

JUNE 2005

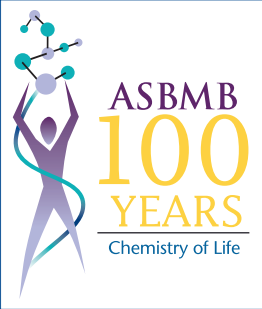
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# ASBMB *Today*

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AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

## Painkilling Drugs from Deadly Snails



Molecular Structure

Genome Dynamics

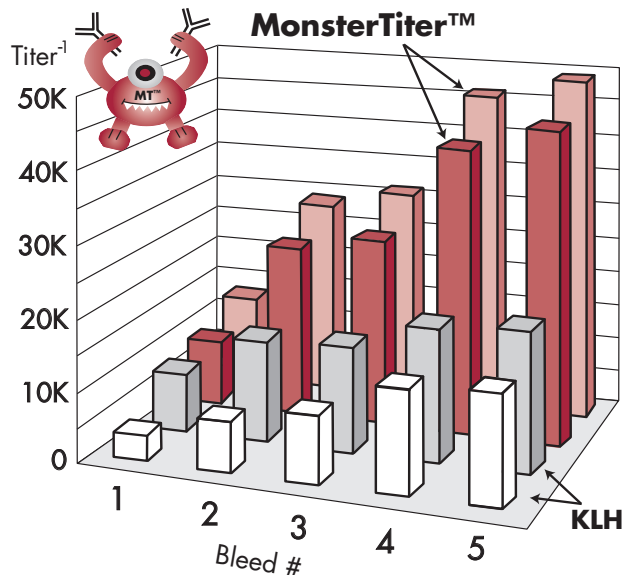
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AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

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Volume 4, Issue 3

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# Articles and Videos of Scientific Stars Will Highlight Centennial Year

By Nancy Rodnan, Director of Publications

**A** Centennial Celebration will be held April 1-5, 2006 in San Francisco to honor the 100 years of achievements and contributions to science made by the *Journal of Biological Chemistry* (JBC) and the American Society for Biochemistry and Molecular Biology (ASBMB). Among the special events planned are video clips of several distinguished scientists that touched and influenced the success of the American Society of Biological Chemists (ASBC), ASBMB and the JBC with their accomplishments, contributions and dedication. In the coming months *ASBMB Today* will feature articles on Arthur Kornberg, Joan Steitz, Thomas Cech, Mildred Cohn, Mike Brown and Joseph Goldstein, Edwin Krebs, Edmond Fischer, Howard Schachman, and Herbert Tabor. Once you read the upcoming articles and see the videos you will quickly understand why these candidates were selected.

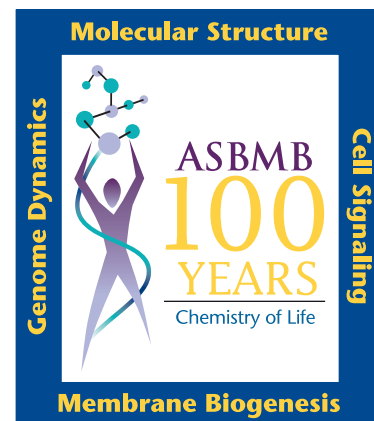
All of these distinguished individuals have been written about and video taped on several occasions over the years. One just needs to 'Google' their names to get lists of their accomplishments, papers written and interviews. So why are we doing this?

Well, we wanted to capture something a little extra. Along with each person's connection to biochemistry, their training, and how they became biochemists, we are going to include their special impact on and role in ASBC, ASBMB, and JBC.

There are many wonderful stories, facts, and insights that have not been shared before. We are very excited about this project and hope you will find the articles and videos of great enjoyment and interest.

## Tell Us What You Think

We appreciate receiving letters that are suitable for publication regarding issues of importance or commenting on articles appearing in *ASBMB Today*. Letters should be sent to the editor, John Thompson, at the address found at left. Letters must be signed and must contain the writer's address and telephone number. The editor reserves the right to edit all letters.





Dr. Judith Bond

## The Evolving Story of Open Access, NIH Sponsored Research, and the ASBMB

**T**he final NIH policy on 'Enhanced Public Access to NIH Research Information' went into effect on May 2, 2005. The bottom line is that the NIH strongly encourages and requests authors who publish work supported by the NIH to deposit the final accepted version of their manuscripts in PubMed Central within 12 months of the date of acceptance by a journal. The rationale and a description of the NIH policy can be found at <http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-05-022.html>. Submission instructions for authors can be found at: <http://nihms.nih.gov>.

In order to enable authors of ASBMB publications to comply with this policy, we have issued the following policy (available on the ASBMB website: [www.asbmb.org](http://www.asbmb.org)).

ASBMB, as copyright holder, grants permission to all authors, for the sole purpose of compliance with the NIH request, to deposit their accepted manuscripts in PubMed Central.

ASBMB will allow authors to transmit their manuscripts to NIH for release free to the public anytime after the day they are published as Papers in Press. We require that the same exact version of the manuscript be deposited in PubMed Central as was accepted and published in Papers in Press. It is also our expectation that the version appearing on the PubMed Central site contain an indication that the paper is

available free on the JBC/JLR/MCP site and that links be provided by PubMed Central to the Papers in Press version and ultimately to the final, redacted version of the paper on the JBC/JLR/MCP web site.

There are innumerable questions as to how this system will work, what it will contribute to 'public access' and whether it is worth the added expense. For JBC, only about 40 percent of the articles will be deposited in PubMed Central, and for many life sciences and chemical journals a much smaller percentage of their articles are from NIH sponsored research and will be deposited in PubMed Central. The NIH will use the depository to manage its portfolio, and the new policy does make some government-funded research more accessible to the 'public.'

The debates about open access, the costs of publishing, finding financial strategies to sustain journals, and archiving journals for the next century are still very much with us. In a recent session at the National Press Club in Washington, DC, a representative of the Public Library of Science (PLOS) continued the aggressive advocacy for an 'authors-pay' model for scientific publication. PLOS alleges that both for-profit and not-for-profit publishers charge libraries, subscribers and other users too much for access, and that they are denying adequate access to the scientific literature. PLOS now admits that the average cost to an

author or sponsor will exceed \$1500 per article. PLOS remains elusive on who is to pay for the up-front costs for publication, and who will pay for the ongoing costs of archiving the literature reliably for years to come. PLOS is reluctant to acknowledge the many innovations that have accrued in scientific publishing, the strides that have been taken to make biomedical data understandable to 'the public,' and that many not-for-profit publishers have made the content of their articles available on-line at no cost to the reader. The saga continues, and the ASBMB will continue to search for innovative solutions in publishing, and to work with other not-for-profit publishers to serve our authors, the scientific community and 'the public.'

*Judith Bond, President, ASBMB*

### CORRECTION

Due to a typographical error, a reference in President Bond's message in the May issue of *ASBMB Today* stated incorrectly that ASBMB (originally the American Society of Biological Chemistry) dates back to December 2006. ASBMB, originally the American Society of Biological Chemists, was founded December 26, 1906, and incorporated September 12, 1919. The name of the Society was changed to American Society for Biochemistry and Molecular Biology in 1987.



by Peter Farnham, CAE, ASBMB Public Affairs Officer

# Key Legislator Calls for Tripling Basic Federal Science Budget

**A** key member of the House Appropriations Committee, Rep. Frank Wolf (R-VA), on May 3 called publicly for tripling federal basic research and development spending over the next decade. Wolf is chair of the House Appropriations Subcommittee on Science, State, Justice, and Commerce, which took over jurisdiction of most science programs at the beginning of 2005.

In a letter to the President on May 3, Wolf said, "America today finds herself at a crossroads when it comes to leading the world in science and innovation. We can continue down the current path, as other nations continue to narrow the gap, or we can take bold, dramatic steps to ensure U.S. economic leadership in the 21st century and a rising standard of living for all Americans."

Wolf then recited a litany of problems America faces in competing with the rest of the world, including producing only a small fraction of the world's

science and engineering graduates—China produces more than twice as many as we do; the declining number of American scientific papers relative to those from elsewhere in the world; a decline in the number of U.S. patents; and a decline in the number of Nobel Prize winners. While the U.S. still enjoys a lead over any single nation in most of these areas, our once dominant position has eroded to close to parity in some cases.

Citing the recent doubling of the National Institutes of Health budget as an example, Wolf urged the president to "make a similar bold commitment to invest in the future of our country by tripling the innovation budget—federal basic research and development—over the next decade....I understand the difficult budget environment the nation is facing. But bold leadership from the White House will help establish this as a national priority in your next budget request to the Congress."

At a press conference on May 12, Wolf—accompanied by several other prominent House members—announced plans for an "innovation sum-


*Science Committee chairman Sherwood Boehlert (R-NY) and, at right, Vernon Ehlers (R-MI) supported call to tripling funding for scientific research and development.*



*Frank Wolf (R-VA), Chair of the House Appropriations Subcommittee on Science, State, Justice, and Commerce, has called for a tripling of federal basic research and development spending over the next decade.*

mit" to be held this fall. The purpose of the summit is to help raise public awareness of these trends and their implications for jobs, industry and national security in the not-too-distant future.

"He gets it," said Science Committee chairman Sherwood Boehlert (R-NY) of Wolf, as he seconded and enthusiastically supported the idea of the summit. A summit "can help forge a national consensus on what is needed to retain U.S. leadership in innovation. A summit like this, with the right leaders, under the aegis of the federal government, can bring renewed attention to science and technology concerns so that we can remain the nation that the world looks to for the newest ideas and the most skilled people."

Summit planning is expected to begin in the next several weeks. 



# Stem Cell Research Bill Close to House Consideration

**I**n a sign of how much the political situation is changing in Congress relative to the stem cell issue, a bill introduced in February—H.R.810, the Stem Cell Research Enhancement Act of 2005—is expected to come up for a vote on the House floor sometime in the next several weeks. H.R.810, which seeks to expand the amount of stem cell research that can be federally-funded, has 198 cosponsors—out of a total of 435 House members. Thus, the number of cosponsors is only 20 short of a majority of the House.

The bill, introduced by Rep. Diana DeGette (D-CO) and Rep. Mike Castle (R-DE), allows donated human embryos from IVF clinics to be used for federally-funded stem cell research. This change in the law would potentially make available for stem cell research tens of thousands of human embryos, currently stored in IVF clinics and destined for eventual disposal. Restrictions on their use in the bill include that the embryos involved can be available only after informed consent and without any sort of financial compensation or inducements for the donor. In addition, before an embryo can be donated for stem cell research, it must be determined that the embryo will never be implanted in a woman and would otherwise be discarded.

The bill does not address creation of embryos for research purposes through somatic cell nuclear transfer—so-called “therapeutic cloning.” It merely allows an expansion of the sources where embryos can be obtained for research purposes. Senators Arlen Specter (R-PA)


and Tom Harkin (D-IA) have introduced companion legislation in the Senate.

Rep. Castle said of the bill, “Embryonic stem cell research is the greatest medical hope of the 21st century. That is why we are standing together today as Republicans and Democrats in the House and the Senate, attempting to rid the current federal policy of obstacles so science can move forward. Make no mistake about it, today we are introducing this legislation for the millions of patients who suffer nationwide. Not one more day should be wasted in the search for a cure.”

