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ASBMB Today

AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

ASBMB Today: Our "New" Newsletter

Dr. Robert D. Wells, President

This issue of *ASBMB Today* represents our "new and improved" newsletter. *ASBMB Today* replaces *ASBMB News* which had served as our newsletter for approximately the past ten years. As you can see, *ASBMB Today* (Volume 1, Number 1) has a new format which is attractive and easy to read. Mr. John Thompson [Editor] has made numerous improvements which will help to convey news of our Society to our members. In addition, appreciation is conveyed to Mr. Peter Farnham who has overseen the activities with *ASBMB News* in the past and continues to participate with the improvements in *ASBMB Today*.

New content included in *ASBMB Today* will focus on budget issues with Federal agencies, administrative policies by the Council of your Society, Federal and State regulatory issues, conferences and meetings, news related to scientific publications, biotechnology developments, and other topics including diversity and undergraduate education. We hope that you will enjoy *ASBMB Today*.

Mr. Thompson welcomes articles from our membership as well as comments and suggestions. Please correspond with him at jthompson@asbmb.faseb.org or 301-530-7145.

We invite your remarks and participation.

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ASBMB Today

AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

APRIL 2002, Volume 1, Number 1

features

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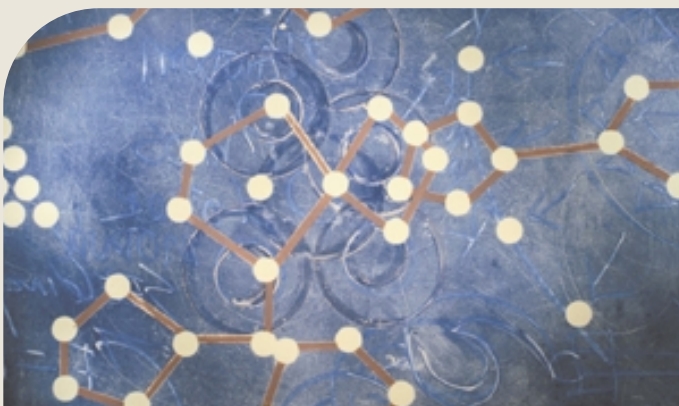

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Open the Door for Foreign Scientists

I read Dr. Weiner's letter in the February issue of *ASBMB News* with great interest.

It has been a long-standing issue that U.S. high school and college students lack interest in science studies. As you pointed out, many graduate programs have trouble recruiting Ph.D. students. As result, over the past two decades, many foreign students/scientists have supported and made tremendous contributions to the U.S. scientific community.

The key issue here is, in my opinion, the job market for Ph.D. students and postdoctoral fellows. Unless this is addressed, the U.S. will have to continue its dependence on foreign scientists to support its science effort. The issue of employing a foreign workforce is not a unique one for the scientific community. Other industries such as computer science and some medical communities have heavily relied on foreign engineers, and MDs as well.

Over the past two decades, many foreign scientists have supported and made tremendous contributions to the U.S. scientific community.

The U.S. should improve the job market for its scientists and continue to open its doors to scientists, engineers, and medical doctors from other countries to support its science mission, engineering program, and medical service. This will ultimately benefit this country.

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Tell Us What You Think

We appreciate receiving letters that are suitable for publication from ASBMB members 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.

John Edward Porter Receives First Schachman Public Service Award

John Edward Porter, former chairman of the House Appropriations Subcommittee on Labor, HHS, Education, and Related Agencies, is the first recipient of the ASBMB's Howard K. Schachman Public Service Award. ASBMB is recognizing Mr. Porter for his role in bringing into existence the plan for doubling the budget of the National Institutes of Health in five years.

The NIH budget stood at just over $13 billion in 1997, and if all goes well, will exceed $27 billion by this fall. This stunning accomplishment would not have happened without Mr. Porter's staunch and early support for it during his chairmanship of the subcommittee that funds NIH. Mr. Porter, who served in the House of Representatives for 21 years from the 10th Congressional District of Illinois, chaired the Appropriations Subcommittee on Labor, HHS, Education, and Related Agencies from early 1995 through the end of his congressional service in January 2001.

Mr. Porter's award lecture, "Issues Related to the National Institutes of Health," will be delivered at 12:15 pm, Tuesday, April 23, 2002, in Room 226, Morial Convention Center, New Orleans, Louisiana, in conjunction with ASBMB's annual meeting. The lecture is open to any attendee at the meeting.

"I can't think of a more deserving recipient of the first Schachman Award than Chairman Porter," ASBMB Public Affairs Committee Chairman William R. Brinkley told *ASBMB Today*. "Through his passion for health and his firm belief that basic biomedical research is the only answer for finding cures and prevention of diseases, Chairman Porter, more than anyone else, should be credited with the successful orchestration in Congress of the concept of doubling the NIH budget in five years. Although he retired from Congress before the doubling was completed, Chairman Porter works tirelessly as a member of the Board of Directors of Research!America and the Campaign for Medical Research. He continues to believe in the campaign to double the NIH budget, and to maintain a level of NIH funding in the future that will assure continued success long after doubling."

For his part, Mr. Porter said he was "very pleased to receive this award, and I'm honored the Society thought of me."

A Lifetime of Service

Mr. Porter finished his service in the House of Representatives in 2001, and upon his retirement became a partner in the law firm of Hogan & Hartson. He practices in the firm's Washington, D.C. office and is a member of the firm's Health group. Mr. Porter concentrates his practice on health law and education matters, including administrative and regulatory, international, legislative strategy, and education and health policy.

Mr. Porter's service in Congress not only included his chairmanship of the appropriations subcommittee overseeing NIH. He also served as Vice-Chairman of the Subcommittee on Foreign Operations, and as Vice-Chairman of the Subcommittee on Military Construction.

Mr. Porter was founder and co-chairman of the Congressional Human Rights Caucus, a voluntary association of over 250 Members of Congress working to identify, monitor and end human rights violations worldwide. ⊛

Senate Debate Due on

by Peter Farnham, ASBMB Public Affairs Officer

Somatic cell nuclear transfer (SCNT), loosely referred to as "cloning," continues to occupy a major portion of Congress' attention as the year proceeds. Senator Sam Brownback (R-KS) is the chief proponent of a Senate bill that would ban all forms of SCNT. S.1899, "The Human Cloning Prohibition Act of 2001," would complement House passage of the Weldon bill last year.

The Weldon bill outlawed SCNT for any purpose, both reproductive (intended to produce what the bill refers to as an "embryo," which would then be implanted) and so-called "therapeutic cloning" (that is, SCNT intended to produce stem cells which could be used in research and for possible therapies).

Sen. Sam Brownback

The Bush administration supported the Weldon bill in the following statement issued last July 30:

"The Administration supports a ban on the cloning of human beings by somatic cell nuclear transfer. The Administration unequivocally is opposed to the cloning of human beings either for reproduction or for research. The moral and ethical issues posed by human cloning are profound and cannot be ignored in the quest for scientific discovery . . .

"The Administration is strongly opposed to any legislation that would prohibit human cloning for reproductive purposes but permit the creation of cloned embryos for research. Thus, the Administration would strongly oppose any substitute amendment . . . which would permit human embryos to be created and developed solely for research purposes."

Last year, as the first session of the 107th Congress was winding down, Senate Majority Leader Tom Daschle (D-SD) was trying to clear the Senate calendar of anything controversial in order to expedite the start of the holiday recess. As part of this maneuvering, he promised Brownback a vote on his bill this Spring in exchange for his withdrawal of it from the Senate calendar (a debate would have badly delayed the Senate's departure for the holidays). It now looks like the promised vote will take place this month, after the Easter recess.

As the Senate debate on the Brownback bill approached, frantic lobbying efforts were underway by both supporters and opponents. At press time the outcome is too close to call, but the number of uncommitted senators was clearly dwindling.

A March 5 hearing focused on SCNT, featured prominent activists on both sides of the issue. The hearing was before the Senate Health, Education, Labor and Pensions Committee, and was chaired by Senator Ted Kennedy (D-MA) and later by Senator Jim Jeffords (I-VT). The hearing followed dueling press conferences in support of the Brownback bill and of the Feinstein bill (which would ban SCNT for purposes of reproduction, but allow it for therapeutic or research purposes).

Actor Christopher Reeve, paralyzed five years ago in a terrible riding accident, spoke eloquently about the need to allow scientific research to proceed by not banning therapeutic cloning. Dr. Paul Berg, Stanford University, was equally eloquent in discussing the potential of somatic cell nuclear transfer and the promise of the resultant stem cells for research and possible therapies. The other witness supporting

Christopher Reeve

Your efforts to persuade your senators to oppose passage of the Brownback bill would be most appreciated. All senators can be reached through the U.S. Capitol switchboard at 202-224-3121. In addition, the Senate website (www.senate.gov) has contact information for each senator. Simply click on the link, "List Senators by State," and you can get directly to your senator's website.

Brownback 'Cloning' Bill

SCNT was Thomas Murray, President, The Hastings Center. Opponents of SCNT who testified were Judy Norsigian, Founder, The Boston Women's Health Book Collective; Dr. Stuart Newman, New York Medical College, and Sen. Mary Landrieu (D-LA).


