complexes and the movement of proteins from one cellular location to another is a tightly-controlled process. Therefore, it is not surprising that numerous signaling molecules have evolved as regulators of this cellular traffic. This symposium will focus on exciting new developments in vesicle traffic, and Dr. Emr who will chair the symposium will discuss how genetic analyses in yeast have afforded detailed insights into the mechanisms by which phosphoinositide signaling pathways regulate trafficking. This theme will be reinforced by Dr. Malhotra, who has been investigating vesicle transport to and from the Golgi apparatus, and the importance of a kinase, Protein Kinase D, in this process. To conclude the symposium, Dr. Bankaitis will discuss PTP, the phosphatidylinositol transfer protein, a master regulator of mem-


brane traffic which is necessary for the efficient traffic of a distinct class of membrane phospholipids, the phosphoinositides.

### Structural Basis of Signaling

**Chair:** David Barford, The Institute of Cancer Research, UK: Structural basis for regulation of protein kinases and phosphatases.

**Speakers:** Mark Lemmon, University of Pennsylvania School of Medicine: Activation and inhibition of EGF receptor signaling; Frank Sicheri, Samuel Lunenfeld Research Institute, University of Toronto: Substrate Recognition and Presentation by the SCFCdc4 Ubiquitin Ligase

A detailed molecular picture of the three-dimensional structure of signaling molecules is of paramount importance for understanding the specificity underlying signaling cascades, and

equally importantly, how deregulation of such cascades leads to human disease. This symposium will focus on the molecular resolution of signaling pathways, with emphasis on the structure-function basis of a number of signaling molecules. Much insight into the specificity attributed to signaling by protein kinases and phosphatases has been gained from the three-dimensional crystal structures of such molecules, and this will be highlighted by Dr. Barford, who will chair this symposium. In a similar vein, Dr. Lemmon will discuss how a detailed molecular analysis of the epidermal growth factor-receptor has provided new insights into the detailed mechanism of action of this important receptor tyrosine kinase. Finally, Dr. Sicheri will highlight how molecular resolution of a ubiquitin ligase has provided new and important information about this intriguing class of enzymes. 

## Genetic Time Bomb continued ...

*Continued from previous page*


microarrays to analyze gene databases that were generated from multiple other forms of heart muscle disease. What they found was that a growth-factor gene called BMP-10 was expressed 500 times higher in Nkx2-5-deficient mice, as compared to normal mice, and the gene was unique to this specific form of congenital heart disease. Normally, BMP-10 is only active during fetal heart development, not later in life.

The team went on to engineer animals that have high levels of BMP-10 growth factor in the heart and

observed the same form of heart disease found in Nkx2-5 deficient mice and in patients that harbor mutations in this gene.

Because the AV node is under-formed in the Nkx2-5-deficient mice, when the animal grows and there is excessive expansion of the heart muscle due to BMP-10 expression, the small AV node is unable to keep up with the growth. The result is a mismatch between the AV node electrical switch and the surrounding cardiac muscle, causing the AV node to deteriorate.

"Because a major portion of the muscle defect is due to BMP-10, we will

conduct further tests to see if blocking the persistent expression of this single growth factor will have an effect on the late stages of cardiac dysfunction, including the excessive overgrowth of the heart and the potentially deadly arrhythmias," Dr. Chien said. "Further work will determine whether this may hold to be true for other forms of congenital heart disease, and to see if blocking the BMP-10 growth factor might have a therapeutic effect in halting the onset of massive cardiac overgrowth and associated conduction system disease." 

*\*ASBMB member.*

# U.S. Graduate Students Gain Research Experience in East Asia and Australia

**A**merican students are happy to find jobs during the summer to help pay for their schooling. Others are more fortunate to be part of intern programs that prepare them for their eventual professional lives. For some others, however, the summer prospects are even more rewarding. How about an opportunity to construct carbon nanotubes in a Sydney, Australia laboratory? What about the chance to study with a molecular virologist in Taipei to search for a potential HIV cure? Or maybe do research based on a fossil fuel carbon emission model created in Seoul to better understand the effects of greenhouse gases?

The National Science Foundation's 2004 East Asia and Pacific Summer Institutes Program (EAPSI) for U.S. Graduate Students provided just such opportunities for 150 advanced science and engineering students this past summer in Australia, China, Japan, Korea, and Taiwan. In 2005, NSF will again support U.S. students as they work with foreign counterparts in fields such as cancer research, humanoid robotics, computational neuroscience, and nanofabrication.


