JULY 2004

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ASBMB Today

Constituent Society of FASEB

AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

ALSO IN THIS ISSUE

A Message from ASBMB's New President Judith S. Bond

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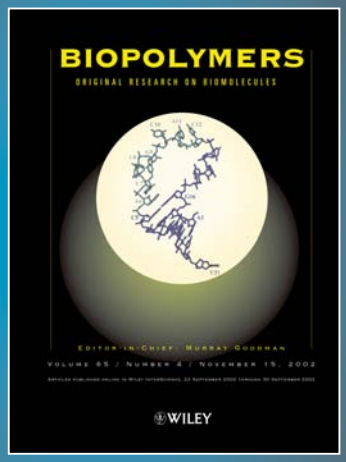
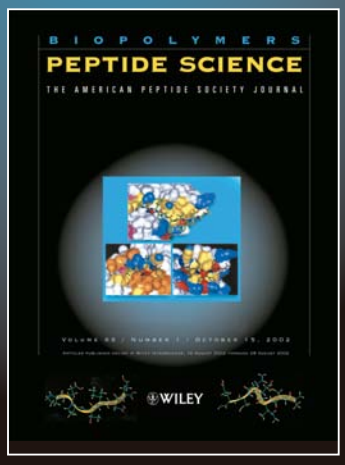
Presenting a New Unified Biopolymers

BIOPOLYMERS and PEPTIDE SCIENCE—
ONLINE SUBMISSION AND PEER REVIEW!
PEPTIDE SCIENCE — NEW EDITOR!





BIOPOLYMERS

The Biospectroscopy and Nucleic Acid Sciences sections are now fully integrated into *Biopolymers* to present a unified publication. Biospectroscopy and nucleic acid science articles will appear regularly in issues of *Biopolymers*. This truly international journal publishes original research papers on the structure, properties, interactions and assemblies of biomolecules. *Biopolymers* covers organic and physical chemistry, experimental and theoretical research, and static and dynamic aspects of structure. Papers from world-renowned laboratories offer the latest research on the development of experimental and theoretical studies of the structure of biologically significant molecules.

PEPTIDE SCIENCE

Throughout her distinguished career, Dr. Lila Gierasch, the new Editor of *Peptide Science*, has used biophysical approaches to explore the relationship between amino acid sequence and preferred conformations of peptides and proteins, with an emphasis on the impact of a cellular environment. Current thrusts of her work are the mechanism of folding of a class of predominantly ß-sheet proteins, the structure and function of Hsp-70 molecular chaperones, and the roles of signal sequences in protein targeting. She has effectively utilized synthetic peptides to dissect and probe complex biological systems.

Peptide Science is the sole affiliate Journal of the American Peptide Society. This section of *Biopolymers* is designed to provide a forum for current topics in peptide research and to publish articles that correlate research results between the subdisciplines of the peptide sciences. *Peptide Science* will continue to publish reviews on "Current Trends in Peptide Sciences" as well as original research papers.

ONLINE SUBMISSION AND PEER REVIEW SYSTEM FOR AUTHORS

In taking a step toward facilitating seamless international scholarly communication, *Biopolymers* and *Peptide Science* offer web-based submission and peer review. This process makes it easier than ever for you to submit a paper to the Journals.

For detailed instructions, visit:

Biopolymers: bip-wiley.manuscriptcentral.com

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ASBMB Today

AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

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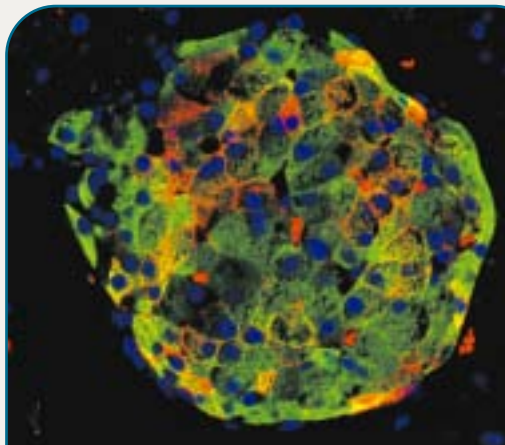