Rep. DeGette added, “Americans of all stripes—conservative and liberal, Republican and Democrat—want government to oversee medical research ... Our legislation brings millions of Americans closer to a cure and furthers the culture of life we all embrace by preserving the strict controls that only NIH can impose.”

Federal funding for human embryonic stem cell research is limited to cells derived from a handful of human stem cell lines that existed prior to August 9, 2001, the day President Bush announced his policy on this type of research. Although there are no restrictions in the private sector on human embryonic stem cell research, there is growing concern in the biomedical research community that such research would be greatly enhanced if the current federal policy were to be broadened to include more lines eligible for federal funding and support. DeGette and Castle have offered their bill as a way to

expand the number of embryos available from which lines could be developed, while at the same time avoiding a protracted fight over SCNT, which continues to be controversial in the House.

A bill banning SCNT has passed the House overwhelmingly in each of the last two congresses, but has not been able to clear the Senate. So far this year, no ban on SCNT has been introduced in either legislative body. 

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## International Scientists, Engineers Essential to Competitive U.S.

To maintain America’s leadership in science and engineering research, a comprehensive effort is needed to improve the recruitment, education, and training of a cross section of U.S. students for careers in these fields, while continuing to attract the most talented scholars worldwide, says a new report from the National Academies. These twin goals are critical, given increasing global competition for top-notch graduate students and researchers.


The continued vitality and excellence of the nation’s science and engineering enterprise are essential to America’s interests, emphasized the committee that wrote the report. Highly talented people are the driving force behind scientific and technical advances in this knowledge-driven economy, and the contributions of international graduate students and postdoctoral scholars are important.

# NIH Issues Guidance on Submitting Manuscripts Under Public Access Policy

**N**IH issued guidance on April 29 concerning how it intends to implement its policy on enhanced public access to publications derived from NIH-funded research. The guidance document appeared in the April 29 issue of the *NIH Guide to Grants and Contracts*.

The document summarizes the NIH policy on enhanced access (which took effect on May 2, 2005), and then discusses a password-protected, Web-based, NIH-Manuscript Submission (NIHMS) system, developed to "facilitate the submission process." More information on this system is available at [www.nihms.nih.gov](http://www.nihms.nih.gov).

The notice then describes how to submit a manuscript. Upon logging into the NIHMS system, PIs will be asked to categorize themselves as extramural or intramural investigators. At this point, PIs will be asked to provide basic information about themselves and their manuscripts. They will then load the complete text of the manuscript into the NIHMS system, as well as any corresponding or supplemental image files such as figures or tables. PIs will next confirm that manuscripts and supplemental material have been successfully received; review and approve the terms and conditions of the submission agreements and specify the timing of posting of the final

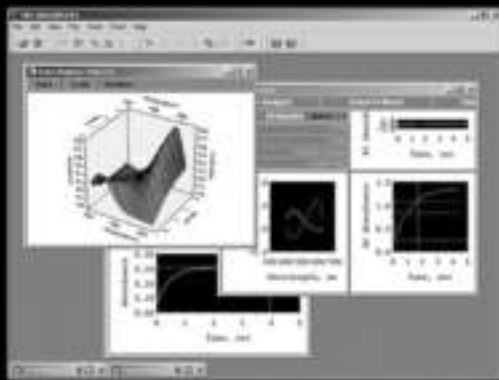
manuscripts. Finally, PIs will be notified by NIH when their manuscripts are ready for posting; PIs should then review their manuscripts once more and correct any errors that may have appeared. After PI-final approval, the manuscripts will be made publicly available after the specified time-delay. 

*Note: Extramural PIs must first obtain an NIH eRA Commons account number in order to enter into the NIHMS system and submit final manuscripts. For more information contact the Sponsored Research Office at your institution or contact the NIH eRA Commons Help Desk at [commons@od.nih.gov](mailto:commons@od.nih.gov) (or phone at 866/504-9552).*

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# National Academies Release Guidelines for Embryonic Stem Cell Research

**T**he National Academies debuted guidelines for research involving human embryonic stem cells (hESC) in late April, and urged all institutions conducting such research to establish oversight committees to ensure that the new guidelines are followed. The guidelines are intended to enhance the integrity of privately funded hESC research by encouraging responsible practices.

“Heightened oversight is essential to assure the public that stem cell research is being carried out in an ethical manner,” said Committee Co-Chair Jonathan D. Moreno, University of Virginia. “The oversight we call for will in many instances set a higher standard than required by existing laws or regulations.”

“A standard set of requirements for deriving, storing, distributing, and using embryonic stem cell lines—one to which the entire U.S. scientific community adheres—is the best way for this research to move forward,” added Committee Co-Chair Richard O. Hynes, Massachusetts Institute of Technology.

The guidelines call for creation of Embryonic Stem Cell Research Oversight (ESCRO) committees. These would be in addition to already existing research compliance bodies such as institutional review boards. In addition to scientists, ESCRO committees would include legal and ethical experts, and representatives of the public.

The ESCRO committees would review proposals for research that takes stem cells from excess blastocysts at *in vitro* fertilization clinics or from

blastocysts created expressly for stem cell research. They also would review any proposed use of blastocysts created by nuclear transfer, often referred to as therapeutic cloning.

The guidelines reiterate previous Academies’ statements (and those of most other scientific bodies, including ASBMB) that reproductive cloning must not be allowed. In fact, the guidelines state that blastocysts used for research should not be grown in culture for longer than 14 days.

Human embryonic stem cells, says the guideline, should be introduced into nonhuman mammals only under circumstances where no other experiment can provide the information needed. Experiments where there is a possibility that human cells could contribute in a “major organized way” to the brain of an animal require strong scientific justification, the committee stated.

There are a number of recommendations (Rec.#8-23) regarding the protection of human subjects, informed consent, and tracking of stem cell lines. Perhaps the most noteworthy of these is that all donors involved must give informed consent and should not be reimbursed beyond basic medical expenses. This would include sperm donors, who under the current system are often anonymous and sometimes compensated. The committee acknowledged that this could




Senator Sam Brownback  
(R-KS)

potentially exclude a large number of existing hESC lines, but thought that this was important given the immortality of the lines and the potential for future therapeutic uses.

The Academies’ guidelines also address how far scientists should go in mixing human and animal cells to create so-called chimeras, which researchers may need to do in order to test the therapeutic potential of human stem cells in animal models. The guidelines say no animal embryonic stem cells should be transplanted into a human blastocyst, and approval by an ESCRO committee should be secured before any human embryonic stem cells are put into an animal. Also, no animal into which human embryonic stem cells have been introduced should be allowed to breed. In addition, no human embryonic stem cells should be put into nonhuman primate blastocysts.

The committee urged the formation of a national independent body to periodically review whether the guidelines need to be updated in light of unforeseen advances in stem cell science and evolving public attitudes.

As might be expected, the report met with strong criticism from those opposed to hESC research. Senator Sam Brownback (R-KS) blasted the report, saying “these so-called guidelines for destructive human embryonic stem cell research try to put a good face on an unethical line of research. We should not be destroying young human lives for the benefit of others.”

An online copy of the guidelines can be found at: <http://books.nap.edu/catalog/11278.html> 

# Pain-Killing Drugs

By Nicole Kresge, Staff Science Writer

**T**he *Conus* snail is a carnivorous sea animal that relies on its venom to stun its victims, including fish bigger than itself. Once immobilized, the hapless prey is devoured by the snail. This rapid-acting venom contains hundreds of small toxic peptides, which have been the subject of more than 30 years of intensive research by Dr. Baldomero M. Olivera\* at the University of Utah.

In the early 1970s, Dr. Olivera started to systematically collect venom from *Conus* snails and purify their biologically active components. "We started working on *Conus* because we had to find a project in the Philippines that required no equipment (we had an empty lab, initially)," explained Olivera. "We decided to investigate components of the venom of the geography cone, *Conus geographus*, since this species of cone snail was known to be able to kill people. We originally thought this was going to be a really short-term research project."

Dr. Olivera discovered that each *Conus* snail's venom consists of a diverse mixture of small, structurally constrained peptides (conopeptides), and that the complement of peptides found in one species' venom is strikingly different from that found in another species.

The conopeptides are mostly 12 to 35 amino acids in length and are highly cross-linked. The total repertoire of different peptides expressed in the venom of a single species ranges from 50 to 200, and each conopeptide is a highly specific ligand, targeted to a

certain isoform of a receptor or ion channel. Combinations of these peptides produce the fast-acting, immobilizing action of the venom the snails rely on for catching fish.

The first venom peptide to be purified was a competitive nicotinic antagonist named alpha-conotoxin GI from *C. geographus*. This was followed by the characterization of the mu-conotoxins, also from *C. geographus*, which were found to be sodium channel blockers. Over time, many other *Conus* peptides were purified and characterized. "We have probably purified over 150 peptides from venoms, and know the sequence of over 2,000 by molecular techniques," says Dr. Olivera.

Because they specifically target a variety of pharmaceutically important

ion channels and receptors, are fast-acting and potent, and are easy to manufacture due to their small size, the conopeptides have garnered much attention as potential therapeutics.

"Conopeptides make good pharmaceutical leads because they are so very highly specific for their targets," explains Dr. Olivera. "Many of the receptors and ion channels in the nervous system are present in many different molecular isoforms, and a pharmaceutical agent that interacts with multiple closely related isoforms can have bad side effects. The interest in conopeptides is their extraordinary specificity and their ability to discriminate between closely related molecular isoforms."

*C. striatus* ingesting a fish.



Photo by K.S. Matz.

# from Deadly Snails

One conopeptide, omega-conotoxin MVIIA, was recently approved by the Food and Drug Administration (FDA) for chronic, intractable pain suffered by people with cancer, AIDS, injury, failed back surgery or certain nervous system disorders. The conopeptide was originally isolated from the venom of *C. magus* by J. Michael McIntosh, then an undergraduate student working in Dr. Olivera's lab.

Omega-conotoxin MVIIA blocks the calcium channels in nerve cells that transmit pain signals, making it an ideal candidate for a painkiller. Indeed, studies showed that omega-conotoxin MVIIA is a potent analgesic, approximately 1,000 times more potent than morphine. The peptide also relieves neuropathic pain, which is generally unresponsive to opiates, and no tolerance occurred during chronic treatment.

*C. monachus ingesting a fish.*



Photo by K.S. Matz.

*C. bullatus harpooning/stinging fish.*

Currently, omega-conotoxin MVIIA is being manufactured by Elan Corporation under the name Prialt (ziconotide intrathecal infusion). The painkiller became available in January and is the first example of a gene-

encoded invertebrate polypeptide to be used clinically.

There are several other conopeptides that have reached human clinical trials. Contulakin-G, an agonist of the neurotensin receptor, was shown to be a potent analgesic in animal models, and conantokin-G, an NMDA receptor antagonist, has therapeutic potential for epilepsy; these compounds have been through Phase I clinical trials. Omega-conotoxin CVID is in Phase II trials for treatment of chronic pain.