Sen. BIll Frist

Few positions seemed to have changed as a result of the hearing. However, Senator Bill Frist (R-TN), a heart surgeon, all but stated that he intends to support the Brownback bill, a disappointment to many activists working for SCNT. However, Frist also indicated that he has considerable doubt about a provision in the Brownback bill that would ban importation of any therapies that were dependent on SCNT. "I think this section needs work," he said. This was the first indication from those supporting the Brownback bill that it might be modified.

It would be very helpful to get some key conservative senators to support SCNT to produce stem cells, and there is some hope that this might occur. Senator Strom Thurmond (R-SC) supported stem cell research when it was debated in 1998, as did Senator Orrin Hatch (R-UT), who in February alluded to the promise of stem cell research in public remarks.


Sen. Orrin Hatch

However, he is under enormous pressure to vote in favor of the Brownback bill (the National Right to Life Committee has bought radio ads in Utah attacking his position), and had not yet publicly stated his position. ⊛

Language To Be Key Factor In Brownback Debate

One of the subtleties of the debate on the Brownback bill is expected to be the language used to describe the different elements of the process. "Language is important, semantics are important," says one lobbyist on the SCNT issue. So far, however, the scientific community is not having much success in controlling what words get used in public statements, either in Congress or in the general media.

For example, is it accurate to refer to the product of somatic cell nuclear transfer as an embryo? An embryo is the result of a union between an egg and a sperm cell. However, if there is no fertilization of the egg, but rather, an asexual process in which the nucleus of another cell is inserted into it, should the resultant cell mass be called an embryo? Wouldn't it be more accurate to refer to it as an asexually produced—or even unfertilized—blastocyst?

Or take the word "cloning" itself. A more accurate and less emotional term is "somatic cell nuclear transfer," but the word "cloning" has entered the debate and is used as a kind of shorthand to describe the process at issue in the Brownback bill. Use of the term "therapeutic cloning" is even more problematical, with the prestigious National Academy of Sciences weighing in against its use. The Academy prefers the term, "nuclear transplantation to produce stem cells."

Other linguistic formulations have been proposed and tried out, but none of them have caught on so far. One formulation that has been suggested is "DNA therapies for human diseases and disabilities." Senator Orrin Hatch (R-UT) used a similar formulation—"DNA regenerative therapy"—in a public statement on stem cells. However, this formulation, according to an article in *Science's* February 15 issue, was dismissed as being "beyond comprehension" by a biologist at the Max Planck Institute.

Unfortunately, supporters and opponents of the Brownback bill freely use the terms "cloning" and "embryo" in congressional deliberations on the subject. Some may argue that this is not really that important; use of the term "embryo" to describe an asexually produced, unfertilized blastocyst is merely shorthand that makes the process easier for most Senators and staff to understand. But, others argue that by referring to an asexually produced, unfertilized blastocyst as an "embryo," one is conceding an important language issue to opponents of somatic cell nuclear transfer for research and therapeutic purposes. It implicitly surrenders to Brownback's supporters the right to define the terms used in the debate.

Scientific and Medical Aspects of Human Reproductive Cloning

By Maxine Singer, Carnegie Institution of Washington

On January 18, 2002, the National Academies published a report entitled *Scientific and Medical Aspects of Human Cloning*. The report was prepared by a distinguished panel of biologists and physicians who together brought to the task considerable expertise in the basic science and clinical aspects of mammalian reproduction. Irving L. Weissman was the chair of the panel which was established in June, 2001 under the joint aegis of the Academies' Committee on Science, Engineering and Public Policy (COSEPUP) which I chair and the National Research Council's Board on Life Sciences, chaired by Corey Goodman (the full report is available at www.nationalacademies.org/humancloning).

The panel was charged to examine the scientific and medical issues relevant to human reproductive cloning, including the protection of human subjects, how human reproductive cloning differs from stem cell research, and whether a moratorium on human reproductive cloning was advisable. An examination of the broader societal, ethical, and religious issues that surround the question of human reproductive cloning was not part of the panel's charge.

The panel undertook an extensive study of the published methods and outcomes associated with reproductive cloning of experimental and farm mammals. Its aim was to determine whether those methods are sufficiently reproducible and safe to be extended to humans. A public workshop was held in August to hear world leaders in relevant technologies present up-to-date data. Among the participants were persons who had publicly announced their intention to clone human beings. The panel also examined whether human participants in reproductive cloning could be adequately advised and protected by the procedures now standard for medical experimentation. Hundreds of scientific and clinical papers were considered and are listed in the report's useful bibliography.

In reproductive cloning, the nucleus of a body cell is transplanted into an egg whose nucleus has previously been removed and the egg is stimulated to divide to form a blastocyst of approximately 150 cells. The blastocyst is then placed into a uterus where it can continue to develop into a fetus and full term, newborn organism.

Nuclear transplantation of a body cell nucleus into an enucleated egg followed by stimulation and blastocyst formation are also the first steps in a procedure for the production of stem cells. In this case, cells from the inner cell mass of the blastocyst are separated from those blastocyst cells that would become the placenta, and the inner cell mass cells are cultured to initiate a stem cell line. Such stem cells are unspecialized and can develop into most if not all kinds of body cells. The panel avoided using the terms 'therapeutic' or 'research' cloning to describe this process because neither term reflects the common scientific usage which applies the word cloning to processes that produce a copy of an organism, cell, or DNA molecule.

The panel concluded that the data from reproductive cloning of animals demonstrate that the process is currently extremely inefficient. Only a small percent of the attempts are successful in producing healthy clones and the percent varies from species to species. Some of the eggs containing transplanted nuclei fail to produce viable blastocysts while others yield (implanted) clones that die during all stages, including late stages, of gestation. Newborn animal clones often die soon after birth and others are abnormal. Additionally, the procedures carry serious risks for the mother, including, in some species, abnormally large placenta and fetuses.

In view of these findings, the panel unanimously approved the following recommendation:

"Human reproductive cloning should not now be practiced. It is dangerous and likely to fail. The panel therefore unanimously supports the proposal that there should be a legally enforceable ban on the practice of human reproductive cloning."

The scientific and medical considerations related to this ban should be reviewed within five years. The ban itself should be reconsidered only if at least two conditions are met: (1) a new scientific and medical review indicates that the procedures are likely to be safe and effective, and (2) a broad national dialogue on the societal, religious, and ethical issues suggests that a reconsideration of the ban is warranted."

Scientists place a very high value on the freedom of inquiry—a freedom that underlies all forms of scientific and medical research. The panel recognized that a recommendation for legal restrictions on research must be based on compelling reasons. It was convinced that in the case of human reproductive cloning, the potential dangers to the implanted fetus, the newborn, and the woman carrying such a fetus constitute just such compelling reasons.

In contrast, the panel found no scientific or medical reasons for a ban on the production of stem cells by nuclear transplantation because no blastocyst is implanted in a uterus. Embryonic stem cells produced by nuclear trans-

plantation from patients with heritable risks of various diseases would allow important novel research for the fundamental understanding and the possible treatment of such diseases. Moreover, such cells, when derived with a nucleus from a patient, could yield tissues that stand a good chance of being accepted by that patient's immune system and thus provide improved therapies for diseases such as Parkinson's and Alzheimer's. For these reasons, the panel also unanimously recommended the following:

"Finally, the scientific and medical considerations that justify a ban on human reproductive cloning at this time are not applicable to nuclear transplantation to produce stem cells. Because of the considerable potential for developing new medical therapies for life threatening diseases and advancing fundamental knowledge, the panel supports the conclusion of a recent National Academies report that recommended that biomedical research using nuclear transplantation to produce stem cells be permitted. A broad national dialogue on the societal, religious, and ethical issues is encouraged on this matter."

About the Author

Maxine Singer received the Ph.D. in Biochemistry in 1957 from Yale University. Her interest in nucleic acids began during her post-doctoral work in Leon Heppel's laboratory at NIH and has never flagged. Until 1975, she was a Research Biochemist in the Institute of Arthritis and Metabolic Diseases, NIH, where she worked on the synthesis and structure of RNA and applied this experience to the work that elucidated the genetic code. By 1970 she had become interested in animal viruses and took a sabbatical leave in the laboratory of Ernest Winocour at the Weizmann Institute of Science, Israel. There she began work on aspects of simian virus 40.

Moving to the National Cancer Institute in 1975, she continued this work studying defective SV40 viruses whose genomes contain regions of DNA from the host monkey cells. She also carried out investigations on interaction between histone H1 and DNA as it relates to the structure of chromatin. In the same year she served on the organizing committee for the Asilomar Meeting on Recombinant DNA molecules, the first public discussion of the implication of these new methods. The work on defective SV40 led to an interest in highly repeated DNA sequences in primates, including human genomes. This led, in turn, to the discovery of a transposable element (jumping gene) in human DNA.

Dr. Maxine Singer

In 1988 she became President of the Carnegie Institution of Washington, retaining her laboratory and the title Scientist Emeritus at the NIH. At Carnegie she has renewed her interest in the range of sciences investigated at the Institution's departments: earth science, astronomy, plant and developmental biology. She has also initiated programs designed to improve scientific understanding by the general public including the training of elementary school teachers and a Saturday program for children—First Light.

In 1988, Dr. Singer received the Distinguished Presidential Rank Award, the highest honor given to a civil servant, and in 1992 she received the National Medal of Science, the nation's highest scientific honor bestowed by the President of the United States "for her outstanding scientific accomplishments and her deep concern for the societal responsibility of the scientist." In 1999 she received the Vannevar Bush Award presented by the National Science Board of the National Science Foundation. ⊛

ASBMB Welcomes New Ph.D.'s

ASBMB extends its congratulations to these individuals who recently received their Ph.D. degrees from the Department of Biochemistry at the University of Wisconsin. In recognition of their achievement, ASBMB is also presenting them with a free one-year membership in the Society. The new Ph.D.'s are listed below with their current affiliation.