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ASBMB Sponsors United Nations Conference on 'Human Cloning Issues in All its Aspects'

By William R. Brinkley, Ph.D., Chair,
Public Affairs Advisory Committee, ASBMB

The Genetics Policy Institute (GPI) hosted a conference on stem cell research to openly discuss the repercussion of an international ban on therapeutic cloning and to draw a clear distinction between cloning of human beings (reproductive cloning) vs this potential life-saving methodology of therapeutic cloning. The meeting was organized by lawyer Bernard Segal, Executive Director of GPI, who succeeded in bringing some of the world's most renown investigators on this topic to New York for this landmark meeting on June 2, 2004. "A UN vote to ban this important scientific research would be tragic and would destroy the hopes of millions suffering from Alzheimer's, diabetes, cancer , spinal cord injuries, heart disease, ALS, and other devastating conditions for which no cure is known," said Segal. Christopher Reeve addressed the gathering via a taped commentary and urged everyone to do everything possible to support stem cell research and to persuade the UN not to prohibit this vital area of research.

I attended the one-day meeting for President Bettie Sue Masters, who was unable to participate. ASBMB was recognized as one of the sponsors of this meeting which featured speakers such as "Dolly" cloner Ian Wilmut, of the Roslin Institute in the United Kingdom, Shin-Yong Moon and Woo Suk Hwang of Seoul National University in the Republic of Korea. The latter two investigators were the first to clone a human embryo and to legitimize the application of somatic nuclear transfer (SCNT) for the production of human stem cells to use to successfully repair spinal chord injury. Speakers from the U.S. included Gerald D. Fischbach from Columbia University, who served as moderator; Rudolf Jaenisch, Whitehead Institute, whose research has rescued mice with genetic defects through therapeutic cloning and gene therapy; Douglas A. Melton, Harvard, a noted authority on stem cell technology; Camillo Rocordi of the Diabetes Institute, University of Florida; John Wagner of the University of Minnesota; and William Dalton Dietrich, Miami Project to Cure Paralysis,University of Miami School of Medicine. Other U.S. speakers included Lawrence S. B. Goldstein, UC San Diego, a very active member of the American Society for Cell Biology in the science policy arena, who presented an excellent overview of human cloning and stem cell biology at the opening of the conference; and Dr. Gerald Schatten of the University of Pittsburgh School of Medicine who is recognized internationally for his work on primate reproduction and stem cell technology.

This was, by far, the most effective public policy forum on stem cells that I have attended and the program attracted world-wide participation. Speakers were factual, but careful not to over-sell this promising technology. Each speaker was especially cautious to define SCNT and stem cell methodology accurately, and to state clearly that legitimate scientists around the world are totally and unequivocally opposed to reproductive cloning of human babies. On the positive side, with the remarkable findings by the Koreans, the genie is out of the bottle–SCNT and stem cells,

Continued on page 4

ISE Presents Two New Events For 2004!

CBA-2004

1st International Conference on Cell Based Assays for Drug Discovery & Development:

Applications of Primary Cell Cultures, Engineered Cells, and High Throughput Approaches for the Drug Efficacy, Metabolism, and Toxicity Evaluation

September 20-21, 2004

Renaissance Philadelphia Hotel Airport; Philadelphia, PA, USA

Monday, September 20, 2004

Session 1: Primary and Engineered Cell Systems

Chairs: Albert P. Li and Alan M. Goldberg

•Keynote Lecture: The Importance of Cell Based Assays in Biomedical Research (**Alan M. Goldberg**, Department of Environmental Health Sciences; Baltimore, MD)

•A Novel In Vitro Angiogenesis Assay Suitable for Drug-Screening (**Chris C.W. Hughes**, University of California, Irvine; Irvine, CA)

•Assays for Adipocyte Differentiation and Function (**Lucas Armstrong**, Chemicon International, Inc. Temecula, CA)