There are over 500 species of *Conus*, each of which have anywhere between 50-200 distinct, biologically active conopeptides in their venom. This means that there are more than 50,000 different conopeptides present in the venoms of living species of *Conus* and the possibility of many more potential drugs to be discovered. ∞

\*ASBMB Member

Courtesy Dr. Baldomero M. Olivera, photo by K.S. Matz





# Researchers Make Gains in Understanding Antibiotic Resistance

**H**oward Hughes Medical Institute researchers chipping away at the problem of antibiotic resistance now have a detailed explanation of how the drugs' main cellular target in bacteria evolves to become resistant to some of these medications. The findings are already leading to new antibiotics that are being engineered to circumvent resistance, which is a major worldwide health problem.

Led by Thomas A. Steitz,\* a Howard Hughes Medical Institute Investigator at Yale University, and Peter B. Moore, a Yale Professor of Chemistry, the research team published its findings in the April 22, 2005, issue of the journal *Cell*.

Dr. Steitz and his colleagues studied the structural basis of bacterial resistance to a group of antibiotics that, while chemically quite different, all jam the activity of the protein-making factory in bacteria in much the same way. They studied the MLSBK antibiotics, an acronym for a group of antibiotics which include macrolides, lincosamides, streptogramin B and ketolides. MLSBK antibiotics work by binding to the RNA, near the peptidyl-transferase center, of the large subunit of the ribosome. The ribosome is the molecular machine responsible for translating the genetic information on messenger RNA into the long strings of amino acids called polypeptides that are used to build the cell's enzymatic machinery.

"These antibiotics are clinically very important, and resistance to such antibiotics is a major health problem," said Dr. Steitz. "It is becoming critical to understand the precise structural

basis of resistance and even more important to do something about it." Steitz cited, for example, recent statistics published in the journal *Nature*, stating that hospitals in the United States see some two million cases of antibiotic-resistant infections each year; 90,000 patients die annually from such infections.

In their experiments, he and his colleagues used x-ray crystallography to do high-resolution structural analyses of the large ribosomal subunits bound to a number of the MLSBK antibiotics. In this analytical technique, intense beams of x-rays are directed through crystals of proteins. The underlying atomic structure of the proteins is deduced by analyzing the pattern of diffraction of the x-rays.

Dr. Steitz's group used ribosomal subunits from the archaeobacterium *Haloarcula marismortui* (Hma), which is found in the Dead Sea. They chose Hma ribosomes for their studies because they crystallize well enough to yield high-resolution structural data, but these ribosomes, like those from eukaryotes, are resistant to most MLSBK antibiotics.

The researchers analyzed the structure of erythromycin—among the most widely prescribed macrolide

*"It is becoming critical to understand the precise structural basis of resistance and even more important to do something about it."*

—Thomas A. Steitz

antibiotics—bound to a mutated version of the Hma ribosome that corresponds to a form found in pathogenic bacteria. Their studies revealed details of



Dr. Thomas A. Steitz

erythromycin binding to the mutant form of the Hma ribosome that do not agree with similar analyses by other researchers, according to Steitz. The studies by Steitz's group yielded new information about the basic chemical principles that underlie binding of the antibiotic to the ribosome, as well as new data about how mutation confers drug resistance.

Dr. Steitz and his colleagues also analyzed the structure of five other clinically important antibiotics - azithromycin, telithromycin, clindamycin, and virginiamycin M and virginiamycin S - bound to the large mutated ribosomal subunit. He said these studies provided new details about the nature of drug resistance involving these antibiotics. Furthermore, the studies of the two forms of virginiamycin offer an explanation for how the two forms of that antibiotic work synergistically to kill bacteria.


Finally, the researchers used x-ray crystallography to explore at high resolution the structural basis of a particular ribosomal mutation dubbed L22 that confers resistance to macrolides such as erythromycin. In a seeming paradox, said Steitz, this mutation confers resistance, even though the antibiotic still binds to the mutant ribosome.

The new structural data indicate that the L22 mutation increases the size of a "tunnel" in the ribosome, through which the growing peptide chain moves during synthesis. This tunnel is normally blocked by macrolide antibiotics. In the mutant form, the tunnel widens, which may explain why macrolide antibiotics are no longer effective.

According to Dr. Steitz, insights about the ribosomal origins of antibiotic resistance are already being applied to the development of new antibiotics. One company lead-

ing the way is Rib-X Pharmaceuticals, which was founded by Steitz and colleagues at Yale.

"About half of current antibiotics target the ribosome, and most of them target the large subunit," he said. "So, such advances have the potential for significant clinical impact. The general strategy of Rib-X to overcome resistance is to create new hybrid antibiotics that possess the ability to bind to interact simultaneously with different, nearby sites on the ribosome represented by different classes of antibiotics," he said.

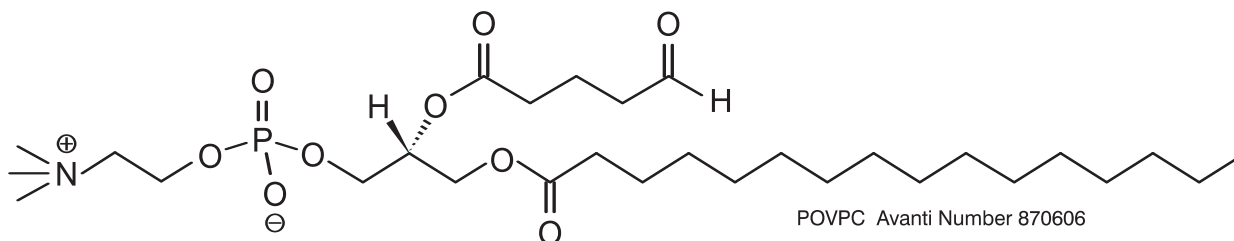
"The idea is to take a bit of one antibiotic and tie it to another. So, if resistance arises due to a mutation in one site, there is still another binding site that can be targeted. It's like multiple drug therapies for HIV, in which the drugs attack several sites at once. And if the virus mutates to avoid the effects of one drug, it still gets hit by another. However, in the case of these antibiotics, the binding sites are linked in one molecule. It's like a multi-drug treatment, but in one compound," Dr. Steitz concluded. 

\* ASBMB member.

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Leitinger, N., *et al.* (1999). *Proc Natl Acad Sci.* Oct 12;96(21):12010-5.

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# Heidi E. Hamm, President-Elect of ASBMB

**H**eidi Hamm, Earl W. Sutherland, Jr. Professor of Pharmacology and Chair of the Department, was elected President-elect of the American Society for Biochemistry and Molecular Biology at the society's annual meeting in San Diego in April. Dr. Hamm, who previously served as the organization's Secretary (1995-1998), and Program Chair in 1998, will serve as President-elect for one year starting this July 1, followed by a two-year term as President beginning July 1, 2006.

In her term as president, she hopes to be a strong advocate of support for biomedical research in this country. "Broad investments in science have been an engine for better health and longer life in this country, and we are in a period of incredible discovery," says Dr. Hamm. "A flat or decreasing research budget will erode the catalytic effects of the recent doubling on medical research breakthroughs. Hardest hit during this funding environment are young people who have been superbly trained and whose contributions will continue for many years. If funding levels do not improve, we will lose them to other careers, and the investment the scientific community has made in their training will be lost. It is a high priority for me to work with ASBMB and FASEB and other organizations to improve future science funding.

"Another goal I have for these next years is to increase the involvement of young people in the society, continue to make progress in keeping a broad and diverse representation of scientists in ASBMB, and promote their active participation in ASBMB and the annual meeting."

Dr. Hamm obtained her Ph.D. in Zoology in 1980 from the University of Texas-Austin and performed her post-

doctoral training at the University of Wisconsin-Madison from 1980-1983. Her initial research centered around circadian clocks and melatonin synthesis in the avian retina; her postdoctoral work investigated the role of transducin in visual transduction using blocking monoclonal antibodies. She held faculty appointments at the University of Illinois at Chicago School of Medicine and Northwestern University before moving to Vanderbilt in 2000 as the Earl W. Sutherland, Jr. Professor and Chair, Department of Pharmacology.

For more than 20 years, she has focused her research efforts on understanding G proteins, a class of cell membrane proteins that transfer signals across the cell membrane. G proteins play a key role in numerous physiological processes, particularly in the brain where many neurotransmitters use G-protein-regulated cascades to send their messages to the inside of the cell. This makes G proteins and receptors that interact with them targets of many pharmaceutical therapies.

Dr. Hamm's research has uncovered many details about how G proteins

work, how they turn on and off, and how they interact with receptor proteins and with the proteins that are next in the message chain. For her research accomplishments, Dr.

Hamm has received numerous awards, including the Glaxo Cardiovascular Discovery Award, two Distinguished Investigator Awards from the National Alliance for Research in Schizophrenia and Depression, the Faculty of the Year award from the University of Illinois College of Medicine, and the Stanley Cohen Award "For Research Bringing Diverse Disciplines, such as Chemistry or Physics, to Solving Biology's Most Important Fundamental Problems" from Vanderbilt University in 2003. She gave the Fritz Lipmann Lecture at the ASBMB Annual Meeting in 2001.

In addition to her research, Dr. Hamm has had the privilege of serving as mentor to 23 postdoctoral fellows and thesis advisor to 17 predoctoral students.

"Because G proteins are involved in so many physiological processes," says Dr. Hamm, "I continue to study a variety of cellular systems that span neuroscience, cardiovascular biology and drug discovery. More recently, my lab has begun to identify systems functions of G protein subunits within the context of integrated physiological responses and apply mathematical modeling approaches to understand these networks of G protein signaling pathways." ☞



Dr. Heidi E. Hamm

*"Broad investments in science have been an engine for better health and longer life in this country... A flat or decreasing research budget will erode the catalytic effects of the recent doubling on medical research breakthroughs."*



# ASBMB Publications...

## *Impacting Life Science*

The Journal of Biological Chemistry



*The  
most cited  
life science  
journal in  
the world.*

Molecular and Cellular Proteomics

*#1 Impact  
Factor in  
Proteomics.*



Biochemistry and Molecular Biology Education



*The leading  
biochemistry  
education  
journal.*

Journal of Lipid Research

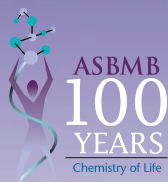
*#1 Impact  
Factor in  
Lipids.*



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# Celebrate: Reserve the Dates!

**T**he American Society for Biochemistry and Molecular Biology (ASBMB)/ *Journal of Biological Chemistry (JBC)* Centennial Celebration will be held in San Francisco, California, in conjunction with Experimental Biology on April 1-5, 2006. The Society will honor a century of achievements and contributions of the ASBMB and the *JBC* with an integrated and stimulating scientific program, and numerous special events during the meeting including a Centennial Opening Celebration, An Evening with the San Francisco Symphony, and A Taste of San Francisco.

Myriad award lectures will punctuate scientific sessions and social activities, including the opening Herbert Tabor/*JBC* Lectureship, the ASBMB Amgen Award, the ASBMB-Merck Award, the FASEB Excellence-In-Science Award, the new ASBMB Award for Exemplary Contributions to Education, the Avanti Award in Lipids, the William C. Rose Award, the Fritz Lipmann Lectureship, the Howard K. Schachman Public Service Award, and the Schering-Plough Research Institute Award.

At the heart of the Centennial Celebration is the scientific program organized by the ASBMB Program Planning Committee. The committee, co-Chaired by Dr. George M. Carman and Dr. Laurie S. Kaguni, has organized a dynamic and diverse scientific program that embraces the fundamental interest of the ASBMB membership, namely the "Chemistry of Life."