Miguel A. Cabrita, University of Alberta

Finghui Feng, Harvard Medical School

Marie-Josee LaForest, University of Montreal

Susan A. McDowell, University of Cincinnati

Ashok B. Ramalingam, Johns Hopkins School of Medicine

Karl J. Staples, Imperial College of Science, Technology & Medicine

Jean-Claude Twizere, Texas A & M University

Johns Hopkins Radiologist Expected To Be Bush Choice To Head NIH

Two years after Harold Varmus' departure from the directorship of the National Institutes of Health, the administration has apparently settled on a nominee for a permanent successor—Adam "Elias" Zerhouni, MD, Executive Vice Dean of Clinical Practice of the Johns Hopkins University School of Medicine. Dr. Zerhouni's scientific expertise is in radiology. An announcement of his candidacy was expected soon.

It has been widely reported that Zerhouni became the nominee after assuring the administration that he opposes use of cloned human embryos in research. He is also reported to support the anti-cloning legislation introduced earlier this year by Senator Sam Brownback (R-KS). This bill outlaws all human cloning regardless of purpose, whether reproductive or therapeutic (see related story, page 4).

However, other sources indicate that the Algerian-born radiologist strongly supports stem cell research, and just one year ago, according to press reports, Zerhouni was instrumental in securing a $58 million private gift to Johns Hopkins to create the Institute for Cell Engineering, which is devoted partly to stem-cell research.

Dr. Zerhouni, characterized by colleagues as a talented administrator and an excellent although little-known scientist, has not commented publicly on any of these matters, and undoubtedly will not do so before his confirmation hearings (assuming he is in fact the President's nominee). Based on press reports, Senate reaction to his nomination was neutral to cautiously favorable, although some overt opposition to his nomination will undoubtedly develop if his alleged support for a ban on therapeutic cloning and the Brownback bill turns out to be accurate.

Zerhouni's expected nomination comes as a surprise to virtually everyone following the administration's sometimes tortured search for a new NIH Director. Most observers expected that the eventual nominee would be Dr. Anthony Fauci, Director of the NIH's National Institute of Allergies and Infectious Diseases. However, after months of negotiations, Dr. Fauci's candidacy was squelched by the White House. According to senior administration officials, Fauci was taken off the list of candidates because he wanted to continue to conduct and supervise research at NIAID in addition to taking on the top job at NIH. However, social conservatives with close ties to the Bush administration take credit for Fauci not becoming the nominee; he was deemed "insufficiently pro-life" by many of them.

Zerhouni, if nominated and confirmed, would preside over an institution located on a 300-acre campus in the midst of a major building boom, 15,000 employees, and a budget expected to grow to more than $27 billion this year. He will also have to find directors for six NIH institutes, some of which have been without top leadership for almost two years. ⊛

Synchrotrons, Math, Physical Sciences All Essential to 21st Century Biology

"The synchrotron is an absolute requirement for state-of-the-art research," declared NIGMS Director Marvin Cassman in addressing a luncheon meeting of the Congressional Biomedical Research Caucus. Equally essential for biologists in the 21st century, he said, is input from mathematicians and engineers.

"For most of the 20th century the driving force in biology was chemistry," he said, but added, "Biologists of the future will need significant mathematical skills to understand those controls, and we will need physical scientists to help us."

To explain this need, Cassman compared biology to the structure of a 747 jet—the wings, flaps, engines, landing gear, etc., but not the control system. "Biologists," he said, "need the help of mathematicians and engineers to understand the controls and how they work." He cited protein structure research at synchrotron facilities as an example of how the physical sciences strongly affect the biological sciences. "There's no way to separate these things anymore," declared Cassman.

An obstacle to adding physical science's expertise into the medical research is, in Cassman's opinion, the compartmentalization of U.S. academic institutions. "We need to break the barriers down," he stated.

The physical sciences' link to biology is exemplified by the increased role of the synchrotron, noted the NIGMS Director. Demand for the use of synchrotrons by biologists is going up rapidly and construction of a major synchrotron installation is now underway at Stanford University. However, in view of the $750 million cost for the Advanced Light Source at Argonne National Laboratory, Cassman sees it as unlikely that another synchrotron will be built in the U.S. any time soon. Planning, though, is underway to maximize the output of existing facilities.

The NIGMS Director, who will be leaving that post in mid-May to become the first director of QB3, the University of California Institute for Quantitative Biomedical Research, reported that a February meeting of an interagency consortium on increasing efficiency at research facilities had discussed the development of robots to automate research processes, and the creation of uniform computer software. He indicated that the use of robots in protein structure determination could speed the process, and that uniform software which could be used "everywhere by everybody" would be a substantial improvement.

That consortium, which is chaired by Cassman, includes representatives from NIH, NSF, and DoE. It was formed in 2000 to solicit input from biological science communities and, he said, "figure out where we can optimally leverage our resources to provide the greatest benefit."

Other strategies to improve efficiency could be coordination of the different synchrotron projects and collaboration among research groups, as well as technological improvements to the accelerators that would make it possible to speed the rate of protein structure determination. "There are some real needs in terms of upgrading synchrotron capabilities so that they are even faster than they are now," said Cassman.

The U.S. currently has six synchrotron facilities. Argonne, Brookhaven, the University of California-Berkeley, and Stanford University have facilities overseen by DoE. NSF supports facilities at Cornell University and Louisiana State University's Center for Advanced Microstructure and Devices in Baton Rouge.

Tufts University Alzheimer's Research Uses Unique Neural Thread Protein Test

Researchers at the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University announced a collaboration with Nymox Corp. to use the company's diagnostic test for neural thread protein (NTP) in its research on nutrition, cognitive functioning, dementia and Alzheimer's disease.

Tufts scientists will include the Nymox NTP test in their evaluation of two important groups of study participants—a population of home-bound elderly people, and a group of aging veterans who are followed as outpatients. Tufts' research already has shown a relationship between cognitive functioning and blood homocysteine levels (related to B vitamin nutritional status.) The NTP test confirms chemical changes in the brain strongly correlated with dementia and Alzheimer's disease.

"We believe the neural thread protein test will provide us with additional valuable information in our study of the causes and prevention of this devastating and incurable condition," said Irwin H. Rosenberg, M.D., senior scientist at the center and dean of the Gerald J. and Dorothy R. Friedman School of Nutrition Science and Policy at Tufts. Initial research findings are expected late this year.

Mayo Clinic Professor Renowned for

Dr. Cynthia T. McMurray is a professor and staff consultant at the Mayo Clinic in Rochester, Minnesota. She was recently recognized for her scientific contributions by being named Distinguished Investigator at the Mayo Clinic and Foundation. This honor came with a $500,000 prize for her research.

She holds a primary appointment in the Department of Molecular Pharmacology and Experimental Therapeutics and the Department of Biochemistry and Molecular Biology, and also is a member of the Mayo Cancer Center and the Molecular Neurosciences Program.

She received her Ph.D. in biophysics in 1987 under Kensal van Holde. After a postdoctoral fellowship at the Vollum Institute of Neurobiology with Edward Herbert, she came to the Mayo Clinic in 1991 as a senior associate consultant and assistant professor. She was promoted to full professor in 1999.

McMurray is internationally renowned for her work on the mutational mechanism called DNA expansion. Instability at repetitive sequences is prominent in cancers and expansion is the underlying cause for a number of progressive neurodegenerative diseases, including Huntington's Disease (HD).

The mutation referred to as "trinucleotide expansion" occurs when the number of CAG triplets present in a mutated gene is greater than the number found in a normal gene. Additionally, the number of CAG triplets in the disease gene continues to increase as the disease gene is inherited (See figure A.). The CAG triplet codes for the amino acid glutamine. As the CAG repeat number grows, the growing polyglutamine tract produces an HD gene product (called huntingtin) with increasingly aberrant properties that cause the death of brain cells controlling movement.

"We hope to develop 'cures' for patients by developing therapeutics to both stop the mutation process as well as to stop the faulty gene products from causing disease, and some of these approaches will be applicable to cancer," says McMurray. Her work touches on cancer biology and neurodegeneration, two of the major focuses of modern biology and medicine. Work from her laboratory has, over the years, revealed features of how DNA is unstably passed on and how unstable DNA causes disease.

McMurray was one of the discoverers of the mechanism for the expansion mutations in mammals. Her work together with a number of colleagues spawned the cover article in the *NIH Journal of Research* as early as 1995. This branch of her work includes understanding the basic mechanisms of DNA repair and its role in gene amplification events.

"We hope to develop 'cures' for patients by developing therapeutics to both stop the mutation process as well as to stop the faulty gene products from causing disease."

—Dr. Cynthia McMurray

Dr. Cynthia T. McMurray

Her recent work on DNA repair and expansion has moved into animal models, and, as reported in a recent issue of the journal *Nature*, she has shed light on part of the mutational mechanism that has been puzzling for years. She has shown that the expansion in germ cells (the heritable part of the mutation) is not associated with replication but rather is likely to be a gap repair process arising from strand breaks (See figure B.). At the sites of breakage, CAG repeats in the HD gene can form unusual secondary structures that appear to elude the natural repair machinery. These loops comprising the CAG repeats are not excised and become incorporated into the DNA giving rise to expansion in the next round of replication.