•Utilization of P-glycoprotein Transport Assay in CNS Drug Discovery (**Liyue Huang**, AstraZeneca, Wilmington, DE)

•Establishment of SAR to facilitate the development of drugs with high potential for CNS penetration (**Jerome H Hochman**; Merck and Co.; West Point, PA)

•Ion Conductance Microscope for Locating and Studying Ion Channels and Receptors in Surface Membranes of Living Cells (**Yuri Korchev**, Imperial College; London, UK)

•Integrated Multiple Organ Culture System (IdMOC) - A Cell-Based Assay for the Evaluation of Multiple Organ Effects (**Albert P. Li**, Ph. D., Advanced Pharmaceutical Sciences, Inc., Baltimore, MD)

Tuesday, September 21, 2004

Session 2: High Throughput Screening Approaches

Chairs: Thomas Fletcher and Serguei V. Kozlov

•Managing Cell-based Assays with Flow Cytometry (**John F Dunne**, BD Biosciences San Jose, CA)

•Ultra-High Throughput Cell-Based Assays for Liver X Receptors (**Lyndon J. Mitnaul**, Merck and Company; Rahway, NJ)

•Cell-Based Screening Assays for Compounds Which Induce Apoptosis or Disrupt the Cell Cycle (**Dianne M. Fishwild**; Guava Technologies Inc.; Hayward, CA)

•Antiviral Discovery for SARS - Rapid Development and Execution of Cell-Based HTS Screening in Response to an Emerging Pathogen Outbreak (**Thomas M. Fletcher III**; Southern Research Institute; Birmingham, AL)

•Proteome-Wide High Throughput Cell-Based Assay for Activators of NFkB (**Hans Biebuyck, John Kenten, Stefanie Nelson, John Joern, Pankaj Oberoi, and Jacob Wohlstadter**; Meso Scale Discovery; Gaithersburg, MD)

•In "Coopetition" with NF-kB: Development of Analytical Tools for Rapid Assessment of Inflammatory [Potential of Test Substances (**Serguei V. Kozlov**, National Cancer Institute at Frederick, Frederick, MD)

•Development of Calcium-Based Assays for Screening and Characterization of GABA-A Receptor Modulators (**Tino D. Jorgensen**, NeuroSearch A/S; Ballerup, Denmark)

ISE Training Courses in Drug Development

Dr. Christopher A. Lipinski

Adjunct Senior Research Fellow, Pfizer Global R&D, Groton New London Labs (Groton, CT)

Dr. Albert P. Li

Founding Chairman, President & CEO; Advanced Pharmaceutical Sciences, Inc. (Baltimore, MD)

August 5-6, 2004

San Francisco Marriott Hotel; San Francisco, CA, USA

Thursday, August 5, 2004

Physical and Chemical Compound Properties in Drug Discovery

Dr. Christopher A. Lipinski

Length of Lecture: 1 day

Course syllabus:

•Definition of chemistry physical and chemical compound properties. Current status of compound properties; comparison to drugs: Cost, time, and challenges.

•Quality chemical structures in drug discovery.

•Medicinal chemistry and the chemistry structure
--Structural features to avoid
--Solving problems using bioisosteres
---Structural features to include
--Privileged structures, molecular anchors, masterkeys

•Solubility
--Importance of aqueous and DMSO solubility
--Computational and experimental approaches to solubility
--Compound handling, storage and when to change the chemistry isolation procedure

•Permeability
--GI and blood brain permeability - how it depends on the chemical structure
--Computational and experimental approaches to permability
--How chemistry can improve permeability

•Chemistry structure and the discovery process
--Chemistry and HTS screening errors
--Lead-like versus drug-like
--Hit to lead and lead optimization chemistry

•Summary of lecture and open discussion.

Friday, August 6, 2004

In Vitro Evaluation of ADMET Drug Properties

Dr. Albert P. Li

Length of Lecture: 1 day

Course syllabus:

•Definition of ADMET. Current status of drug development: Cost, time, and challenges.

•Role of in vitro ADMET systems in drug development.