The chemical nature and dynamics of cellular structures and macromolecules will be addressed in the Molecular Structure Thematic Meeting. Themes include Macromolecular Structure and Dynamics (Chair: Andrej Sali, UCSF), Proteomics and Bioinformatics (co-Chairs: Michael Snyder, Yale University, and David Eisenberg, UCLA), Chemical



*2006 Meeting Organizers George M. Carman and Dr. Laurie S. Kaguni.*

Genetics and Drug Discovery (co-Chairs: Chaitan Khosla, Stanford University, and Kevan Shokat, UCSF), and Glycobiology and Extracellular Matrix (Chair: Carlos B. Hirschberg, Boston University).

The Genome Dynamics Thematic Meeting will address the central dogma of molecular biology through the themes of Genome Dynamics: Replication, Repair and Recombination (Chair: Laurie S. Kaguni, Michigan State University), Chromatin Structure, Expression, Regulation (Chair: Sharon Dent, University of Texas M. D. Anderson Cancer Center), RNA: Structure, Function, and Regulation (Chair: Alan Frankel, UCSF), and Protein Synthesis, Folding, and Turnover (Chair: William Merrick, Case Western Reserve University).

The synthesis, assembly, and metabolism of cellular membranes will be addressed in the Membrane Biogenesis Thematic Meeting, which includes the themes Biochemistry and Molecular Biology of Lipids (co-Chairs: George M. Carman, Rutgers University and Christian R. H. Raetz, Duke University Medical Center) and Structure, Function, and Biogenesis of Cell Membranes (Chair: William Dowhan, University of Texas-Houston Medical School).

Meetings on cell signaling have been very popular in recent ASBMB meetings and for the 2006 meeting, three themes have been organized for the Cell Signaling Thematic Meeting. These include Metabolic Regulation (Chairs: Richard W. Hanson, Case Western Reserve University and Daryl K. Granner, Vanderbilt University), Signaling in Growth and Development (Chair: Michael B. Yaffe, MIT), and Signaling in Aging and Disease (Chair: Natalie Ahn, University of Colorado).

Each theme in the four thematic groups hosts a symposium that will be held in morning or afternoon sessions on each of the four days during the meeting. Allied theme symposia will be scheduled at alternate, rather than concurrent times to offer attendees greater flexibility in planning their activities. Three short presentations are scheduled in each symposium that will be presented by individuals selected from submitted abstracts. In addition, attendees will have the opportunity to present their work in poster sessions that will be held during each day of the meeting.

The ASBMB continues its commitment at the Centennial Celebration to highlight the research of junior scientists at the undergraduate, graduate, and postdoctoral levels, and to promote their interactions at the meeting. In particular, the Education & Professional Development theme (Chair: J. Ellis Bell, University of Richmond) and the Minority Affairs theme (Chair: Juliette Bell, Fayetteville State University) will offer special programs involving a number of Nobel Laureates and prominent scientists. Future issues of *ASBMB Today* will present full-length articles describing the meeting themes, and present detailed information on the multifarious special events planned for the Centennial Celebration. ∞

# ASBMB 2006

April 1-5, 2006 • San Francisco, CA • In conjunction with EB2006

## ASBMB/JBC Centennial Celebration

Honoring 100 Years of Achievements and Contributions to Science

### Thematic Meetings

#### MOLECULAR STRUCTURE

*Macromolecular Structure and Dynamics*  
Andrej Sali, UCSF

*Proteomics and Bioinformatics*  
Michael Snyder, Yale University  
David S. Eisenberg, UCLA

*Chemical Genetics and Drug Discovery*  
Chaitan Khosla, Stanford University  
Kevan Shokat, UCSF

*Glycobiology and Extracellular Matrix*  
Carlos B. Hirschberg, Boston University Goldman School of  
Dental Medicine

#### GENOME DYNAMICS

*Genome Dynamics: Replication, Repair,  
and Recombination*  
Laurie S. Kaguni, Michigan State University

*Chromatin: Structure, Expression, and Regulation*  
Sharon R. Dent, University of Texas M. D. Anderson  
Cancer Center

*RNA: Structure, Metabolism, and Regulation*  
Alan D. Frankel, UCSF

*Protein Synthesis, Folding and Turnover*  
William Merrick, Case Western Reserve University

#### CELL SIGNALING

*Metabolic Regulation*  
Richard W. Hanson, Case Western Reserve University  
Daryl K. Granner, Vanderbilt University

*Signaling in Growth and Development*  
Michael B. Yaffe, MIT

*Signaling in Aging and Disease*  
Natalie G. Ahn, University of Colorado at Boulder

#### MEMBRANE BIOGENESIS

*Biochemistry and Molecular Biology of Lipids*  
George M. Carman, Rutgers University  
Christian R.H. Raetz, Duke University

*Structure, Function, and Biogenesis of Cell Membranes*  
William Dowhan, University of Texas-Houston  
Medical School

#### EDUCATION AND PROFESSIONAL DEVELOPMENT SYMPOSIA

J. Ellis Bell, University of Richmond

#### MINORITY AFFAIRS SYMPOSIA

Juliette Bell, Fayetteville State University

### 2006 Program Co-Chairs

George M. Carman, Rutgers University

Laurie S. Kaguni, Michigan State University

### Special Events

Centennial Opening Celebration

An Evening with the  
San Francisco Symphony

A Taste of San Francisco

### Award Lectures

Herbert Tabor/Journal  
of Biological Chemistry Lectureship

ASBMB Amgen Award

ASBMB Award of Exemplary Contributions to  
Education

ASBMB-Merck Award

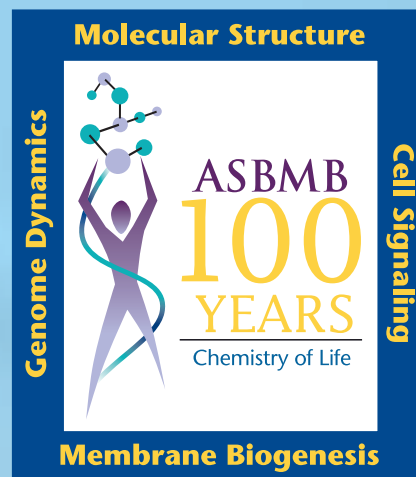
Avanti Award in Lipids

Herbert A. Sober Lectureship

Howard K. Schachman Public Service Award

Schering-Plough Research Institute Award

William C. Rose Award



[www.asbmb.org/meetings](http://www.asbmb.org/meetings)





# Meet the New Members

In addition to President-Elect Heidi Hamm, seven other members were elected to positions on the Council. Below are brief summaries of their backgrounds and their thoughts about ASBMB and the challenges it and the science community as a whole currently face.



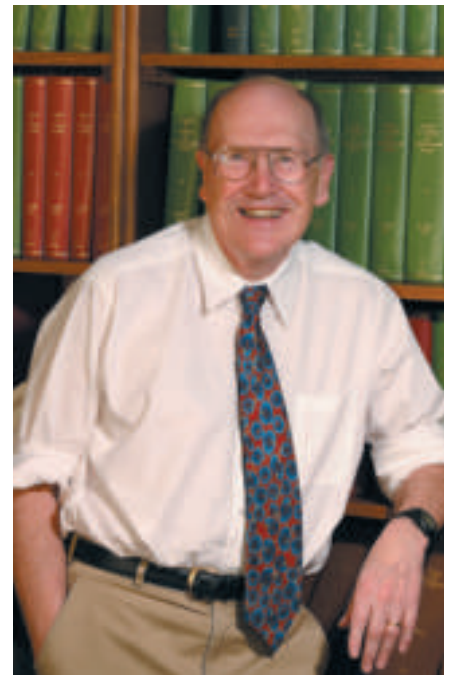
**Merle Olson**  
**Treasurer-Elect**

ASBMB's new Treasurer-Elect is Merle Olson, Dean of the Graduate School and Professor of Biochemistry at the University of Texas Health Science Center in San Antonio. Dr. Olson has been with UTHSC San Antonio since 1976, after spending 8 years at the University of Arizona College of Medicine. He received his B.A. from St. Olaf College in 1962, his Ph. D. in Biochemistry from the University of Minnesota, Minneapolis in 1966 and did a postdoctoral interval from 1966-68 in the Johnson Research Foundation at the University of Pennsylvania. Dr. Olson will take office as Treasurer on July 1, 2006.

The primary interests of his research laboratory for the past 37

years concerned the role of various lipid and peptide mediators in inflammatory or trauma responses in several tissues including the liver, pancreas and bone and the characterization and the regulation of several multienzyme complexes in complex biological/metabolic systems. Dr. Olson's research activities were funded by the National Institutes of Health and the Robert A. Welch Foundation; access to this funding enabled the educational/training process for 18 doctoral students and nearly 80 postdoctoral fellows. For 19 years Dr. Olson served as the Chair of the Department of Biochemistry at the Health Science Center at San Antonio prior to becoming the Dean of the Graduate School.

Dr. Olson's background and interests in issues financial as it pertains to the ASBMB have been instructed by significant intervals of service on the ASBMB and FASEB finance committees and the ASBMB Council. Additionally, and for what it is worth, Dr. Olson derives from a long family lineage of attorneys and tax collectors.



**Anthony E. Pegg**  
**Publications**  
**Committee Chair**

Anthony E. Pegg, the new Chair of the Publications Committee, is currently J. Lloyd Huck Professor of Molecular and Cell Biology and Evan Pugh Professor of Cellular and Molecular Physiology at Pennsylvania

# of the ASBMB Council

State University College of Medicine. Dr. Pegg has published more than 500 papers in his two fields of interest, which are polyamine synthesis and function and the repair of alkylated DNA. He has spent the last 30 years in the Department of Cellular and Molecular Physiology at the Pennsylvania State University College of Medicine. He has been a member and chairman of NIH study sections and has been continuously funded by the NIH for both research interests since coming to Pennsylvania State University College from the University of London. He has been a member of numerous editorial boards, and has organized several scientific meetings including Gordon Research Conferences on both polyamines and DNA repair.

"I think that the publications are a major achievement of the ASBMB," says Dr. Pegg. "I am sure all of the membership is very grateful for the huge amount of work contributed to the publications by the editors, members of the Editorial Boards and others associated with them. The ASBMB has pioneered the rapid movement of scientific journals to electronic publication and the development of tools to provide researchers and others with more rapid access to critical information. The success of the publications is essential to the ASBMB's mission and finances. I hope to help the publications committee to continue to support and provide advice as needed on how to maintain the outstanding record of the ASBMB in publications."



**Suzanne Pfeffer**  
Council member

New Council member Suzanne Pfeffer says she fell in love with Biochemistry as an undergraduate at U.C. Berkeley because it satisfied her interest in understanding the molecular basis of human physiology. After a PhD at UCSF and postdoctoral training at Stanford, she joined the Stanford Biochemistry Department Faculty in 1986 and begins her eighth year as Chairman of that Department.