In addition, the Mayo Clinic professor has identified a key mismatch repair complex that causes expansion, and efforts are underway for drug design to target key proteins and stop the mutation from growing. Her work has

Research on DNA Expansion

generated worldwide interest and was commented on in *Nature News* and Views (2001). She has recently been able to link the expansion mechanism underlying a group of neurodegenerative disorders to some instability events leading to cancer, and reports that she is on the road to developing a drug that may be able to offset both by aborting a common mechanism of action.

McMurray's work on neurodegeneration and pathophysiology of Huntington's Disease has also received attention. The mechanism by which the abnormal Huntington gene kills brain cells is poorly understood. However, a long polyglutamine tract creates an unusually "sticky" molecule that can bind to and interfere with cellular molecules and their functions. Therefore, it is generally accepted that Huntington-mediated aggregation is part of the cell-death mechanism. A recent article in *Nature* (genetics), reported that results from her laboratory have challenged a widely held theory of disease called the toxic peptide theory. This model posits that proteolysis and the release of small fragments containing the polyglutamine tract accumulate and cause toxicity.

This article received extensive press coverage by Associated Press, Reuters News, ABC News, *Science*, and *The Lancet*. Based on her findings, McMurray is currently developing novel therapeutics that have already shown promise in animals. Together with members of the Mayo Clinic's Department of Neurology, she is beginning initial studies to test the feasibility for translation of such therapeutics to human patients.

McMurray recently co-organized a three-site research forum uniting all national sites within the Mayo Clinic. This forum links research among basic scientists and clinicians who share their ideas about approaches to solve human disease, and has been adopted as an annual event.

The Mayo Clinic professor also organizes the annual West Coast Chromatin Meeting, which focuses on chromosome and chromatin structure, epigenetics, and the role of chromatin in cellular regulation and repair. ⊛

Genetics and Pathophysiology of Huntington's Disease and other expansion disorders

Figure A

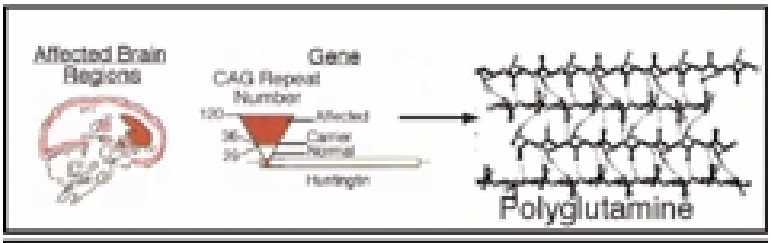


Figure B

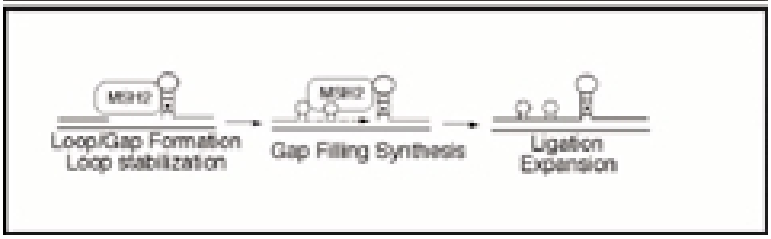


Figure A: The relationship between CAG repeat number and HD pathophysiology. (right) Schematic representation of the HD gene: the open bar represents the coding region of the Huntington's gene (called huntingtin); the lines indicate the non-coding portions of the gene; the small red bar indicates the position of the CAG repeat stretch located within the N-terminal portion of the coding sequence. Upside down triangle represents increasing number of CAG repeats. Base of triangle in white represents normal unaffected individuals with 6-29 CAG repeats. Dotted lines indicate unaffected carriers for disease with 29-35 CAG repeats. Red part of the triangle indicates affected individuals with 36-120 CAG repeats. (left) Regions of neuronal loss in HD. Red regions indicate the major areas of neuronal loss in HD patients with 36-120 CAG repeats. These brain regions control movement. C/P is the caudate/putamen; CTX is the cortex; GP is globus pallidus; STN is subthalamic nucleus; VL is ventrolateral thalamic nucleus; SN is substantia nigra.

Figure B: Model for trinucleotide expansion by gap repair. At CAG repeats, a break is fromed creating a gap of unpaired DNA. Intra-strand, hyrogen-bonded loops comprising CAG repeats are stabilized by the mismtach repair proteins, preventing their re-annealing to the partner strand. The loops are trapped into DNA by a polymerase fill-in reaction and ligation. The loops are the precursors for expansion in the next round of replication.

New Orle

ans A Very Different Place

Just like New York, New Orleans is a large metropolitan city, an international port, and a "melting pot" of many races and cultures. It is also very different from any other city in the U.S.—and maybe anywhere, for that matter. It is not New York nor San Francisco, certainly not Boston, and despite its French origins it is not Paris, or even that other Orleans in France. It's tropical—more like Martinique than Miami. For those of you who will be in the Big Easy for the ASBMB Annual Meeting and EB 2002, here are just a few samplings of the uniqueness of this city.

Le Flotant

New Orleans essentially is an "island." (Possibly the only "inland island" in the United States). It is squeezed between the Mississippi River and the nation's seventh largest lake (Pontchartrain), and surrounded on all sides by a giant oak-cypress swamp. Napoleon, who sold it and the rest of the Louisiana Territory to the U.S., referred to it as the Isle d'Orleans. Early French settlers called it "le flotant," the floating land.

As such, Island Orleans was both isolated and insulated from the mainland for almost 250 years. Thus, it was able to develop—and retain—its own unique culture: jazz, Creole cuisine, Mardi Gras, above ground burial sites ("cities of the dead"), and the famous jazz funerals.

Native Orleanians grew up in separate sections, or faubourgs (French for suburbs). These neighborhoods were, in effect, individual hamlets. Since 90% of the area originally was swamp or water, they were scattered sites, built where "ridges" or natural levees offered elevation above the recurrent floods.

Until 1890, the area was a collective of disconnected suburbs—neighborhoods without neighbors. In many cases they were divided by language. The original French Creoles spoke French and disdained the "Americans" who arrived 90 years later. The Germans, Irish, Italians, and West Indians added to the "unbelievable babble of a dozen languages and scores of dialects in the city's marketplaces."

The ASBMB Annual Meeting and EB will be in the Big Easy April 20-24, 2002. Here are just a few samplings of the uniqueness of this city.

The attachment to neighborhood remains so strong that many third and fourth generation residents take pride in living in their "grandfather's house." In addition, many neighborhoods have maintained much historical character. Ten are now listed as National Historic Districts.

Cajuns And Creoles

As a noun with a capital "C", a Creole is a person, but by some definitions, virtually everyone in New Orleans seems to be a Creole. By others, there's hardly anyone who measures up. Strictly speaking, a New Orleans Creole is a descendant of an early French or Spanish settler, "born in the colony," not in Europe.

According to most dictionaries, Creole comes from the same Latin root as the word "create," with the French

creating their "Creole" from the Spanish "criollo." Over time, this went from denoting a person born of Spanish parents overseas to a person born similarly of French parents—a child of the colonies, in either case.

The Cajuns of South Louisiana are descendants of French colonists who settled Canada's Nova Scotia and New Brunswick. They called their home in the New World "l'Acadie" and were known as Acadiens. "Cajun" is is how that word was mispronoounced by the British, who took over those Acadia in the 18th century and expelled the "Cajuns," thousands of whom eventually settled in Southern Louisiana.

Which Way Is Up?

If you're alert, determined, and here long enough, you might be able to figure out which way is north, south, east or west. New Orleanians tend to shun such mundane directions, because the serpentine Mississippi renders them virtually useless. Instead, the waterways call the shots: downriver for downtown, upriver for uptown, lakeside toward Lake Pontchartrain, and riverside toward Old Man River. ⊛

New Orleans Talk

Colloquialisms are not unknown in most parts of this country, but in the Crescent City—far more than most places—the locals have some unique touches to their vernacular. Following are a few samplings of New Orleans talk.

Alligator Pear: What the locals call an avocado.

Banquette: Pronounced "Ban Ket" in New Orleans, this means, simply, a sidewalk.

Beignet (Ben Yeah): French-style donuts drowned in powdered sugar and customarily served with cafe au lait.

Big Easy: Like Crescent City, a euphemism for New Orleans. It is attributed to a gossip columnist for the *Times Picayune*, who conceived of it in the '70s as an answer to the "I Love New York City" hype. The concept is that if New York is the Big Apple then New Orleans is the Big Easy, where everything is slower, simpler, and easy-going.

Cajun (Kay Jen): There are three meanings for this word. The first refers to the French Acadians who settled into the bayous of Louisiana from Novia Scotia in the 1700s. The second meaning, which involves a rather hot debate, refers to a style of cooking. The last meaning describes a unique dialect of French spoken by the "cajuns."

Chickory: A root that is ground and roasted to add flavor to coffee. Cafe au Lait is made with coffee, chickory and boiled milk.

Crawfish: Crawfish are sort of like little lobsters. Locals have "crawfish parties" where friends gather to feast on pounds and pounds of crawfish that are highly seasoned and boiled with onions, new potatoes, whole garlic cloves, sausage and anything else that adds flavor to these delicious crustaceans. Yankees sometimes call crawfish "crayfish."