•Evaluation of drug absorption
--Mechanisms of drug absorption
--Cell-based systems for drug absorption
--Artificial membrane systems

•Drug metabolism
--Drug metabolizing enzymes
--Metabolic stability evaluation
--Metabolite identification
--Species comparison

•Drug-drug interactions
--Examples of drug-drug interactions
--Enzyme inhibition
--Enzyme induction
--Transporter-based drug interactions

•Toxicity screening
--Examples of toxic drugs and toxic mechanisms
--Screening for acute drug toxicity including general cytotoxicity, hepatotoxicity, neurotoxicity, and cardiotoxicity
--Genotoxicity evaluation
--Toxicogenomics

•Summary of lecture and open discussion

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by Peter Farnham, CAE, ASBMB Public Affairs Officer

House Appropriations Process Begins

After weeks of partisan wrangling, the House Appropriations Committee released its 302(b) allocations on June 2. Unfortunately, the news is not very good. It appears as though the best the National Institutes of Health can expect this year is something along the lines of the President's budget request for the agency, that is, about $729 million, a 2.6% increase over FY 2004. Prospects for the National Science Foundation are even more grim.

In theory, under the annual budget process, the House and Senate were supposed to have completed work on a budget resolution by May 15. The budget resolution sets overall spending priorities, and the total budget is divided into several broad categories—mandatory spending (that required by law); interest on the national debt; and discretionary spending. Discretionary spending is further divided into defense and non-defense discretionary spending.

The total amount of discretionary spending available under the budget resolution is then divided up among the 13 appropriations sucommittees.

In practice, Congress' actually sticking to this schedule is very rare; it has happened only twice in the last 20 or so years. This year is no different. While both House and Senate have completed work on budget resolutions, there is no progress on setting up a conference, and the spending goals and amounts for programs contained in the two resolutions are quite different. The numbers below are from the House budget resolution. As of this writing, the Senate had not divided discretionary spending among its subcommittees.

House Allocations

The two subcommittees we are most interested in—Labor/HHS (which funds NIH), and VA/HUD (which funds NSF), both got slightly more than the President had asked for last spring.

Rep. Ralph Regula (R-OH) chairs the House Appropriations Subcommittee on Labor/HHS and that subcommittee got only about $300 million more than the President's request, for a total of about $142.3 billion. This small amount of additional money probably gives Regula the room he needs to fund NIH at the President's request level ($729 million above last year). Thus, is it quite unlikely, without a last-minute infusion of new money from somewhere, that NIH will do much better than the President's request level this year, as far as the House is concerned.

Regarding the VA/HUD subcommittee allocation, it got $92.9 billion, about $800 million more than the President had asked for. However, this allocation does not begin to address what is needed in this large and diverse bill. Subcommittee Republicans believe they need at least $4 billion above the President's request, but subcommittee Democrats think the figure needed is actually more like $7 billion. Of course, this means that the National Science Foundation is probably going to get squeezed, as VA medical care is short about $1.2 billion of what is needed to make it whole this year.

Thus, barring some surprises—always possible in an election year—it is likely that we are in for more contentious times when Congress begins seriously grappling with appropriations (not expected until after Labor Day).

A brief footnote on NIH—in the Senate, there is some hope that Senator Arlen Specter (who chairs the Senate Appropriations Subcommittee on Labor/HHS) might be able to improve on the President's number, but unless he gets a better allocation than Rep. Regula got, this is probably a reach. It is unlikely, however, that Senator Specter will be able to do much better than $1 billion over FY 2004 for NIH, about a 3% increase.

UN continued ...

Continued from page 2

derived from left-over human embryos destined to be frozen or discarded, can be used to repair damaged cells and tissues and potentially cure many of the world's most daunting and horrific diseases. UN resolution 56/93 of December 12, 2001, from the Ad Hoc Committee to consider prohibition of all forms of human cloning, including therapeutic cloning, will potentially close the door to future medical research involving this technology.