For example, Matthew Averill, a graduate student at the University of Texas at El Paso, this year worked on earthquake prediction with researchers at the University of Tokyo. Sarah Rothenberg from the University of California, Los Angeles, worked on modeling urban water demand at China's Institute of Geographical Sciences and Natural Resources.


"This was the largest contingent of U.S. graduate student participants in the program's 14-year history," according to Larry Weber, who manages the EAPSI program. "These research experiences abroad offer exciting discovery opportunities for talented American science and engineering graduate students, and the program will enable them to have the skills necessary to operate in a competitive international research arena and global marketplace in the future."

The institutes provide U.S. graduate students in science and engineering with first-hand research experiences in Australia, China, Japan, Korea or Taiwan, as well as an introduction to the culture and language of the region. The institutes also offer students first-hand knowledge of the research infrastructure and science policies of their international partners.

The summer institutes last approximately eight weeks from June to August. Each EAPSI awardee receives from NSF an international round-trip air ticket and a stipend of \$3,000. Sponsoring organizations in these East Asia and the Pacific communities support students' local living expenses.


NSF administers and manages the EAPSI program through its Office of International Science and Engineering. The National Institutes of Health (NIH) co-sponsor the summer institute in Japan.

Applications are being sought for the 2005 summer institutes. The deadline for submitting those applications is December 10, 2004. 



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by John D. Thompson, Editor

## WTO Puts U.S. on Hold in Biotech Dispute with EU

The United States will have to wait until next year to see its fight with the European Union (EU) over biotech foods resolved, as the result of a decision by the World Trade Organization (WTO) to accede to an EU request to bring scientists into the debate.

A WTO panel in Geneva decided on August 20 to allow expert testimony before deciding on the complaint filed last year by the United States, Canada, and Argentina over the EU's moratorium on approving genetically modified foods for sale in Europe. That means the panel's report, initially expected before the end of this year, now will be delayed until late March,

according to WTO documents. The U.S. had argued that scientific advice was not needed because the case revolved around legal issues, while the EU has sought to move the debate from trade rules to health and environmental protection.

Last May the EU had ended its six-year moratorium and allowed into the market a modified strain of sweet corn grown mainly in the U.S. Another herbicide-resistant corn was approved for animal feed in September, but in both cases the decision was made by the EU's executive commission after ministers from the 25 member governments deadlocked on the applications. The United States has

said it will continue with its WTO case until it sees a "predictable, ongoing process" based on science, not politics. It also opposes the EU's strict labeling, saying it unnecessarily scares away consumers.

Biotech crops have been widely grown in the United States for years, including corn and soybeans genetically modified to resist insects or disease, and U.S. exporters claim the ban has stopped about \$300 million in annual sales of bioengineered corn to Europe. In addition, U.S. officials have expressed concerns that Europe's anti-biotech sentiment is spreading to developing countries as well, exacerbating global hunger.

## China's Government Supports Attempts to Overturn Patents

Foreign pharmaceutical manufacturers in China are facing new challenges as local drug companies find government support in their attempts to overturn the validity of domestically issued patents.

Last July, China's State Intellectual Property Office (SIPO) revoked patent protection for Pfizer's Viagra (sildenafil citrate), saying that Pfizer's application had failed to accurately explain the use of the drug's key ingredients.

This ruling was followed in August, by the announcement that 17 Chinese pharmaceutical companies had formed an alliance to produce a generic version of Viagra. The alliance plans to sell its product for 40 to 50 yuan (about \$5 U.S.) per tablet, and some

industry sources predict the price could fall to as low as 20 yuan if local companies are allowed to produce the drug. Pfizer's price in August was 99 yuan.

Pfizer has had many frustrations since bringing Viagra to China. Cheap counterfeit products immediately appeared on shop counters and in airport shops around the country, despite regulations restricting sales to government-authorized doctors and hospitals. Pfizer claims 90 percent of the Viagra sold in China is fake or counterfeit.

Pfizer has 3 months to make an appeal in the Beijing First Intermediate People's Court, and Chinese lawyers say it could take 2 years for the court to make a ruling. If it loses this appeal,

the company can take the case to the Beijing Higher People's Court for a final decision. Should Pfizer lose both appeals, Chinese pharmaceutical companies will be able to use sildenafil to produce drugs.