Creole (Kree Yol): This word refers to the French and Spanish descendents in New Orleans and also describes a style of cooking.

Etoufee (A Two Fay): There are many variations to this dish. Most etoufees start with a roux and consist of rice, shell fish or meat and vegetable.

Grillades (Gree Yods): Broiled veal served in gravy. Usually, grillades are served for breakfast with grits.

Gumbo: This word comes from an African language and means okra. Gumbo is a traditional Southern soup-like dish. It can be made with just about anything, but all gumbos start with a rich roux and usually include either sea food or sausage.

Muffaletta (Moof a lot a): Said to have been invented at "Central Grocery" on Decatur Street in the French Quarter, a Muffaletta is a very large sandwich served on an Italian bread loaf. The muffaletta is made from ham, salami, and provolone cheese, and is garnished with an olive relish.

Neutral Ground: In most cities this is called the "median," that little strip of ground in the middle of a road. Legend has it that the neutral ground got its name from early New Orleans when the French and Spanish could do business between sections of the city by standing on the "neutral ground."

Po'Boy: Any sandwich made with a loaf of French bread. Called a Po'Boy because one sandwich can feed an entire family.

Roux (Rew): Made from flour and oil, it is the base for many popular New Orleans dishes.

Scientists Must Take Lead In Bioterrorism Security

Scientists whose research involves working with materials that could become weapons for bioterrorists must take the lead in developing security safeguards, or see research restricted by the heavy hand of government.

That was the gist of the message heard by some 200 business, policy, and academic leaders attending a summit, Preserving an Open Society in an Age of Terrorism, held March 5-6 in New York City's Plaza Hotel.

The summit, billed as the first to examine from a strategic perspective the impact of the war against terrorism on both the public and private sectors, was presented by *Scientific American* and the Center for Strategic and International Studies. Speakers from academia, business, and government discussed the measures needed to protect society against biological warfare, how to protect our critical infrastructure, and what this means when much of the cyberworld is in private hands, as well as what future public/private partnerships will look like.

Charles B. Curtis, President of the Nuclear Threat Initiative, told them that the same university and industry researchers who customarily handle the materials for chemical and biological weapons must be "the authors, the implementers, and the enforcers" of procedures for their safe transfer, said. Failing that, he cautioned, scientists risk a government response that may put in jeopardy the very mechanisms on which they depend.

The events of September 11 must change the way some scientists communicate, agreed Adel Mahmoud, President of the vaccine division at Merck. "We can't just say the only drive for science is openness and transparency," he told *BioMedNet News*. "The fact is, there are people out there watching us, trying to use our information against us."

Much attention about bioterrorism has focused on countries such as Iraq and the former Soviet Union, but top biological labs in the U.S. have the same "porous approach to security," according to Curtis. He noted that a memo, discovered by the *Wall Street Journal* on the hard drive of a computer Al-Qaeda left in Kabul, recommended that would-be terrorists enter bioweapons programs in educational institutions, because they allow easy access to specialists in biowarfare and their work.

He suggested that, instead of responding to someone else's security plan, researchers propose their own plans for scientific communication that exercises reasonable judgment, and is enforced by their peers. "No less is required of our nation's research universities and the science community," said Mahmoud.

Business as usual cannot be the norm, he said, and scientists may need to restrict some presentations to closed meetings with controlled attendance. This could run the risk of excluding some valuable contributions, he acknowledged, "but you have to be pragmatic."

Panelists at the summit were unanimous in agreeing that microbes will be the weapons of choice for terrorists in the future. With rapid advances in biotechnology and biomedical research, they are simple to produce, easily available, and easy to conceal.

NAS Urges Anthrax Vaccine Research

Even as the summit on Preserving an Open Society in an Age of Terrorism was meeting, a National Academy of Sciences panel was urging the government to support research into a better anthrax vaccine.

Speakers at the New York summit commented that vaccine technology has not advanced much in the two centuries since Jenner conquered smallpox. Vaccine research, they indicated, is not profitable and only four companies now make vaccines compared to 20 in the 1980s.

"Nobody considered vaccines an important priority - not just industry," said Michael Friedman, Chief Medical Officer for Biomedical Preparedness at Pharmaceutical Research and Manufacturers of America and a former deputy commissioner for operations at the Food and Drug Administration, a speaker at the summit. Although infectious diseases still cause nearly a third of deaths worldwide, he said, NIH funds minimal research into infections other than HIV, and in academia and industry alike, the high-profile diseases are Alzheimer's, diabetes, and cancer.

> ***"The fact is, there are people out there watching us, trying to use our information against us."***
>
> **—Adel Mahmoud, Merck**

The awakened interest in infectious diseases mandates a greater contribution from industry researchers, supported by academia and the government, added Mahmoud. "We have to invest in both the basic science and the clinical science that will help us deal with these microbial threats," he said. They have been with us and will remain, he added, and "they are very, very smart critters." ⊛

Research Funding's Broad Impact

Just as Uncle Sam's funding for military installations boosts the economy of the surrounding area, so too can federal support for scientific research at universities and other institutions be a boon for the communities in which they are located. In both cases, there is a ripple affect on employment, wages, real estate values, and business opportunities. The San Francisco and Boston areas are two examples of this impact.

Boston has long been by far the nation's top beneficiary of a five-year plan to double the federal medical research budget, with the city's universities, hospitals, and businesses receiving more than $1 billion per year in grants. And in the San Francisco Bay area, federal grants for biomedical research and consequent patents are among the few high spots of an otherwise dismal economy.

For Boston and environs, $1.6 billion in NIH grants pays the equivalent of about 10,000 researcher salaries, supporting everyone from top-flight doctors to local college students who help staff the labs. Massachusetts General Hospital receives more NIH money than any other hospital in the country; the federal dollars pay for 2,500 jobs.

"It is hard to exaggerate the economic impact on the Bay State," wrote columnist Michael Kranish in a recent issue of the *Boston Globe*. "The five independent hospitals in the nation that receive the most money from NIH are all in Boston. In Cambridge, the Whitehead Institute Center for Genome Research, which has ties to MIT, receives the nation's largest NIH grant—$60 million annually—for five years."

Another Boston institution, Massachusetts General Hospital, receives $181 million per year from NIH.

The economic spin-off from federal funding is worth at least another $1 billion per year to the state, according to the Massachusetts Technology Collaborative, and there is further impact on the state when research projects are turned into biotechnology businesses.

A typical example is Genzyme Corp., which employs 4,000 people in Massachusetts. The company started 20 years ago after then-Tufts University researcher Henry Blair decided he needed more room to run his NIH contract. Blair co-founded Genzyme to create his own lab space, and his research became the basis for what today is Genzyme's major product, a drug for the treatment of Gaucher's disease.

To Blair, the NIH money cycle in Massachusetts is driving the research that helps drive the economy. He told the *Boston Globe*, "Genzyme would not have existed without that NIH contract."

The reliance on funding for research could, for the Boston area and New England as a whole, could conceivably be the equivalent of leaning on a weak reed.

Why? Because in some regions state funding and grants, from individuals and foundations, are outpacing those in New England. For example, Texas has established two new research funds that are expected to each grow to over $100 million in the next 17 years, and California plans to spend at least $225 million in the next three years on research projects teaming the state university system with private industry.

In contrast to such state largesse, New England states contribute less than three percent of research funding at the region's universities. According to *The Chronicle of Higher Education,* that's less than half of what states elsewhere give to their institutions.

Others May Be Eyeing The NIH Bonanza

Politicians from other areas are beginning to cast covetous eyes on the funding that has benefited the Boston and San Francisco areas, as well as other centers of medical research.

Especially outspoken, according to the *Boston Globe's* Kranish, is Senator Thad Cochran (R-MS) who helped lead the effort to double the NIH budget five years ago. His state, Mississippi, gets just $18 million in federal medical money compared with Massachusetts' $1.6 billion.

"It isn't fair," the senator said. As he sees it, the "peer review" method in which experts are gathered to grade grant applications is a process dominated by scientists from the handful of states that get most of the grants. "Those who decide where the money goes are in many cases in those cities that do so much of the research," Cochran said. "If you are not a peer, you don't get the money."

Cochran is the number two Republican on the Senate Appropriations Committee. Mississippi's other senator, Trent Lott, is minority leader. Cochran said he may try to change the allocation method when NIH's budget comes up for consideration, but he acknowledged that this would be a long shot.

Research Funding Helps Keep San Francisco Afloat

Research grants are seen as a key factor in the San Francisco Bay area's economic vitality. Thanks to the region's culture of innovation and its plethora of research institutions, a recent analysis by a business group, the Bay Area Council, forecasts economic growth for the Bay Area of more than 4.2%—and as much as 5.1%—during the next three to five years.