The time has come for scientists, especially members of ASBMB, to pick up the gauntlet and define and defend a technology that promises to end suffering and provide hope for all humanity; the United Nations is a good place to start. Support a ban on reproductive cloning but oppose the Costa Rican proposal to ban therapeutic cloning. At the same time, we must carry the message to our various state legislatures.

Troublesome Clauses: The Importance of Seven Words

by Peter Farnham, CAE, ASBMB Public Affairs Officer

A Reagan-era national security directive, hailed at the time as a major victory for science, is looking considerably less helpful almost 20 years after it was issued. This is the main message of a report released recently by the Association of American Universities and the Council on Government Relations. The report, called "Restrictions on Research Awards: Troublesome Clauses," notes various restrictions included in research contracts between a variety of government agencies and universities because of a seven-word clause in National Security Decision Directive 189, issued in September 1985.

NSDD 189 was a policy statement indicating that "to the maximum extent possible," the Reagan administration's policy was not to restrict dissemination of the products of fundamental research. "It is also the policy of this Administration that, where the national security requires control, the mechanism for control of [research] information…is classification." The directive went on to instruct federal agencies on how to determine if a research project needed to be classified, and ended with the following statement: "No restriction may be placed upon the conduct or reporting of federally funded fundamental research that has not received national security classification, except as provided in applicable U.S. statutes."

This statement was widely praised at the time by most of the scientific community as a major victory for freedom of scientific communication. You may recall the era—the Reagan administration was actively engaged in battling the Soviet Union in a variety of Third World hotspots from Afghanistan to Africa and Central America. As part of the same strategy of active opposition and confrontation, the Reagan administration launched major efforts to restrict foreign access to U.S. technology. The scientific community worked very hard to carve out basic research as an area where such restrictions would not be put in place since science could only advance effectively if basic research was freely and openly available. The result of the science community's lobbying was the seemingly benign directive cited above.

The Bush Administration noted in November 2001 that it continues to support this policy and will ensure that it is followed. Unfortunately, this assurance is not as helpful as initially thought, since the last seven words of the directive—"except as provided in applicable U.S. statutes"—have become a key tool for the imposition of restrictions on basic research (in seeming contrast to the clear language of the directive) in the post-9/11 era.

It turns out that a number of federal agencies are using "applicable U.S. statutes" to restrict publication or foreign student access to research produced under certain contracts, and the practice is growing. The task force report notes that at least 105 research awards include language that restricts publication of results or the access of foreign nationals to the research. While many of these restrictions are found in Department of Defense contracts (as might be expected), a wide variety of federal agencies, including the National Science Foundation and the Department of Health and Human Services, also include such restrictions in at least some of their contracts.

The problems for academic research are several. First, the Department of Defense, for example, often requires that contractors not disseminate any unclassified information generated by the contract to anyone outside the contractor's organization. This means that unclassified work cannot be published in an open journal. Further, industrial contractors sometimes subcontract work to universities, and routinely include such restrictions in the subcontract to the university if the company has to comply with the restriction itself.

However, it is not jut companies passing along such restrictions. Depending on the research involved, the DoD sometimes requires universities to comply with this language when they are the contractors. A few universities have turned down contracts containing this language. However, most have not.

A second problem is related to students at universities. Thousands of foreign nationals study science and engineering at American universities, and if a researcher has a contract that restricts foreign student access to unclassified information generated from the work, the researcher could be in a situation where one student could work on the project, but another student sitting beside the first could not.

Continued on next page

Research!America Ads Promote Investment in Science

This spring, Research!America, in partnership with the Universities Research Association, Inc., and the Science Coalition, launched an advertising campaign to promote the importance of investment in the basic science. The campaign consisted of ads in the Washington Post, a medium selected because it is considered a must read by Washington policy makers. The theme of the advertising was:

Research in Basic Science Brings Innovations That Improve Our Lives … like MRI. Science is an important investment for America, even when government resources are scarce.