"With the arrival of genomics and developmental biology during the previous decade, biochemistry lost a great deal of its perceived sex appeal," noted Dr. Pfeffer. "Now, with renewed recognition of the importance of understanding metabolism, and broad interest in the molecular basis of disease, Biochemistry returns to the fore. If we are to understand molecular pathways comprised of hundreds of players, and discover new drugs to target pathways more specifically, we must support the teaching, training and practice of Biochemistry. The ASBMB has long recognized the importance of its youngest members—they represent our future. I will work to ensure that the activities we support nurture Biochemists in training—at

the undergraduate, graduate and post-doctoral levels."

Pfeffer was President of the American Society for Cell Biology in 2003 and is the recipient of numerous awards including a merit award from the NIDDK. She has recently become an avid scuba diver, and was 60 feet underwater off the coast of Thailand during the tsunami of 2004. Lucky for Pfeffer, the 100-foot boat she was living on was in relatively deep water and far enough from shore so that she only experienced an unusually "high current" dive. The next morning, her ship rescued six stranded, Thai park rangers from a small, devastated island and ferried them to a Thai Navy vessel anchored off the Similan Islands. Two days later, the boat was able to return to its dock on Phuket Island where tourist evacuation was well underway.



**Linda Pike**  
Council member

New Council member Linda Pike says, "Of all the activities sponsored by the ASBMB, two stand out in my mind

as deserving of our attention in the immediate future: the national meeting and our lobbying efforts on behalf of scientists, and in particular, biochemists. The national meeting is important because it represents an opportunity for biochemists to get together and participate in a multi-disciplinary examination of issues that cut across all sub-disciplines in our field. The introduction of 'themes' within the meeting has provided an organizing principle for this broad-ranging meeting. I would like to work toward a greater engagement of our membership in defining the themes and setting the agenda for the national meeting. The meeting should reflect the interests of our membership and serve their need for a forum for their work that is broadly attended by their colleagues.

"In this age of limits on discretionary spending at the federal level," Pike added, "it is more important than ever that ASBMB play a leadership role in ensuring that biomedical research is supported at a level that will allow adequate funding for investigators at all career stages and will maintain our competitiveness as a nation in this arena. In addition, ASBMB needs to work to ensure that governmental policies are established based on the best possible science, not on ideological grounds."



**Bruce Alberts**  
**Nominating Committee**

Elected to the Nominating Committee was Bruce Alberts, President of

the National Academy of Sciences and Chair of the National Research Council since 1993, he is a respected biochemist recognized for his work in biochemistry and molecular biology. He is noted particularly for his extensive study of the protein complexes that allow chromosomes to be replicated. His term as NAS president ends in 2005.

Born in 1938 in Chicago, Illinois, Alberts graduated from Harvard College in Cambridge, Massachusetts, with a degree in biochemical sciences. He earned a doctorate from Harvard University in 1965. He joined the faculty of Princeton University in 1966 and after ten years was appointed professor and vice chair of the Department of Biochemistry and Biophysics at the University of California, San Francisco (UCSF). In 1980, he was awarded the honor of an American Cancer Society Lifetime Research Professorship. In 1985, he was named chair of the UCSF Department of Biochemistry and Biophysics.

For the period 2000 to 2005, Alberts is the Co-chair of the InterAcademy Council, a new advisory institution in Amsterdam governed by the presidents of the science academies of 15 different nations, designed to provide science advice to the United Nations and other international organizations. He has served in different capacities on a number of prestigious advisory and editorial boards, including: as chair of the Commission on Life Sciences, National Research Council; on the advisory board of the National Science Resources Center, a joint project of the National Academy of Sciences and the Smithsonian Institution working with teachers, scientists, and school systems to improve teaching of science; as well as on the National Academy of Sciences' National Committee on Science Education Stan-

dards and Assessment. Until his election as President of the Academy, he was president-elect of ASBMB. Alberts is one of the original authors of *The Molecular Biology of the Cell*, the leading advanced textbook in this field and now in its fourth edition. His most recent text, *Essential Cell Biology*, is intended to present this subject matter to a wider audience.



**Ruma Banerjee**  
**Publications Committee**

Newly elected to the Publications Committee is Ruma Banerjee, the George Holmes University Professor and Willa Cather Professor (emerita) of Biochemistry at the University of Nebraska. She is the Director of an NIH-NCRR funded Redox Biology Center. Her research interests are in the area of redox enzymology, homocysteine biochemistry and inborn errors of B12 metabolism.

Dr. Banerjee views the excellent quality of the publications supported by the ASBMB as one its major contributions to the life sciences community. The pervasiveness of science and technology in every aspect of society increases the urgency for enhancing scientific literacy, for public access to the literature and more effective communication between the specialists and the lay audience. She views the discussions in the community about the changing culture of publications and access as being timely and looks forward to contributing to these as a member of the publications committee.





**Robert Rhoads**  
**Publications Committee**

It is an honor to be elected to the Publications Committee of the ASBMB, and I wish to express my thanks to the society's membership for electing me. I am a big fan of the ASBMB's publications and consider the JBC to be the gold standard. I co-authored my first JBC paper in 1971 and my most recent one in 2005, so I have lived with the JBC for most of my scientific career. My post-doctoral mentor was Bob Schimke, who was an Associate Editor of the JBC at the time. Consequently, I was asked to give opinions about submitted manuscripts as early as 1971. I am now in my fourth five-year term as a JBC Editorial Board member, so reviewing manuscripts for the Journal has been a nearly continuous part of my scientific career as well. (During my first term, someone had told me that one could be asked to serve on the Editorial board for only two terms, so I gladly accepted my second term, but this turned out to be a cruel fiction.) Why do I review 50 plus papers a year? Speaking from an altruistic standpoint, the JBC is one of the pillars of biochemistry and I want to help support it. Speaking selfishly, I want the JBC to be there when I am ready to publish papers from my lab. I greatly appreciate the crisp and fair turnaround of my submitted manuscripts and try to return the favor for other submitting authors. There is absolutely no comparison between the reviewing process of the JBC and that of other major biochemical and molecular biological journals with regards to speed, fairness, rigor, evenhandedness, predictability, and consistency. In addition to the review process, the JBC has led the way in numerous areas of scientific publication: electronic submission of manuscripts, free access to published articles, putting the entire opus of the Journal on-line, making articles available immediately after acceptance, etc. I have found that participating in the activities of high quality organizations is a pleasure (the converse is true as well). I therefore look forward to working with the ASBMB staff and other members of the ASBMB publication committee to 'keep up the good work.' ☺



## **DESPERATELY SEEKING!!**

### **Seeking What? Who?**

#### **Seeking Your Memories and Reminiscences of your years as a member of The American Society for Biochemistry and Molecular Biology!**

As part of the 2005–06 Centennial Celebration of ASBMB and the *Journal of Biological Chemistry* (JBC) we are asking you to tell us what it was like:

- ✦ At the Atlantic City meetings.
- ✦ When you gave your first lecture at an ASBMB Annual Meeting.
- ✦ Serving as an ASBMB officer or Council member.
- ✦ Getting your first paper accepted—or rejected—by the JBC.
- ✦ Being a post doc in that first lab.
- ✦ Running your own lab.
- ✦ Great teachers and professors and what you learned from them.
- ✦ The first ASBMB meeting you attended.
- ✦ Students you taught or went to class with and their successes in research.
- ✦ What ASBMB membership has meant for you and what it can mean to today's undergrads and postdocs.

These are just some of the things we are looking for to help us in celebrating our Centennial and to tell your fellow members and potential new members about what ASBMB means in terms of camaraderie, research, and science's contribution in making this a healthier and happier world.

Please send your comments and any photos you have—particularly those from years past—via email to John D. Thompson, Editor, *ASBMB Today*, at [jthompson@asbmb.org](mailto:jthompson@asbmb.org).

# Careers In Industry: Some Pointers and Comments For Considering Industry Positions

**T**hose attending the Careers in Industry session at the ASBMB Annual Meeting in San Diego had the opportunity to get some informed advice on job hunting from scientists working in industry. In addition, two experts in the human resources field. John Dowd, Manager of Human Resources at BD Technologies, and Tom Koellhoffer of T.J. Koellhoffer & Associates, an executive search firm that specializes in technology-oriented search assignments, provided the answers needed to a slate of questions pertinent to today's job hunters.



*Attendees at both the Careers in Industry and Women's Mentoring Session found career advice invaluable.*

## **What would industry like to find in a candidate?**

Commercialization of products in a milestone-driven environment is the ultimate goal in industry. We do like to find the candidate who is able to transcend some of the differences between the university and industrial research environment.

## **What skill sets are useful?**

While technical research expertise is critical, we assume a candidate already possesses technical excellence, as well as skills in project management and leadership. BD also evaluates candidates against a broad range of "competencies" correlated with success. A few of these traits are categorized as: "Promotes an Inclusive Work Environment," "Teamwork," and "Managing, Leading and Developing Others."

## **Should you respond to ads? Are "random" or "cold call resumes" useful?**

It is always good to get the word out that you're going to become available for employment and it is best to do so several months prior to your availability date. Always respond to ads that are of interest to you and be sure to name the job you're interested in being considered for in a letter of introduction. Try to get the name of the hiring manager or HR person who is filtering the responses, and ask if there is any further information you can provide about your background. Follow up via e-mail on a periodic basis.

## **Should you use a headhunter?**

Every good reference library should have a copy of the directory of executive

recruiters (ISBN: 1-885922-64-7). This is a nationwide directory of recruiting firms that lists firms by size, geographic location, and recruiting specialty. Look for firms listing specialties in your field and try to develop a conversational relationship with the recruiter.

## **Are career objectives really useful on a CV or is that better placed in a letter?**

The general-purpose CV probably isn't the place to state one's career objective. A well-crafted cover letter that addresses the requirements of a specific opportunity is always advisable, and a little up-front research on the company's mission statement can go a long way to helping a candidate craft an eye-catching cover letter that states career objectives in the context of the company's stated mission.

# Structure of Key Protein in Innate Immune Response Solved

By Nicole Kresge, Staff Science Writer

**What types of jobs, experiences, benefits, and employment stability are found in industry?**

At BD Technologies, as one example, we hire researchers from a variety of scientific/engineering disciplines, and at the BA/MS/PhD levels.

The industrial researcher can expect to be paid at a rate more competitive than academia but both would offer a comprehensive benefits package. However, with regard to employment stability, no industry or company can offer guarantees to anyone.

**What are some pros and cons of working in industry as compared to academia?**

In academia, the researcher's work is dependent on the funding, with a fair amount of freedom in the choice of projects. In industry, if the company decides to terminate a particular project, funding is cut and the research halted.

Publishing in industry varies, depending on the company, research project and research position. Usually however, the concept of "publish or perish" is not characteristic of industry. ❧

*The questions were posed and edited by Marilee Benore Parsons, Associate Professor of Biochemistry at the University of Michigan, Dearborn, who organized the Careers in Industry session.*

**T**he cellular receptor CD14 plays an extremely important role in immunity—when bacteria invade the body, it recognizes molecular components of the pathogen and initiates the cellular defense mechanisms. Now, in a report published as a *Journal of Biological Chemistry* "Paper of the Week," scientists in Korea announced their elucidation of three-dimensional structure of CD14 and showed how it is perfectly suited to bind to certain bacterial products (2005, 280: 11347-11351).