Academic institutions will be a prime factor in this growth, according to the *San Francisco Chronicle*. Consider, for example, the University of California at San Francisco (UCSF):

- Studies have indicated that UCSF now injects as much as $2 billion into the local economy. Similarly, data for the University of California at Berkeley reveal that every dollar spent by that campus generates another 67 cents in local spending, resulting in a total impact on the Bay Area of $1.4 billion.
- UCSF employs more than 17,000 Bay Area residents with an annual payroll of $932 million, making it the second-largest employer in San Francisco. Spending by the employees in turn supports many more jobs in the region.
- UCSF received $340 million in federal grants for biomedical research last year, including nearly half of the $608 million awarded by NIH to all Bay Area institutions.
- Since UCSF's co-discovery of genetic engineering more than 25 years ago, the discoveries of UCSF scientists have led to the founding of nearly 70 life sciences companies, including biotechnology leaders Genentech and Chiron. The Bay Area is now home to 713 biomedical companies employing more than 80,000 people, according to a study recently released by the California Healthcare Institute.
- UCSF holds more than 500 patents, including five of the University of California system's top 11 revenue producers—hepatitis B vaccine, human growth hormone, a cochlear implant helping deaf people hear, a technique for delivering medicines into the body's cells and a form of recombinant DNA used for the production of therapeutic agents.
- UCSF's patents generated $434 million in the past five years—76 percent of the revenue from all patents in the University of California system in the same period.
- During the next three years, UCSF plans to develop 1.3 million square-feet of new research and teaching space, spending approximately $650 million in construction and other project costs.

The economic spin-off from federal funding is worth at least another $1 billion per year and there is further impact on the state when research projects are turned into biotechnology businesses.

Boston and San Francisco are just some of the municipalities and regions that benefit economically from the side affects of funding for scientific research. Others that have yet to develop as major research centers can be expected to seek development in this area, just as have other regions sought to duplicate the high tech success of Silicon Valley. For the potential political implications, see sidebar **"Others May Be Eyeing The NIH Bonanza."** ⊛

NSF: Small, Underfunded, Important

Many of you either have now, or have had, research support from the National Science Foundation at some point in your careers. ASBMB itself has had NSF support for various travel and education programs over the years. We bet you don't know, however, just how important NSF is in so many areas of academic biology and other related sciences. Below are a few "fast facts" about NSF, taken from recent NSF publications.

- Budget for 2002: $4.789 billion. Only 5% of budget is for internal operations, including staff salaries and expenses.
- Share of total annual federal spending for R&D: 4%.
- Share of federal funding for basic academic research: 23%.
- Share of academic research funding:
  Physical Sciences 36%
  Environmental Sciences 49%
  Engineering 50%
  Mathematics 72%
  Computer Science Research 78%
  Anthropology 100%
- Number of organizations receiving NSF funds each year: 1800.
- Number of proposals reviewed each year: 32,000.
- Approximate number of total awards funded each year: 20,000.
- Approximate number of new awards funded each year: 10,000.
- Number of reviewers (scientists and engineers) who evaluate proposals for NSF each year: 50,000.
- Number of reviews done each year: 250,000.
- Number of students supported through NSF's Graduate Research Fellowship Program since 1952: 36,000.
- Number of people (teachers, students, researchers, postdoctorates and trainees) that NSF directly supports: nearly 200,000.
- ASBMB is supporting a five-year doubling of the NSF budget, aiming at a total budget of $8 billion by 2005.

UK Endorses Embryonic Cloning; But Only for Research Purposes

Britain's position in pioneering stem cell research hardened when the UK's House of Lords signaled an unequivocal go-ahead to the controversial cloning of embryonic tissue.

Even if cell nuclear replacement is not itself used directly for many stem cell-based therapies, "there is still a powerful case for its use ... as a research tool to enable cell-based therapies to be developed," declared a report from the House of Lords Select Committee on Stem Cell Research.

The report, demanded early last year by critics of embryonic stem cell research, examined regulations drafted to extend the provisions of the 1990 production to research aimed at "increasing knowledge" and "enabling any such knowledge to be applied in developing treatments for serious disease."

It comes down heavily in favor of the existing regulations as long as they continue to come under the strict control of the government's watchdog, the Human Fertilization and Embryology Authority (HFEA).

The report also stresses that the regulations are concerned only with research, not treatments, and notes that the committee "unreservedly endorses the legislative prohibition on [human] reproductive cloning."

Richard Harries, the Bishop of Oxford and Chair of the Lords committee, said, "Research on early human embryos raises difficult moral and scientific issues, on which there are strong and sincerely held views. After looking at all the issues very carefully, the committee was not persuaded that it would be right to prohibit all research on early embryos."

The committee examined the feasibility of using adult stem cells as an alternative supply of readily-available stock, but Harries said it concluded "that as yet research on adult stem cells has not, as some claim, made research on embryonic stem cells unnecessary."

Response to the report came swiftly from the Wellcome Trust.

"The Lords deserve congratulations on their clarity of thought on an issue that others have attempted to hijack with inflammatory and misleading interventions," said Mike Dexter, Director of the Wellcome Trust. "Scientists can now get on with finding treatments for life-threatening diseases, such as Parkinson's, diabetes and cancer, thanks to this commonsense report."

> ***"Research on early human embryos raises difficult moral and scientific issues, on which there are strong and sincerely held views. After looking at all the issues very carefully, the committee was not persuaded that it would be right to prohibit all research on early embryos."***
>
> **—Richard Harries, Bishop of Oxford**

Germany Also Approves Stem-Cell Research

Earlier this year, Germany's researchers got the go-ahead to use a limited number of human embryonic stem-cell lines. However, the Bundestag's 340-265 vote to permit such use met a cautious reception from researchers, who expressed concerns about restrictions in the new law.

Germany will now permit embryonic stem-cell lines created before January 30 of this year to be imported. Only research on projects that are ranked as a high priority by a newly created regulatory body will be allowed. Permission must be obtained from the parents of the embryo from which the cell line was extracted, and there must be no alternative means of doing the research. Applications will have to be approved by a new national ethics committee.

Despite the restrictions in the new law, its passage was welcomed by Oliver Brustle and Otmar Wiestler, the University of Bonn neuroscientists whose application for funding from DFG, the nation's primary research agency, set off the debate. Their grant to study the production of neural precursor cells from stem cells was approved the day after the parliamentary decision.

"The ice is broken," Brustle told *Nature* magazine. "We would have preferred a more liberal solution, but the new rules are helpful, provided they will not be used to create further delays." German researchers should have ready access to all the lines listed in the National Institutes of Health registry, he said.

Gunter Stock, head of research at Berlin's Schering Company and a strong supporter of stem-cell research, said, "It is the smallest possible 'yes,' but I am grateful for the vote." ⊛

Chilled Neutrons To Solve Cell Membrane Puzzles

Cell membrane researchers are eagerly bracing for a long-awaited cold wave. A new partnership involving the National Institute of Standards and Technology (NIST), the University of California-Irvine (UCI), and other organizations will use beams of super-chilled neutrons to probe the elusive structure and interactions of cell membranes and their components, gathering information key to improving disease diagnosis and treatment.

Led by UCI biophysicist Dr. Stephen White, an ASBMB member, the Cold Neutrons for Biology and Technology (CNBT) team received $5 million from NIH's National Center for Research Resources to build the nation's first neutron-beam research station fully dedicated to biological membrane experiments. Located at the NIST Center for Neutron Research (NCNR) in Gaithersburg, Maryland, the CNBT team will exploit the NIST center's ability to generate high-quality beams of "cold" neutrons. Stripped from the nuclei of heavy atoms and then cooled by liquid hydrogen, these uncharged particles are ideally suited for exploring the disordered, continually changing landscape of cell membranes.

Dr. Stephen White

"We aim to close a big gap in our understanding of cell-membrane biology."

—Dr. Stephen White

"Cold neutrons provide a powerful tool for studying cell membrane systems," says White, "but the demand for beam time at the handful of neutron facilities in the United States is so great that the tool was nearly unavailable for this kind of research. Yet, for many challenges in biology and medicine, neutron probes offer the only realistic hope for answers."

For example, White says that only neutron probes can glimpse the process by which protein fragments, or peptides, are assembled into membrane-borne sentries that ward off harmful microorganisms.

To ease the neutron crunch for biologists, NIST offered to open a new port in a beamline at its NCNR. White then organized the CNBT partnership, which includes researchers from UCI, NIST, the University of Pennsylvania, Rice University, Carnegie Mellon University, the Duke University Medical Center and the Los Alamos National Laboratory.

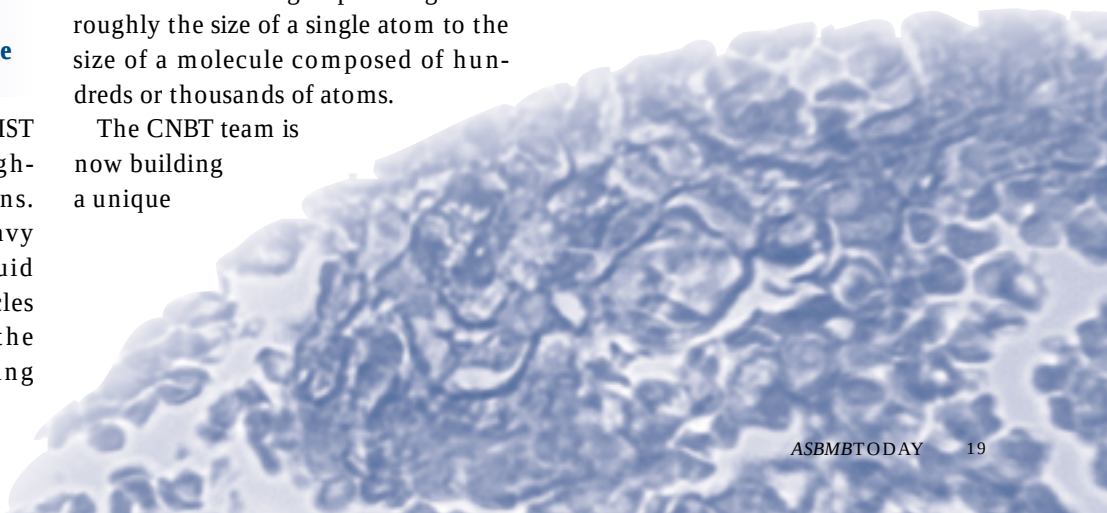
Neutrons are non-destructive, highly penetrating probes, valuable for studying changes in membranes over time. Because they behave like tiny waves of energy, neutrons also make excellent rulers. Depending on temperature, the length of the neutron ruler can be tuned over a range spanning from roughly the size of a single atom to the size of a molecule composed of hundreds or thousands of atoms.