Until a court ruling is made, Pfizer's patent will continue to be protected under Chinese law. Pfizer is expected to try to keep the case tied up in Chinese courts for much of the remaining validity of the patent, which expires in 2014. However, Chinese legal experts say that if local companies decide to produce the drug in the interim, the government may decline to take any action on the grounds that the patent is under dispute.



## Monsanto Rivals Seeking a Bigger Piece of the Biotech Crop Pie

The agricultural biotechnology field, dominated since its inception by Monsanto Co. of St. Louis, is becoming more crowded. At least four major companies are identifying useful genetic traits and engineering them into a variety of crops. If these gain regulatory approval, some will compete head-to-head with Monsanto's products, while others may be sold alongside them.

For farmers this is good news. Industry watchers predict that over the next few years, farmers will have more choices in deciding what to plant, and with financial return will win out over brand loyalty. "Farmers will buy from whatever company will provide them with a better value," according to Marshall Martin, Associate Director of Agricultural Research Programs at Purdue University.

"They're not buying Roundup Ready because it's from Monsanto. They're buying it because it works, and, up until now, Monsanto has been the only one on the market."

Roundup Ready is Monsanto's brand for a genetic trait that gives plants the ability to withstand applications of glyphosate, a broad-spectrum herbicide. The company said 123.9 million acres of soybeans, corn, cotton and canola worldwide included the Roundup Ready trait in its 2003 fiscal year. In calendar year 2003, 92 percent of the 167.2 million acres planted with biotech seeds worldwide contained a Monsanto trait. In most categories, its insect- and herbicide-resistant traits were the only ones available.

Now, though, biotech researchers and product development teams are busy at Syngenta AG, DuPont's Pioneer Hi-Bred International division, Dow AgroSciences LLC and Bayer CropScience, a subsidiary of Bayer AG. Each of these companies predict that over the next five to 10 years, it will be a major player in the industry.

"From a crop biotech standpoint, Monsanto got there first. But we don't see the game as being over," said Pete Siggelko, vice president of plant genetics and biotechnology at Dow AgroSciences.

In a related development, in mid-August a U.S. District Court Judge in San Diego ruled Dow and not Monsanto invented the insect-resistance trait used in Herculex and WideStrike. Needless to say, Monsanto will appeal.

## New ARC Chief Plans to Bring Australia's R&D into 21st Century

With low business research and development (R&D) dragging Australia's overall research expenditure below the Organization for Economic Cooperation and Development (OECD) average, the Australian government has picked a scientist whose career has straddled both pure and applied research to head the Australian Research Council (ARC) for the next five years.

Peter Hoj is moving from managing director of the Australian Wine Research Institute (AWRI) to ARC this month. His responsibilities will increase from an AUD \$9 million (USD \$6.4 million) budget at the AWRI to a council that currently distributes more than AUD \$400 million (USD \$286 million) in competitive grants each annually and in 2005-2006 will reach AUD \$550.

Dr. Hoj earned his Ph.D. in genetics and photosynthesis at the University of Copenhagen, and worked as a research scientist in Denmark and Australia on his way to becoming Foundation Professor of Viticultural Science at the University of Adelaide.

He said the biggest problem facing Australian research today was the low business expenditure on R&D. He said the government was already taking steps to address the problem, such as the Backing Australia's Ability initiatives. But, he said, "until such a time that our gross expenditure on R&D compares well with that of other advanced OECD nations, business must work tirelessly to address this imbalance in partnership with government, R&D communities, and the public."

# Many Students Still Not Ready for College Science and Math Courses

**T**he average national ACT composite score increased in 2004 for the first time in seven years. At the same time, the ACT results—a national indicator of student readiness for college—reveal that an alarming number of graduating high school seniors continue to be unprepared for college science and math courses. The average ACT composite score rose just one-tenth of a point to 20.9 among 2004's high school graduates, compared to 20.8 for each of the past two years.

The ACT Assessment, the nation's most widely accepted college admission and placement exam, is scored on a scale of 1 to 36, with 36 being the highest possible score.

The ACT score results indicate that many high school graduates have not mastered key academic skills. Only a fourth (26 percent) of 2004 graduates earned a score of 24 or higher on the ACT Science Test, while just four in 10 earned a score of 22 or higher on the ACT Math Test. Students who reach these score levels have a high probability (75 percent) of earning a "C" or higher—and a 50/50 chance of earning a "B" or higher—in credit-bearing college biology and algebra courses, respectively. These figures are unchanged from 2003.