The innate immune system uses the CD14 receptor protein to recognize several microbial and cellular products including lipopolysaccharide (LPS), a glycolipid found on the outer membrane of certain bacteria. Once CD14 binds to LPS or another ligand, it presents the molecule to other proteins which initiate a strong pro-inflammatory response that stimulates host defenses.

"Macrophages and monocytes can recognize distinct structural patterns in various molecules from pathogenic microorganisms," explains Dr. Jie-Oh Lee of the Korea Advanced Institute of Science and Technology. "LPS is the most famous and probably the most important inducer of the innate immune response."

Dr. Lee and his colleagues solved the three-dimensional crystal structure of CD14, providing crucial insights into how the receptor binds to its ligands. "Our structure shows that CD14 has a

large hydrophobic pocket near its amino terminus," says Dr. Lee. "We propose that this pocket is the main binding site for LPS because previous biochemical studies demonstrate that amino acid residues comprising the pocket are critical for LPS binding. Most, if not all, of the CD14 ligands compete with LPS for CD14 binding. Therefore, they probably share the same binding pocket with LPS."

Ligands other than LPS can be accommodated in the pocket due to its large size, the flexibility of its rim, and the multiple grooves available for ligand binding. The researchers also discovered that mutations that interfere with LPS signaling cluster in a separate area near the pocket suggesting that the areas around the pocket are important in LPS transfer.

Not only do these findings shed light on how cells recognize pathogens, they also may also lead to the development of drugs to help treat septic shock, an often fatal systemic bacterial infection that is triggered by LPS.

"Pharmaceutical companies have tried to develop anti-septic shock agents for a long time without clear success," explains Dr. Lee. "Since LPS is an important inducer of septic shock, blocking LPS receptors such as CD14 are among the most important targets. Our structure shows the shape of the LPS binding pocket of CD14. Now, drug developers will have better chance to design a molecule that will complement the shape of the pocket." ❧



# Signaling Protein Builds Bigger, Better Bones in Mice

**Some genetically engineered “supermice” with four times the normal bone mass may aid the search for osteoporosis drugs. A new study shows that their bone strength is aided by a signaling protein that stimulates the growth of bone cells and keeps fat tissue from developing.**

**L**eaping tall buildings in a single bound may be out of the question, but the genetically engineered “supermice” in Ormond MacDougald’s\* laboratory at the University of Michigan Medical School are definitely stronger than average. With bone mass up to four times greater than ordinary mice, these research animals could hold the secret to new drugs for preventing or treating osteoporosis and other human diseases.

The secret appears to be a secreted signaling protein called Wnt10b. Known to inhibit the development of adipose tissue in mice, Wnt10b also stimulates the growth of bone cells, according to a new study that was published February 21 in the Online Early Edition of the *Proceedings of the National Academy of Sciences*.

“High levels of Wnt10b expression in bone marrow directly increased bone mass and density in our experimental mice,” says Ormond A. MacDougald, Associate Professor of Molecular and Integrative Physiology in the U-M Medical School. “This is the first identification of a specific signaling protein in the Wnt family that regulates bone formation.”

Wnt10b is one of a family of 19 related proteins that regulate the complex changes that take place as an embryo develops. One step in this process determines the fate of primitive cells called mesenchymal stem cells.

“In bone marrow, mesenchymal stem cells have the potential to become either fat cells called adipocytes or bone-forming cells called osteoblasts,” MacDougald says. “In adult animals, including humans, there’s a reciprocal relationship between bone and marrow fat. Our research indicates that Wnt10b’s signal blocks the fat cell pathway and stimulates the osteoblast pathway, which means less fat and more bone.”

To study the effect of Wnt10b gene expression on tissue development, MacDougald’s research team created an artificial sequence of DNA called a transgene linking Wnt10b to the FABP4 promoter, which is expressed in fatty tissue and in bone marrow. U-M scientists injected the transgene DNA into fertilized mouse eggs, and then bred mice that inherited the new gene to create the transgenic animals used in their research.

Kurt D. Hankenson, a U-M Assistant Professor of Orthopedic Surgery and Laboratory Animal Medicine, and

Christina N. Bennett, a U-M graduate student and first author of the PNAS paper, used micro-computerized tomography to scan femur bones from mice that inherited the FABP4-Wnt10b gene combination and compare them to scans from normal mice.

The two discovered that femurs from the transgenic mice had almost four times as much bone, and were mechanically stronger than femurs from control mice.

“It was a very exciting moment the first time we saw scans showing increased bone mass in transgenic mice,” Bennett says. “Visually, we don’t see any abnormal side-effects in bone from the transgenic mice. Its development and morphology appear to be completely normal.”

Loss of bone often develops with aging, but Wnt10b transgenic mice maintained their high levels of bone mass up to the ripe old age of 23 months, when the study was concluded.

Estrogen deficiency in females is a common cause of bone loss. When U-M scientists removed ovaries from normal mice in the study, they developed reduced bone mineral density and bone volume. But the Wnt10b females

*Continued on next page*

# Antibodies: Two Are Better Than One

**C**ancer patients may one day benefit from treatment with mixtures of customized antibodies. In a study published in the February 8, 2005, *Proceedings of the National Academy of Sciences*, a team of Weizmann Institute scientists have demonstrated how the right combination might form a web that destroys the cancer cell's communication network, ultimately demobilizing the cell.

Three decades of intensive cancer research led to the identification of a family of receptors, known as HER, that sit antenna-like on the outside of the cell membrane and are implicated in certain types of cancer. A team of researchers under Dr. Yosef Yarden, Dean of the Weizmann Institute's Feinberg Graduate School and a professor in the Institute's Biological Regulation Department, had previously found that, under certain conditions, the HER2 receptor amplifies the growth signal received by the cell. Dr. Yarden and Dr. Michael Sela,\* former president of the Weizmann Institute of Science,

and currently a professor in the Institute's Immunology Department, teamed up to create a strategy for the customization of antibodies that work independently to engage these cancer-specific receptors and shut down the attendant signaling network. The study was carried out in cooperation with researchers from Targeted Molecular Diagnostics, Westmont, Illinois.

In experiments conducted in vitro and in lab mice, the researchers exposed the cancer cells to two different antibodies that link up to HER2 receptors. In a synergistic action, the antibodies were shown to cooperate rather than compete for distinctly different attachment points on the architecture of the receptors, resulting in the assembly of a large molecular scaffolding between the receptor towers. The interlocking system grips and pulls the receptors towards each other until they collapse inward like overloaded laundry lines. The stressed receptors become engulfed by the cell, and thus cease signaling. In response, the cell halts growth and,




Dr. Michael Sela

Dr. Yosef Yarden

when chemotherapy is used in combination with the immunotherapy, it dies.

According to Sela, the study sheds light on the synergy at work in the antibody-receptor therapy system. The results demonstrate that with the right combination of antibodies, receptor degradation is accelerated: it's more than three times as effective as a single antibody in inhibiting HER2 signaling.

"Understanding how HER receptor degradation works could enhance weak therapeutic efficacy, as well as provide ways to overcome inherent or acquired resistance to cancer treatment," says Yarden. 

\*ASBMB member.


*Continued from previous page*

showed no bone loss after their ovaries were removed. "Because the transgenic mice have more trabecular bone, or bone within the marrow cavity, to begin with, they are doubly protected from the usual loss of bone density due to estrogen deficiency," Dr. MacDougald noted.

To confirm that Wnt10b was the key to increased bone formation, Bennett and Hankenson scanned bones from a strain of laboratory mice that didn't have a gene for Wnt10b. Lacking the ability to produce Wnt10b protein in bone marrow cells, these mice had 30 percent lower bone volume and bone mineral density than normal mice.

Using PCR analysis of Wnt10b-expressing cells in bone marrow, MacDougald found high levels of collagen and alkaline phosphatase, and expression of transcription factors that turn on genes involved in bone formation.

Bennett discovered another important clue when she found that Wnt10b expression shuts down activity of a gene called PPAR-gamma, which is required for the development of adipocytes or fat cells. "It suggests that Wnt10b's role may be to block PPAR-gamma, shifting development from the adipocyte pathway to the osteoblast pathway," she says.

In future research, MacDougald hopes to unravel the molecular mechanism for Wnt10b's bone-building effect. "It's not only an important scientific question, it's important to the understanding and potential treatment of osteoporosis and other human diseases," he says. "Right now, there is a need for drugs on the market to stimulate new bone formation. Being able to activate Wnt signaling in bone marrow and osteoblasts might help prevent the loss of bone associated with aging or menopause." 

\*ASBMB member

by John D. Thompson, Editor

## Clinical Trials Decreasing in U.S. But Increasing Overseas

**T**he drug industry is conducting significantly fewer clinical trials of potential new medicines now than it did in 2001, and the number of principal investigators leading those efforts in the United States has declined even more steeply, according to a study by a Tufts think tank on drug industry issues.

Using information collected by the Food and Drug Administration, researchers with the Tufts Center for the Study of Drug Development found that, after a major expansion during the 1990s, the number of drug industry-sponsored clinical trials leveled off in 2000 and began to drop after 2002. Study author Kenneth A. Getz told the *Washington Post* that the drop was primarily due to the cancellation of trials entering their final phase.

During that same period, the number of principal investigators leading

clinical trials in the U.S. declined by 11 percent, while the number of investigators working on FDA-approved trials abroad rose 8 percent, indicating that the outsourcing of drug research is beginning to accelerate. "The big message here is that the decline in principal investigators is not solely a function of the short-term decline in clinical projects," Getz said. "If we continue to see this in the longer term, it could diminish our ability to innovate."

The study also looked at the economics of clinical trials, which are becoming less lucrative for doctors and researchers, and found that more clinical trials are being conducted at cheaper sites abroad, and in southern states rather than in more expensive northern states. Between 1994 and 2004, the proportion of principal investigators work-

ing in the South grew by nearly 20 percent, to more than 40 percent of the nation's total. During the same time, the proportion active in the Northeast declined from 23 to 19 percent of the total.

The principal investigators studied are board-certified physicians hired by drug companies to conduct clinical trials that test the safety and efficacy of medications in development. The study found that the number of U.S. investigators peaked at 25,000 in 2001 and was less than 21,000 by 2003.

The number of U.S. sites conducting clinical trials dropped from some 51,000 in 2001 to 48,000 in 2003. During that same period, the number of FDA-approved investigational drug studies in all phases of research rose from about 3,900 to 4,500—but less were being conducted in the U.S.

## MIT launches Center for Biomedical Innovation

This summer the MIT Center for Biomedical Innovation (CBI) is beginning to develop ways to more efficiently and safely move advances in the life sciences from the laboratory into actual public health use. The center will build on MIT's special strengths across the disciplines of science, engineering and management, and will also draw on the expertise of nearby Harvard Medical School. "At MIT, we have a tradition of collaborating across disciplines to work on important challenges. This is an industry under siege, and it is reacting enthusiastically to CBI," said Richard Schmalensee, dean of the MIT Sloan School of Management. "We don't necessarily promise to

be an industry ally, but we offer the promise of neutral ground and unbiased expertise."

Beginning with a two-day "All Stakeholder Summit" set for June 16-17, the center aims to create a "safe harbor" in which major players across the biomedical spectrum—from medical researchers to federal regulators and payers, to experts in finance and marketing—will be able to better appreciate each other's concerns and needs. Serious challenges created by the recent recalls of widely utilized pharmaceutical products make it especially important to break through traditional "silo thinking," said Dr. Frank Douglas, the former Executive Vice President

and CEO of Aventis SA, who will lead the new center.