The CNBT team is now building a unique instrument with dual capabilities: diffractometry and reflectometry. It will detect neutrons that are reflected or otherwise scattered after striking membrane samples. Reflected or diffracted neutrons will provide information on the location, orientation, size and composition of membrane components. In addition, the team is upgrading another instrument useful for studying large molecules—a small-angle neutron spectrometer—that will be shared with researchers in other fields.

The instruments are scheduled to be completed in 2003. They will provide cell membrane scientists with access to powerful technologies well beyond the resources of individual researchers.

Ultimately, the team hopes to use painstakingly gathered experimental data to predict molecular structure and the course of cell-membrane interactions. Computer models already are under development, and UCI chemistry professor Douglas Tobias is working on a computer simulation that can provide three-dimensional images and may even show changes in membrane structure over time.

"We aim to close a big gap in our understanding of cell-membrane biology," says White.



Big Drug Companies More Dependent on Biotechnology

At a time when the industry's best-selling brands face increasing competition from cheap generics, and its pipeline of new products is thin, the big drug companies are becoming more dependent on the biotech sector.

Bristol-Myers' investment in ImClone was one of the biggest deals to date between an established company and a biotech partner. To win access to Erbitux, ImClone's promising colon cancer drug, Bristol-Myers paid $1 billion for a 20 per cent stake in the company and promised further payments of up to another billion.

That relationship went downhill following the FDA's announcement that the drug could not be approved because of faulty data in the clinical trial. Bristol-Myers has demanded more control over drug development of the drug, which ImClone has refused, and ImClone faces legal action from investors charging it gave misleading information about its previous dealings with the FDA. Congressional hearings may also be on the horizon.

The dispute between Bristol-Myers and ImClone comes at a time when pharmaceutical companies are desperate for new products—in the next five years, patents on drugs with annual sales of over $40 billion will expire—while facing political pressure to keep from raising prices.

The biggest problem they face, however, according to The Financial Times, may be the poor results of their own research and development, which is costing more but producing less. Eight of the top 15 pharmaceutical companies did not win approval for a single new drug last year. According to Jean-Pierre Garnier, chief executive of Glaxo-SmithKline, in 1980 the top 20 drug companies spent $2 billion on R&D and 34 new drugs were approved. In 2001, the top 20 spent $26 billion, but only 28 drugs gained approval.

The biotech industry, by contrast, has been getting stronger. The decoding of the human genome led to record fund-raising over the last two years. There are now about 500 biotechnology companies researching new products, and they have about 1,300 compounds in development.

For the pharmaceuticals, the R&D crisis has sparked a debate about what their focus should be. Several have split their research groups off into separate fiefdoms, in an effort to create some of the atmosphere of the biotech world. One senior Glaxo-SmithKline executive has even been quoted as saying that his company might spin off some of its drug discovery components if results failed to improve.

Degussa Group Acquires Genset Oligos

The Degussa Group, Düsseldorf, Germany, will acquire Genset Oligos, the oligonucleotide division of Genset S.A., Paris, France, for $21.5 million, and merge it with Proligo, its subsidiary based in Boulder, Colorado.

The merger with Genset Oligos is expected to make Proligo a fully integrated supplier of nucleic acid specialties (genomics and genetic medicine) and provide Proligo with a global sales channel for its highly specific products (oligonucleotide probes, custom Locked Nucleic Acid, LNATM). The transaction was expected to be closed by the end of March.

Proligo is a dedicated specialist in professional and progressive nucleic acid products. Genset is a genomics-based pharmaceutical company focused on generating a pipeline of drug targets and candidates in the areas of CNS and metabolic disorders.

Celera Protease Inhibitor Enters Development for Chagas' Disease

The Institute for One World Health (IOWH) and the National Institutes of Health (NIH) have initiated development of Celera Genomics' CRA-3316 as a potential new treatment for Chagas' Disease. CRA-3316, formerly known as APC-3116, is a cysteine protease inhibitor discovered by the Celera research team. This parasitic infection is estimated to afflict 16-18 million individuals in South and Central America, with an annual mortality rate of 50,000, based on figures provided by the Centers for Disease Control. The compound targets the major protease produced by a parasite that causes Chagas' Disease. The parasite, *Trypanosoma cruzi*, is related to the agent responsible for African sleeping sickness, and it depends on a cysteine protease, cruzain, to sustain its life cycle.

While Chagas' Disease has historically been limited to South and Central American regions, an increasing immigration north has resulted in an increase in *T. cruzi* infections in the U.S.

Better Mice Help Biotech Start-Up

Mindset, a small biotechnology start-up based in Jerusalem, has engineered a better mouse that has generated a unique source of revenues to sustain the drug-development drive.

"We are a very unusual company in that we have intermediate and long-term sources of revenues," says Daniel Chain, the British-born chief executive and founder of Mindset. "And our source of revenues today is also a source of core drug discovery technology."

That source of revenues is a colony containing thousands of genetically modified mice, housed secretly at an unnamed location in New York State to protect the facility from militant animal rights activists. Mindset's mice have been engineered to include human genes that stimulate signs of full-blown Alzheimer's in just 12 weeks, compared with a year for other test mice.

Big pharmaceuticals companies are queuing up to have Mindset perform their Alzheimer's drug-testing. Initial clients include Lundbeck, the Danish pharmaceuticals group. Talks are under way with 50 other groups and Mindset expects revenues from these services to rise from $2 million last year to at least $8 million this year. Mindset has also raised $15 million in venture financing from MPM Capital, a Boston-based healthcare fund, and Clal Biotechnology, Israel's biggest biotech investment group.

New Antigen Microarrays Open Window to Better Disease Screening

A new microarray-based technology developed at Stanford University Medical Center may help doctors determine which molecules (antigens) come under attack in an autoimmune disease. By identifying these antigens, doctors can pinpoint diseases and treatment options.

"Right now clinicians test each antigen separately — and each one can take weeks," said P.J. Utz, MD, assistant professor of immunology and rheumatology and senior author on the study. "These arrays could enable a clinician to diagnose the disease on the first visit."

The antigen microarrays — developed in collaboration with Lawrence Steinman, MD, professor of neurology and neurological sciences — consist of glass slides dotted with thousands of proteins and other molecules that are often attacked in autoimmune diseases. To use the microarray, doctors draw a blood sample from the patient and incubate it on the array. Those antibodies that attack molecules on the array will locate their target and latch on. Fluorescent molecules are then added to detect the antibodies, creating colored spots on the slide. From there, it's a matter of counting the spots to see which antigens the immune system recognized.

EDITOR'S NOTE

The article, in the February issue of *ASBMB News*, on the NIGMS workshop "Achieving Scientific Excellence Through Diversity" was based on an NIGMS report. The full report can be obtained on the web at http://www.nigms.nih.gov/news/reports/diversity.html.

University of Wisconsin Foundation Resolves Patent Dispute

The University of Wisconsin Foundation and the Geron Corporation have reached a patent licensing agreement expected to ease the way for scientists to develop medical treatments using human embryonic stem cells.

The agreement narrows the exclusive commercial rights that Geron has to embryonic stem cells. It is also expected to reduce concerns that Geron's rights would hamper science or force stem cell companies to move overseas to avoid potential patent infringement charges.

The Wisconsin Foundation holds a fundamental patent on human embryonic stem cells because a university scientist, Dr. James A. Thomson, was the first to isolate them.

Menlo Park, California-based Geron financed Thomson's work and got the exclusive rights to sell treatments based on six types of cells plus options to acquire the exclusive rights to others.

Under the new agreement, Geron will have exclusive commercial rights to only three types of cells made from the embryonic cells—neural cells, heart cells, and pancreatic islet cells.

It will have only nonexclusive rights to develop treatments based on three other cell types—bone cells, blood cells, and cartilage cells—and will no longer have the option to acquire exclusive rights to additional cell types.

"Have it Your Way"

Tailoring Search Results in the New HighWire Portal

In the January issue, *ASBMB News* introduced the new "portal" site from Stanford's HighWire Press, which allows you to search all of Medline plus 300 journals' full-text at once—including the *JBC*, of course! Last month we began a series of short articles highlighting tools or features of this new site for researchers' sore eyes, starting with the ability to quickly see which articles are freely available to you right in your search result. This month we continue the series with a look at tailoring a search result to fit your needs. The new site is at http://highwire.stanford.edu.

The search result pages in the new portal let you change your view of the results with just a click or two. This month we'll look at how to amend, sort, condense, investigate and download search results.

Look at the top of a recent search result for Synaptotagmins (see figure).

The top section of the new search result page makes it easy to adjust your result in several ways:

Amend the result: Your search terms are pre-entered for you in the Quick Search box. You can add or replace terms there and click "go"; or change the scope of your search from searching Medline (as shown in this example) to focus on the 300+ highly-cited journals whose full-text is found at HighWire by checking a different radio button and clicking "go".