In comparison, ACT test-takers in the class of 2004 are more likely to be ready to tackle college coursework in the area of writing. The large majority of students (68 percent) earned a score of 18 or higher on the ACT English Test, which indicates they have a high probability of earning a "C" or higher in a credit-bearing college composition class. At the same time, nearly a third of ACT test-takers do not reach this benchmark, suggesting there remains room for improvement even in this area.

## Too Few Students Take Challenging Courses in High School

One major reason why many students lack college-level skills in math and science is that too few are taking challenging coursework in high school. Fewer than two-thirds (62 percent) of ACT-tested graduates in the class of 2004 took the recommended core coursework for college-bound students—at least four years of English and three years each of mathematics (algebra and higher), natural sciences and social sciences. This percentage has changed little over the past decade, rising just 5 percent since 1994.


Similarly, students who took biology, chemistry and physics outscored those who took general science, biology and chemistry by a full 3 points on the ACT Science Test. Even more impressively, students who took biology, chemistry, and physics outscored those who took less than three years of sci-

ence by more than 4 points.

The percentage of college-bound students who took extensive math and science coursework remained relatively low in 2004. Only 39 percent of all ACT-tested graduates reported taking four or more years of math in high school, while just 42 percent reported taking three or more years of science including physics.

## Scores Higher for Racial/Ethnic Minorities

The national average composite score rose slightly for nearly all racial/ethnic groups in 2004. African American students posted the highest gain, an increase of two-tenths of a point this year compared to last. Scores for African American, American Indian, and Asian American students all increased for the second year in a row.

The average score for Hispanic students remained stable. 

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# Bringing Students into Science through Outreach

By Neena Grover and Marilee Benore-Parsons

**M**ost biochemists and molecular biologists are motivated by a devotion to science coupled with a belief that their work will make a difference. This sense of purpose is not always expressed or appreciated by students until they experience the impact their education and skills can have on their community. This is partially due to the approach traditionally used to teach science as a collection of facts. In this old model of teaching, only experts know enough to make meaningful contributions to science and society.


The last decade has seen a dramatic shift in science education. Faculty are recognizing the need to involve students in learning science and utilizing more active learning approaches. Moreover, students are challenging us to teach and practice science in new and creative ways, including articulating the value of practicing science. Finally, we are beginning to recognize that students can be our best ambassadors.

Volunteer activities and involvement in K-12 education have been used for decades but were generally linked to demonstrations and occasional on-campus activities, with little recognition of the educational impact such activities bestow on the participating students. In the last decade, outreach activities have become increasingly incorporated into undergraduate and graduate education, and are linked to the content of science courses. This relatively new approach is called Service-Learning (SL). Students work with K-12 school systems or with local organizations, such as clinics or senior centers, and get credit for the academic activities associated with such endeavors. In other cases, students serve to tutor or present topics to the university community. The challenges associated with organizing such content-linked out-

reach activities are many, and it is time to share these experiences.

ASBMB offered its first symposium on outreach at the 2004 national meeting in Boston, and the rooms were packed with educators interested in incorporating these approaches. The Education and Professional Development (EPD) committee of ASBMB now has an outreach subcommittee to promote the best practices in outreach activities. Towards these efforts, the *Enzymatic* newsletter of ASBMB will feature articles on science outreach activities, including service learning. Sharing these success stories will serve as a resource for all those interested in learning from these experiences. These approaches have proven to increase student motivation and involve a more diverse population of students to participate in science.

Improved student learning is a goal of ASBMB, campus administrations and agencies such as NSF. Outreach efforts are gaining administrative support and infrastructure, as activities demonstrate the contribution of institutions of higher education to their communities while improving student motivation and learning. Furthermore, a greater emphasis on broader impact and outreach activities required for NSF grants has made us aware of the need to explain science to non-scientists, if we expect tax payers to fund our research and if we wish to increase the number of students who are attracted to science careers.

If you are already using outreach activities for teaching, please share your experiences by submitting articles to *Biochemistry and Molecular Biology Education (BAMBED)* and to *Enzymatic*. 