"It is very clear to me that this industry faces serious issues," said Douglas. "The productivity of large pharmaceutical innovation has decreased. We lack the ability to properly predict the side effects of new compounds, and we don't have good ways to monitor and assess them once they are in the market. Pricing models have become untenable. So has the 'blockbuster' mentality. Across the board, a lot of old models really need to be examined, and CBI is where it can happen. We will bring together stakeholders with the common objective to find solutions that will transform the industry."



## China Offers Research Grants to Bring Overseas Chinese Home

China is seeking to attract scientific talent from Chinese communities in other countries by offering long-term grants to researchers taking up positions in China. The offers of annual grants of one million yuan (US\$120,000) for up to four years, was launched in April by the National Natural Science Foundation of China (NSFC), the country's main funder of basic research. NSFC has so far placed no limit on the number of grants that will be awarded.

To be eligible, applicants must be 'overseas Chinese' — ethnically Chinese but with foreign citizenship. In addition to younger than 45, they must have a doctorate and have been

offered a position in a Chinese university or research institute. Scientists taking up posts in Hong Kong and Macao will not be eligible for funding.

Applicants should be leading scientists in their area of research, and must do full-time research in China during the funding period. Duan Yibing, a senior researcher with the Institute of Science Policy, part of the Chinese Academy of Sciences, says the funding

program shows that China is being increasingly active and practical in attracting international talent.

Considering the low cost of doing research in China, the amount of grant money is considered likely to attract many overseas Chinese. To ensure that returning researchers stay in China, it is also considered likely that the government will adopt strict measures to ensure that the returnees remain in China.

## Bayer Deal: A Major Customer Win for Medidata

A battle to sign a large new clinical technology customer has ended with

Bayer choosing a New York technology concern to supplant Bayer's in-house, laptop-based technology for gathering and managing data in clinical trials.

"Bayer HealthCare views electronic clinical data management as an important component of our global focus on increasing clinical trial capacity while managing costs through standardizing on a common platform," said Johann Prove, head of data acquisition and data management. "A cross-functional team evaluated our alternatives, both internal and external, and concluded that Medidata's Rave solution provided all markets with the most adaptable and extensive capabilities to drive business value and common processes globally."

Bayer was one of the first companies to develop its own software for clinical trials. The architect of its electronic data capture (EDC) system, Sylva Collins, subsequently departed to do it again at Novartis with even more impressive results.

## UNH Grant Helps Firm Developing Instruments To Speed Up Drug Development Process

The University of New Hampshire's Industrial Research Center (NHIRC) has provided a grant to a new company focused on developing instruments designed to speed the analysis of proteins, which scientists believe will have a profound impact on the drug development process. The \$49,990 grant was awarded to Sentry BioScience Inc., with locations in Nottingham, New Hampshire and Knoxville, Tennessee.

Sentry is focused on developing low-cost instruments that have the potential to accelerate the analysis of proteins, and the market for proteomics instrumentation is expected to grow from \$720 million in 2001 to \$1.7 billion by 2006, an 18 percent annual growth rate. Sentry is collaborating with Tom Laue, Profes-

sor of Biochemistry and Molecular Biology, and the Center to Advance Molecular Interaction Science (CAMIS).

The company's initial focus on proteomics takes advantage of microfluidic technology, prototypes of instruments and a detection system that has a patent pending. Sentry also is in the process of raising \$15 million from venture capitalists to commercialize integrated microfluidic methods and instruments for biological applications, which will streamline the drug testing process, shorten the time to receive results and reduce the cost per drug test.

Since 1992 the NHIRC has brought \$225 million in new sales and more than 3,170 new jobs to the state.

# The ASCB 45th Annual Meeting

## December 10-14, 2005, San Francisco

Zena Werb, President ■ Linda Hicke, Program Chair ■ Aaron Straight, Local Arrangements Chair

### KEYNOTE SYMPOSIUM

#### Saturday, December 10 Big Science, Little Science

Linda Buck, Fred Hutchinson Cancer Research Organization/HHMI  
Clare Fraser, The Institute for Genomic Research

### SYMPOSIA

#### Sunday, December 11

##### Quantitative Studies of Cell Signaling Networks—8:00 am

Marc Kirschner, Harvard Medical School  
Garry Nolan, Stanford University  
Peter Sorger, Massachusetts Institute of Technology

##### Prokaryotic Origins of the Cytoskeleton—10:30 am

Harold Erickson, Duke University Medical Center  
Christine Jacobs-Wagner, Yale University  
Dyche Mullins, University of California, San Francisco

#### Monday, December 12

##### Wiring the Nervous System—8:00 am

Hollis Cline, Cold Spring Harbor Laboratory  
Anirvan Ghosh, University of California, San Diego  
Yishi Jin, University of California, Santa Cruz/HHMI

##### Adapting to Stress: Spotlight on Organelles—10:30 am

Tom Rapoport, Harvard Medical School/HHMI  
David Ron, New York University School of Medicine  
Richard Yule, National Institute of Neurological Disorders & Stroke/NIH

#### Tuesday, December 13

##### Reprogramming Cell Fate—8:00 am

Helen Blau, Stanford University  
John Gurdon, Wellcome Trust/Cancer Research UK  
Markus Grömppe, Oregon Health & Science University

##### Host-Pathogen Interactions—10:30 am

Pascale Cossart, Institut Pasteur, Paris  
David Roos, University of Pennsylvania  
Wesley Sundquist, University of Utah

#### Wednesday, December 14

##### Cell Growth & Division—8:00 am

Ernst Hafen, Universität Zurich  
Tim Hunt, Cancer Research UK  
Yixian Zheng, The Carnegie Institution of Washington/HHMI

### MINISYMPOSIA

#### Building Sensory Networks

Herwig Baier, University of California, San Francisco  
Gero Miesenboeck, Yale University School of Medicine

#### Cargo Sorting & Vesicular Transport

Robert Piper, University of Iowa  
Anne Spang, Max Planck Institute, Tuebingen

#### Cell Biology of the Synapses

David Colman, McGill University  
Janet Richmond, University of Illinois

#### Cell Migration/Motility

Peter Friedl, University of Würzburg  
Carole Parent, National Cancer Institute/NIH

#### Chromatin Dynamics

Terumi Kohwi-Shigematsu, Lawrence Berkeley National Laboratory  
Danesh Moazed, Harvard Medical School

#### Coordinating Adhesion & Signaling

Avri Ben-Ze'ev, Weizmann Institute of Science  
Vania Braga, Imperial College London

#### Coordination of Cytoskeletal Networks

William Bement, University of Wisconsin, Madison  
Talila Volk, Weizmann Institute of Science

#### Cytoskeletal Dynamics in Living Cells

Velia Fowler, The Scripps Research Institute  
Steven Gross, University of California, Irvine

#### Cytoskeletal Molecular Motors

Susan Gilbert, University of Pittsburgh  
Margaret A. Titus, University of Minnesota

#### Differentiation & Cancer

John Cleveland, St. Jude Children's Research Hospital  
Xi He, Children's Hospital, Boston

#### Epithelial Morphogenesis & Polarity

David Bilder, University of California, Berkeley  
Heike Fölsch, Northwestern University

#### Extracellular Matrix & Signaling

Josephine Adams, The Cleveland Clinic Foundation  
Joanne Murphy-Ullrich, University of Alabama at Birmingham

#### Formins & Arp2/3: Regulators of Actin

Henry Higgs, Dartmouth Medical School  
Matthew Welch, University of California, Berkeley

#### Intermediate Filaments

Ueli Aebi, University of Basel  
Bisrh Omary, Palo Alto VA/Stanford University

#### Intersection of Signaling & Trafficking: Small GTPases

Jim Casanova, University of Virginia  
Harry Mellor, University of Bristol

#### Lipid-Mediated Signals

Antonella DeMatteis, Consorzio Mario Negri Sud  
Julie Saba, Children's Hospital/Oakland Research Institute

#### The Membrane Cytoskeleton

Vann Bennett, Duke University Medical Center/HHMI  
Elizabeth McNally, University of Chicago

#### Mitosis & Meiosis

Dean Dawson, Tufts University  
William Earnshaw, University of Edinburgh

#### Neuronal Polarity & Axo-Dendritic Growth

Lorene Lanier, University of Minnesota  
Liqun Luo, Stanford University

#### Nuclear Compartments

Joseph Gall, The Carnegie Institution of Washington  
Angus Lamond, University of Dundee

#### Nuclear Envelope Functions

Valérie Doye, Institut Curie, Paris  
Howard Worman, Columbia University College of Physicians & Surgeons

#### Organelle Dynamics

David Chan, California Institute of Technology  
Andreas Mayer, University of Lausanne

#### Pathogens Co-opting Host Cell Functions

Marcia Goldberg, Massachusetts General Hospital  
Michael Way, Cancer Research UK

#### Protein Folding & Quality Control

Judith Frydman, Stanford University  
Jonathan Weissman, University of California, San Francisco/HHMI

#### Protein Misfolding & Disease

William Balch, The Scripps Research Institute  
Harry Orr, University of Minnesota

#### Regulating Intercellular Junctions

Andrew Kowalczyk, Emory University School of Medicine  
Yoshimi Takai, Osaka University

#### Regulation of the Cell Cycle

Alison Lloyd, University College London  
Peter Sicinski, Dana Farber Cancer Institute

#### RNA Silencing Mechanisms

Bonnie Bartel, Rice University  
Greg Hannon, Cold Spring Harbor Laboratory

#### Signaling in the Immune System

Jason Cyster, University of California, San Francisco/HHMI  
Michael Dustin, New York University School of Medicine

#### Signaling in 3D Environments

Jeffrey Hubbell, Swiss Federal Institute of Technology  
Senthil Muthuswamy, Cold Spring Harbor Laboratory

#### Stem Cell Niches

David Scadden, Massachusetts General Hospital  
Allan Spradling, Carnegie Institution of Washington/HHMI

#### Trafficking Proteins & Complexes

James Hurley, National Institute of Diabetes & Digestive & Kidney Diseases/NIH  
Sean Munro, MRC Laboratory of Molecular Biology, Cambridge

For more information, contact the ASCB at 301-347 9300; [ascbinfo@ascb.org](mailto:ascbinfo@ascb.org) or [www.ascb.org](http://www.ascb.org)

# Career Opportunities

## PLANT BIOCHEMICAL GENETICS, ASSISTANT PROFESSOR in BIOCHEMISTRY

### University of Nebraska-Lincoln

A joint, tenure-track Assistant Professor in Biochemistry position is currently available in the Plant Science Initiative and Department of Biochemistry at the University of Nebraska-Lincoln. The position is 80% research/20% teaching. As part of a newly emerging Nutritional Genomics Center, the successful candidate is expected to maintain a vigorous research program focused on biochemical genetics of plants. Research may include plant secondary metabolism, metabolic profiling, nutritional genomics, and genetic regulation of plant metabolism. Teaching responsibilities include teaching one graduate or undergraduate level course annually in a relevant area, and mentoring students. A Ph.D. and post doctoral experience in plant genetics, biochemistry or related field is required. Salary is commensurate with qualifications and experience. Review of applications will begin June 20, 2005, and continue until the position is filled or the search is closed. Applicants should go to <http://employment.unl.edu/> and complete the Faculty/Administrative Information form and then send complete application file, consisting of a statement of research interests, CV and arrange for three letters of recommendation be sent, to Search Committee Chair, Assistant Professor Biochemical Genetics, N300 Beadle Center for Genetics Research, University of Nebraska-Lincoln 68588-0660. UNL is committed to a pluralistic campus community through affirmative action and equal opportunity and is responsive to the needs of dual career couples. We assure reasonable accommodation under the Americans with Disabilities Act. Contact Dr. Sally Mackenzie at (402) 472-6997 or [smackenzie2@unl.edu](mailto:smackenzie2@unl.edu) for assistance.