Sort the result: The default sort for the search engine shows you "best matches"—meaning those articles in which your search terms showed up most frequently and prominently. Clicking on "newest first" will reorder your search result by date, displaying the most-recently-published articles first.

See more per page: By default, the search engine shows you 10 items on each page. You can ask for 25, 40, 60, or 80 results per page just by clicking on the appropriate number. But note that a page that has 40 items on it will take longer to load than one with only 10 items.

Condense the result: The standard form for each citation provides a lot of information, such as a full list of authors, full citation information, which section of a journal an article is in, whether the article is a review, etc. The "condensed" option displays all the basic citation information you'd find in a reference list, plus a bit more, and takes up only a quarter the space! It looks like this:

Working from results: If you've tried the new portal, you might have noticed that it allows you to click on a link in a search result and go to an abstract or PDF by opening a new browser window, without losing your search result; it is almost as if you can "keep your finger on the page" of a search result while going off to explore new pages.

But there are other tools to help you work from results. By clicking in the checkbox to the left of any citation, then clicking the appropriate radio button under the grey box (to the right of the Search Result information) labeled "For checked items" you can do more with any article in a search result.

Download each checked item to your local citation manager database: You can quickly add citations and abstracts to your database in EndNote, ProCite and Reference Manager. Online instructions are provided to be sure everything is set up for an automatic transfer. You can also download an individual article's cita-

tion/abstract to a reference manager when you are viewing it in a HighWire-based journal site.

Expand each checked item to its abstract: A web page of abstracts for the selection citations will come up in a separate window. Each abstract includes a full citation and a link to full-text. As you review pages of search results, you can accumulate possible candidate articles to evaluate further by checkmarking them. Then you can read through the abstracts all at once, print them, or click through to full-text.

Next month we'll look at how you can have the system keep track of your favorite journals, including the *JBC*, *Molecular & Cellular Proteomics*, *Biochemistry and Molecular Biology Education*, and the *Journal of Lipid Research*. ⊛

Is your Directory listing correct?

Update your online record anytime during the year.

To update your online listing in the *FASEB Directory of Members*, visit **www.faseb.org** and click on "Member Directory."

Click "Update Member Info" at the top of your screen to make changes. All changes must be entered before July 31 to be included in the 2003 printed directory.

Please note: There is a time delay between submitting revisions and their actual appearance online.

Calendar of Scientific Meetings

APRIL 2002

ASBMB Satellite Meetings:
I - Transcriptional Regulatory Mechanisms;
II - Scientific and Technical Challenges in the Human Proteome

April 19-20 • New Orleans, Louisiana
Contact: Kelly Gull; Ph. 301-530-7145;
Fx. 301-571-1824; Email: kgull@asbmb.faseb.org;
Website: www.asbmb.org

American Society for Biochemistry and Molecular Biology Annual Meeting in Conjunction with EB2002

April 20-24 • New Orleans, Louisiana
Contact: EB2002 Meetings Office; Ph. 301-530-7010;
Fx. 301-530-7014; Email: eb@faseb.org;
Website: www.faseb.org/meetings/eb2OO2

MAY 2002

8th National Symposium:
Basic Aspects of Vaccines

May 1-3 • Walter Reed Army Institute of Research,
Bethesda, Maryland
Scholarship Application Deadline: March 15
Abstract Deadline: March 31
Contact: Janet O'Brien, Ph. 301-319-9462;
Fx. 301-319-9025; Email: symposium@na.amedd.army.mil
website wrair-www.army.mil/symposia/dmbsym

International Conference on Thiamin, Its Biochemistry, and Structural Biology.

May 18-21 • Rutgers University
Contacts: Frank Jordan; Ph: 973 353-5470
Email: frjodan@newark.rutgers.edu
Mulchand Patel; Ph: 716 829-3074
Email: mspatel@buffalo.edu
Website: www.chemistry.rutgers.edu

Proteomics: The Next Grand Biological Challenge

May 19-22 • Vanderbilt University
Contact: Division of Continual Medical Education
Ph: 615-322-4030; Fx: 615-322-4526;
Website: http://medschool.mc.vanderbilt.edu/proteomics

American Crystallographic Association in Conjunction with American Association for Crystal Growth

May 25-30, 2002 • San Antonio, Texas
Contact: Ph. 716-856-9060, ext 379; Fx. 716-852-4846;
Email: aca@hwi.buffalo.edu; Website: www.hwi.buffalo.edu/aca/

JUNE 2002

45th Annual Canadian Federation of Biological Societies Meeting
Themes: Neurological Development; Physical Activity, Nutrition and Chronic Disease

June 12-15 • Palais des Congres, Montreal, Canada
Contact: wantonious@cfbs.org; Website: www.cfbs.org

Proteomes: Structures, Changes, Interactions, and Function

June 20-23 • Iowa State University, Ames Iowa
Contact: Plant Sciences Symposium Office;
Ph. 515-294-7978; Fx. 515-294-2244; email: bmb@iastate.edu
Website: molebio.iastate.edu/~gfst/phomepg.html

JULY 2002

European Cells and Materials:
ECM III Cartilage & Joint Repair
Tutorials, Basic Research, and Clinical Methods

July 1-3, 2002 • Congress Centre, Davos, Switzerland
Contact: www.aofoundation.org/events/ao/ecm/organiser.shtml

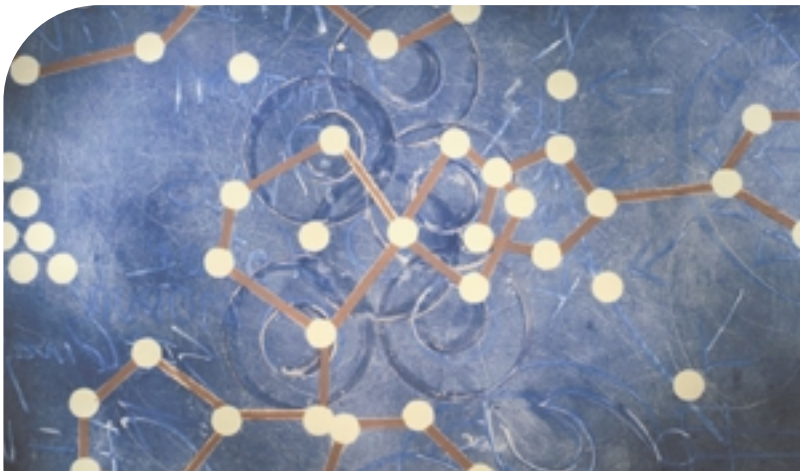
AUGUST 2002

Tissue Remodeling

August 1-4 • Iowa State University, Ames, Iowa
Abstracts and travel grant applications due May 31.
Contact: Growth Factor and Signal Transduction Conferences
Ph. 515-294-7978; Fx. 515-294-2244;
Email: gfst@iastate.edu
Website: molebio.iastate.edu/~gfst/homepage.html

American Society of Cell Biology: Nontraditional Functions of Ubiquitin and Ubiquitin-like Proteins

August 11-14 • Colorado Springs, Colorado
Contact: Delia Zielinski, ASCB; Ph: 301-347-9300
Fx: 301-347-9310; Email: dzielinski@ascb.org



SEPTEMBER 2002

Computational Biophysics: Integrating Theoretical Physics and Biology

September 7-12 • San Feliu de Guixols, Spain
Contact: Dr. J. Hendekovic, European Science Foundation
Ph. +33 388 76 71 35; Fx. +33 388 36 69 87,
Email: euresco@esf.org

Molecular Targets for Dietary Intervention in Disease

September 19-22 • Iowa State University, Ames, Iowa
Contact: Growth Factor and Signal Transduction Conferences
Ph: 515-294-7978; Fx: 515-294-2244; email: gfst@iastate.edu;
Website: http:molebio.iastate.edu/~gfst/homepg.html

7th International Symposium on Dendritic Cells

September 19-24 • Bamberg, Germany
Contact: Prof. Dr. Alexander Steinkasserer
Ph: ++49-9131-853-6725; Fx: ++49-9131-853-5799;
e-mail: steinkasserer@derma.imed.uni-erlangen.de
Website: www.dc2002.de/

OCTOBER 2002

First Joint Symposium of the Growth Hormone Research Society and the

International Society for Insulin-like Growth Factor Research
October 5-9 • Boston, Massachusetts
Contact: Professional Meeting Planners
Ph: 781-279-9887
Fx: 781-279-9875
Email: info@pmpmeeting.com
Website: www.ghigf2002.com

Metabolic Engineering IV: Applied System Biology

October 6-11 • Il Ciocco, Castelvecchio Pascoli Tuscany , Italy
Contact: United Engineering Foundation
Ph: 212-591-7836
Fx: 212-591-7441
Email: engfnd@aol.com
Website: www.engfnd.org
Registration: http://www.engfnd.org/2ay.html

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

The Society is asking department chairs to provide ASBMB with the names and addresses of each new Ph.D. recipient from their institutions. Upon receipt of this information, we will write the new Ph.D.s to congratulate them on their accomplishment and offer the free one-year membership in ASBMB. Names and addresses of the new Ph.D.s should be sent to:

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American Society for Biochemistry
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9650 Rockville Pike
Bethesda, MD 20814
Email: asbmb@asbmb.faseb.org

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