*Last year ASBMB Today received one award, this year we received three APEX Awards for Publications Excellence from Communications Concepts, Inc., which specializes in business publications. Peter Farnham, at left, received an Award for his article in the February 2004 issue, "Happy New Year—Not; 2004 Outlook Tough at Best,"*

*which forecast a difficult year for biomedical research funding. Our designer, Wendie Lubic, received an Award in Design and Layout for "Leading Researchers Highlight Annual Meeting," a feature on the 2003 Annual Meeting. An Award in the Most Improved Magazines and Journals category went to John Thompson, Editor.*



# Calendar of Scientific Meetings

## OCTOBER 2004

### An ASBMB Sponsored Symposium: Redox Signaling in Biology and Disease

October 21–24 • Kiawah Island, South Carolina  
Organized by Larry Marnett, Vanderbilt U. and Roy J. Soberman, Harvard Med. School  
Plenary Lecture: Regulation of Mammalian Clock Genes  
Steven L. McKnight, U. of Texas, Southwestern Medical Center  
Contact: Joan Geiling, Ph: 301-634-7145; Fax: 301-634-7126  
Email: asbmb@asbmb.org; Website: www.asbmb.org

### Inhibition of Matrix Metalloproteinases: Expanding the Horizons

October 23–25 • Crowne Plaza LaGuardia Hotel, New York City  
This meeting will focus on new ideas in development of inhibitors of MMPs to treat disease (done in collaboration with NYAS). Abstracts welcomed.  
Sponsored by Northshore LIJ Medical Center  
Contact: Robert Greenwald; Ph: 516-465-5410  
Fax: 516-465-5454 ; Email: rgreenwald@lij.edu or Stanley Zucker: s\_zucker@yahoo.com

### An ASBMB Sponsored Symposium: Transcriptional Regulation by Chromatin and RNA Polymerase II

October 29–November 1 • Granlibakken, Lake Tahoe, California  
Organized by Ali Shilatifard, St. Louis U. School of Med.  
Keynote Speakers: Joan Conaway and Ronald Conaway  
Contact: Joan Geiling, Ph: 301-634-7145; Fax: 301-634-7126  
Email: asbmb@asbmb.org; Website: www.asbmb.org

## NOVEMBER 2004

### 4th International Congress on Autoimmunity

November 3–7 • Budapest, Hungary  
Deadline for Receipt of Abstracts: June 20, 2004  
Contact: 4th International Congress on Autoimmunity Kenes International—Global Congress Organisers and Association Management Services, 17 Rue du Cendrier, PO Box 1726, CH-1211 Geneva 1, SWITZERLAND  
Ph: +41 22 908 0488; Fx: +41 22 732 2850  
Email: autoim04@kenes.com  
Website: www.kenes.com/autoim2004

### American Association of Pharmaceutical Scientists AAPS Annual Meeting and Exposition

November 7–11 • Baltimore, Maryland  
Ph: 703 243 2800; Fx: 703 243 9650  
Website: www.aapspharmaceutica.com/meetings/futuremeetings/

### First Latin-American Protein Society Meeting

November 8–12 • Hotel do Frade, Rio de Janeiro, Brazil  
Sponsored by The Protein Society, The Wellcome Trust, and Brazilian research funding agencies.  
For more information: Dr. Alberto Spisni  
Brazilian Synchrotron Light Laboratory, Campinas, Brazil, and Dept. Experimental Medicine, University of Parma, Italy  
Caixa Postal 6192 - CEP 13084-971, Campinas, SP, Brazil  
Ph: +55 19 3287-4520; Fx: +55 19 3287-4632  
Email: alberto@lnls.br; Website: www.lnls.br/lapsm

### Second National Meeting of the American Society for Matrix Biology

Nov 10–13 • San Diego, California  
Contact: ASMB, 2019 Galisteo Street, Building I-1, Santa Fe, NM 87505; Ph: 505 989-4735; email: cindi@sciencemanagers.com  
Website: <http://www.asmb.net>

## DECEMBER 2004

### American Society for Cell Biology, 44th Annual Meeting

December 4–8 • Washington, DC  
Ph: 301-347-9300; Fx: 301-347-9310  
Website: <http://www.ascb.org/>

## MARCH 2005

### CSBMCB Sponsored Meeting on Cellular Dynamics

March 16–20 2005 • Banff Centre, Banff Alberta  
This meeting, set in Banff National Park, will feature cutting-edge sessions on Nuclear structure, Organelle Inheritance, Imaging Technologies, Protein Folding, mRNA localization, Organelles of the secretory pathway and Systems approaches to Cell Biology. Keynote Speaker is Günter Blobel.  
Email: rick.wozniak@ualberta.ca  
Website: <http://www.csbmc.ca/2004Meeting/index.ht>