## FACULTY POSITION

### LSU Health Sciences Center

The Department of Molecular & Cellular Physiology invites applications for a tenure track position at the level of Assistant/Associate Professor. Successful applicants will be expected to develop an independent, nationally funded research program. Research areas are open, but preference will be given to individuals with an interest and record of achievement in cardiovascular science, inflammation and/or oxidative stress. Information about the departmental research focus is available at <http://www.shreveportphysiology.com>.

A generous startup package and appropriate space will be offered. Applicants should have a Doctoral degree and relevant postdoctoral experience.

Applications will be reviewed as they are received until the position is filled. Send curriculum vitae and names of three references to: D. Neil Granger, PhD, Boyd Professor & Head, Department of Molecular & Cellular Physiology, LSU Health Sciences Center, 1501 Kings Highway, Shreveport, Louisiana 71130-3932, FAX: 318-675-6005, e-mail: [dgrang@lsushc.edu](mailto:dgrang@lsushc.edu).

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# Calendar of Scientific Meetings

## 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

### **7th International Symposium on Biocatalysis and Biotransformations**

July 3–8 • Delft, Netherlands  
Contact: Biotrans 2005 Secretariat, Department of  
Biotechnology, Julianalaan 67 2628 BC, Delft, The Netherlands  
Email: biotrans2005@tnw.tudelft.nl  
Website: www.biotrans2005.bt.tudelft.nl/

### **FASEB Summer Research Conference on Transport ATPases: Genomics, Mechanisms, and Relevance to Disease**

July 16–21 • Saxtons River, Vermont  
Poster Sessions, Discussions, Young Investigator Forum  
Organizers: Alan Senior & Kathleen Sweadner.  
Applications will be available in March; Website: src.faseb.org.

### **Pathobiology of Cancer**

July 17–24 • Snowmass Village Resort, Colorado  
For information: Email: meetings@aacr.org  
Website: www.aacr.org; Ph.: 215-440-9300

### **BioScience2005—From Genes to Systems**

July 17–21 • Glasgow, UK  
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  
Ph: +44 (0)1206 796351; Fx : +44 (0)1206 798650  
Email: info@BioScience2005.org; www.BioScience2005.org

### **Gordon Research Conference on Molecular & Cellular Biology of Lipids**

July 24–29 • Kimball Union Academy, New Hampshire  
Email: www.grc.uri.edu/05sched.htm#GRC

## AUGUST 2005

### **Ninth International Congress on Amino Acids and Proteins**

August 8–12 • Vienna, Austria  
For Information: Prof. Dr. Gert Lubec, FRSC (UK)  
Medical University of Vienna, Dept. of Pediatrics, Div. of Basic  
Science, Währinger Gürtel 18, A 1090 Vienna, Austria  
Email: gert.lubec@meduniwien.ac.at  
Ph: 0043.1.40400 3215; Fax: 0043.1.40400 3194  
Website: fens.mdc-berlin.de/calendar/?id=485&action=read

### **2005 International Gap Junction Conference**

August 13-18 • Westin Resort and Spa, Whistler, BC, Canada  
Website: www.gapjunctionconference.org  
Abstract And Registration Deadline: April 1  
Contact: Dale W. Laird, University of Western Ontario,  
London, Ontario, Canada, N6A-5C1; Ph: 519 661-2111 x86827  
Fax: 519 850-2562; Email: dale.laird@fmd.uwo.ca

### **7th International Symposium on Mass Spectrometry in the Health and Life Sciences: Molecular and Cellular Proteomics**

August 21-25 • Fairmont Hotel, San Francisco  
This symposium will integrate mass spectrometry perspectives  
with the needs of the biomedical sciences, including: Sub-cel-  
lular separation strategies and sample handling • Analysis and  
automation technologies • Protein identification and quantita-  
tion • Studies of covalent modifications • Modulation of bio-  
logical function • Protein machines and assemblages and  
organelles • Deciphering protein networks and systems •  
Mining genome and proteome databases • Bioinformatics.  
For further information contact the symposium office:  
Phone: (415) 476-4893; Fax: (415) 502-1655  
Email: sfms@itsa.ucsf.edu  
Website: http://ms-facility.ucsf.edu/symposium

## SEPTEMBER 2005

### **Second World Congress on Synthetic Receptors**

September 7–9 • Salzburg Congress Centre, Salzburg, Austria  
Abstract Deadlines: 25 March 2005 (oral and poster papers)  
For information: Conference Secretariat, Elsevier, The  
Boulevard, Langford Lane, Kidlington, OxfordOX5 1GB, UK  
Tel: +44 (0) 1865 843691; Fax: +44 (0) 1865 843958  
Email: jm.seabrook@elsevier.com  
Website: www.syntheticreceptors.elsevier.com

### **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: www.gen.cam.ac.uk/sens2/CSBMCB

**14th Annual Growth Factor and Signal Transduction Symposium: Integration of Structural and Functional Genomics**

September 22 – 25 • Iowa State University, Ames Iowa  
Ph: 515-294-7978; Email: [gfst@iastate.edu](mailto:gfst@iastate.edu)  
Website: [www.bb.iastate.edu/~gfst/homepg.html](http://www.bb.iastate.edu/~gfst/homepg.html)

**International Conference on Enzyme Technology RELATENZ 2005**

September 20–23 • Varadero, Matanzas, Cuba  
Contact: Autopista a Varadero km 3 ?  
Matanzas, C.P.44740, Cuba  
Email [relatenz.umcc@umcc.cu](mailto:relatenz.umcc@umcc.cu)  
Website: [www.umcc.cu/EnzymeTechnology/relatenz.htm](http://www.umcc.cu/EnzymeTechnology/relatenz.htm)

**American Society for Bone and Mineral Research [ASBMR] 27th Annual Meeting**

September 23–27 • Gaylord Opryland Resort and Convention Center, Nashville, Tennessee  
Abstract Submission Deadline: April 27, 2005  
For more information call (202) 367-1161  
Email: [asbmr@smithbucklin.com](mailto:asbmr@smithbucklin.com); Website: [www.asbmr.org](http://www.asbmr.org)

**OCTOBER 2005**

**Supramolecular Chemistry**

October 14-19 • Obernai (near Strasbourg), France  
A European Science Foundation conference. For information:  
Ph: +33 (0)3 88 76 71 35; Fx: +33 (0)3 88 36 69 87  
Email: [conferences@esf.org](mailto:conferences@esf.org)

**North Carolina RNA Society's Symposium on RNA Biology VI: RNA, Target and Tool Theme: Small RNAs and RNPs.**

October 21-22 • North Carolina Biotechnology Center, Research Triangle Park, NC. 2005  
Deadline for registration and abstract submission: July 1  
Email: [stu\\_maxwell@ncsu.edu](mailto:stu_maxwell@ncsu.edu)  
Website: <http://www.med.unc.edu/pmbb/nc-rna-soc.html>

**NOVEMBER 2005**

**International Workshop on Biosensors for Food Safety and Environmental Monitoring**

November 10-12 • Agadir, Morocco  
Contact: Université Hassan II-Mohammedia, Faculté des Sciences et Techniques, B.P. 146, Mohammedia, Morocco  
Email [a.amine@univh2m.ac.ma](mailto:a.amine@univh2m.ac.ma)  
Website: [www.univh2m.ac.ma/biosensors](http://www.univh2m.ac.ma/biosensors)

**DECEMBER 2005**

**Xth PABMB Congress: Panamerican Association for Biochemistry and Molecular Biology**

December 3-6 • Hotel del Bosque, Pinamar, Province of Buenos Aires, Argentina  
Organized by the Argentinian Society for Research on Biochemistry and Molecular Biology (SAIB). The Congress will consist of five Plenary Lectures, eighteen Symposia, nine sessions of oral communications, and three poster sessions.  
For more information contact:  
SAIB President. Ernesto Podestá: [ernestopodesta@yahoo.com.ar](mailto:ernestopodesta@yahoo.com.ar)  
SAIB Secretary Carlos Argaraña: [carga@dqf.fcq.unc.edu.ar](mailto:carga@dqf.fcq.unc.edu.ar), or  
PABMB Chairman Juan José Cazzulo: [jcazzulo@iib.unsam.edu.ar](mailto:jcazzulo@iib.unsam.edu.ar)  
website: <http://www.saib.org.ar>

**Non-Vesicular Intracellular Traffic**

December 15-16 • Goodenough College, London, UK  
Contact: Meetings Office, Biochemical Society, 3rd Floor, Eagle House, 16 Procter Street, London, WC1V 6NX  
Email: [meetings@biochemistry.org](mailto:meetings@biochemistry.org)  
Website: [www.biochemistry.org/meetings/focused.htm](http://www.biochemistry.org/meetings/focused.htm)

**FEBRUARY 2006**

**Third International Conference on Ubiquitin, Ubiquitin-like Proteins, and Cancer**

February 9-11 • The University of Texas M. D. Anderson Cancer Center, Houston, Texas  
This meeting will celebrate the Nobel Prize awarded to Avram Hershko, Aaron Ciechanover, and Irwin Rose for their discovery of the ubiquitin pathway and the 10th anniversary of the discovery of SUMO/Sentrin and NEDD8  
Application and Abstract Submission Deadline: Friday, November 11, 2005; For information contact: Amy Heaton Program Manager, Department Of Cardiology University of Texas M. D. Anderson Cancer Center  
Tel: 713-745-6826; Fax: 713-745-1942  
Website: [www.sentrin.org](http://www.sentrin.org)

**MARCH 2006**

**RNAi2006: Advances in RNA Interference Research**

March 22-23 • St. Anne's College, Oxford, UK  
Conference Organizer: Muhammad Sohail  
Biochemistry Department, University of Oxford  
Tel: +44 1865 275225; Fax: +44 1865 275259  
Email: [muhammad.sohail@bioch.ox.ac.uk](mailto:muhammad.sohail@bioch.ox.ac.uk)  
Website: <http://libpubmedia.co.uk/Conferences/RNAi2006HomeMay2005.htm>

# Fundamentals of Enzyme Kinetics (3rd Edition)

By A Cornish-Bowden (CNRS, Marseilles, France)

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There is no pretence of an encyclopaedic approach, but instead the emphasis is on the principles of enzyme kinetics, and especially on explaining these principles as simply and accurately as possible, so that readers will be well equipped to take the subject as far as they need.

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- Tight-binding and Irreversible Inhibitors
- Reactions of More than One Substrate
- Use of Isotopes for Studying Enzyme Mechanisms
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