## APRIL 2005

### American Society for Biochemistry and Molecular Biology Annual Meeting in Conjunction with EB2005

April 2 – 6 • San Diego  
Nobel Laureates Michael S. Brown and Joseph L. Goldstein will open the ASBMB Annual Meeting with the Herbert Tabor/Journal of Biological Chemistry Lecture.  
Contact: ASBMB 2005, 9650 Rockville Pike, Bethesda, MD 20814-3008; Ph: 301-634-7145; Email: meetings@asbmb.org  
Website: [www.asbmb.org/meetings](http://www.asbmb.org/meetings)

## The 46th ENC Experimental Nuclear Magnetic Resonance

April 10–15 • Rhode Island Convention Center, Providence, Rhode Island

Contact: ENC, 2019 Galisteo Street, Building I  
Santa Fe, New Mexico 87505 (USA); Phone: 505-989-4573  
Fax: (505-989-1073; E-mail: enc@enc-conference.org  
Web page: www.enc-conference.org

### JUNE 2005

#### 7th Annual Plant Sciences Institute Symposium; Meristems 2005

June 2-5 • Iowa State University, Ames, Iowa  
Abstracts due April 1, 2005; Registration Deadline May 2, 2005  
Student Travel Grants: Applications due April 1, 2005  
Contact: Plant Sciences Institute Symposia, Symposium Office,  
3208 Molecular Biology Building, Iowa State University, Ames,  
Iowa 50011-3260; Ph: 515-294-7978; Fax: 515-294-2244  
Email: pbmb@iastate.edu  
Website: www.bb.iastate.edu/~gfst/phomepg.html

### JULY 2005

#### 30th FEBS Congress – 9th IUBMB Conference, 2005 The Protein World; Proteins and Peptides: Structure, Function and Organization; Science is Fun: A Conference for Your Creativity

July 2–5 • Budapest, Hungary  
Contact: Ms. Franciska Morlin, Chemol Travel Congress Dept.  
H-1366 Budapest, P.O.Box 28, Hungary  
Ph:+36-1-266-7032, Fx: +36-1-266-7033  
Email: incoming@chemoltravel.hu; www.febs-iubmb-2005.com

#### BioScience2005 - From Genes to Systems

July 17-21 July • Glasgow, UK  
Focus topics for the meeting: Cell architecture: from structure to function; The nucleus: chromatin, recombination and repair; Cellular information processing; Proteins in disease; Stem cells and development.  
Plenary speakers include: Robert J. Lefkowitz, Wolfgang Baumeister, P. Leslie Dutton, Walter Kolch, and David Stuart. Poster abstract deadline: April 15, 2005, Early registration deadline: May 23, 2005  
For more information: BioScience2005, Biochemical Society, c/o Commerce Way, Colchester, Essex CO2 8HP  
Tel : +44 (0)1206 796351; Fax : +44 (0)1206 798650  
Email: info@BioScience2005.org; www.BioScience2005.org

### SEPTEMBER 2005

#### Strategies for Engineered Negligible Senescence [SENS], 2nd Conference

September 7-11 • Queens' College, Cambridge, England  
Conference organizer: Aubrey de Grey  
Email: ag24@gen.cam.ac.uk)  
Website: http://www.gen.cam.ac.uk/sens2/CSBMCB

## Department Heads Take Note:

# ASBMB Offers Free Membership to New Ph.D.s

ASBMB is now offering a free one-year Associate membership to all students who have, within the past year, earned a Ph.D. degree in the molecular life sciences or related areas.

ASBMB implemented this program as a way to recognize the significant accomplishment of earning the Ph.D., and to provide new Ph.D.s with something tangible and of economic value. Membership in ASBMB brings with it a free subscription to the online versions of the *Journal of Biological Chemistry* and *Molecular and Cellular Proteomics*, as well as subscriptions to *The Scientist* and the Society's magazine, *ASBMB Today*, discounts on other publications, and a host of other benefits.

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Membership at ASBMB  
American Society for Biochemistry  
& Molecular Biology  
9650 Rockville Pike  
Bethesda, MD 20814  
Email: membership@asbmb.org

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