The ads noted that in the twenty-first century, scientific discoveries affect how we live, how we work, how we communicate with the world around us. Yet scientists did not set out to develop many of these now vital technologies. The history of science is rich in stories of how the study of very abstract concepts gave rise to unanticipated major technological advances. In the 1600s, Isaac Newton questioned why objects move and the best way to describe their motion. He introduced a new and abstract concept called gravity and pondered how it could reach across space, even to the planets and stars. His questions became key to mechanical engineering, the use of satellite observatories, the understanding of the geology of our planet and to flight.

The most powerful, yet non-invasive, diagnostic tools of the twenty-first century provide doctors immediate access to detailed images of their patients' bodies. Scientists did not set out to invent MRI, it emerged by applying knowledge learned through our commitment to fund basic scientific exploration. What began as solely laboratory based phenomena evolved into the invention of new tools for the diagnosis and treatment of disease. Today, magnetic resonance imaging (MRI) scans are able to look at the size and shape of organs and body structures, allowing doctors to identify strokes, soft tissue injuries and tumors quickly and prepare a medical response.

ASBMB is a supporter of Research!America.

Troublesome Clauses continued …

Continued from page 5

Obviously, in an academic setting, restrictions on publication and foreign access to otherwise unclassified research findings are unfair, impractical, and not helpful to the advancement of science.

The AAU/COGR report therefore recommends that agencies "adhere to the spirit" of NSDD 189 and "not impose publication and foreign national restrictions" in research contracts. The report also recommends that a distinction be drawn between basic, fundamental research such as that typically done at universities, and the developmental and commercialization work typically done in industry. Further, industry should be instructed in these distinctions, and told they are not required to pass along restrictions that they must deal with when they subcontract work to universities (if the work is basic in nature).

The AAU/COGR report can be found at: www.aau.edu/research/Rpt4.8.04.pdf

The ASBMB Public Affairs Advisory Committee and staff is monitoring this little noticed problem, and would appreciate any information or comments that researchers reading this article may have on the issue. Please contact the Society's public affairs officer, Peter Farnham, at pfarnham@asbmb.org

Top 25 Institutions Receiving NIH Awards in FY 2003

Listed below in rank by dollar amount, are the top 25 institutions that received NIH awards in Fiscal Year 2003. For a complete listing of all institutions receiving awards, the number of awards and total amounts, including training grants, fellowships R&D contracts, and other awards, go to the NIH website.

Rank	Organization	All Awards	Research Grants	R&D Contracts
1	Johns Hopkins University	$414,225,650	$371,244,640	$21,749,426
2	Washington University	368,355,293	341,702,460	10,822,788
3	University of Pennsylvania	359,944,311	331,165,125	991,169
4	University of California San Francisco	350,786,145	305,890,184	28,925,060
5	Duke University	305,405,308	271,877,809	9,292,482
6	University of Washington	290,097,322	266,524,625	1,904,512
7	University of California Los Angeles	264,873,857	247,471,696	8,673,963
8	Yale University	261,706,751	236,996,674	3,347,436
9	University of Pittsburgh	258,276,361	227,703,969	5,268,268
10	Baylor College of Medicine	246,410,097	222,205,006	15,001,107
11	University of Michigan	241,388,940	216,969,254	5,266,169
12	Stanford University	235,522,176	214,966,069	3,859,036
13	Boston University	232,179,841	97,942,051	0
14	Columbia University	220,316,305	199,261,122	4,078,040
15	University of California San Diego	219,646,784	198,583,224	9,900,030
16	University of Alabama at Birmingham	208,229,354	159,169,432	23,901,670
17	Vanderbilt University	205,896,115	188,634,437	1,027,999
18	Case Western Reserve University	203,512,407	183,123,959	13,455,976
19	University of Texas at Galveston	202,863,845	76,952,533	13,262,508
20	University of North Carolina Chapel Hill	199,091,797	174,300,048	14,761,483
21	University of Texas at Dallas	173,839,840	152,430,428	14,890,525
22	University of Colorado Health Science Center	165,148,917	154,913,439	1,688,428
23	Emory University	158,120,873	149,337,231	2,626,946
24	New York University Mount Sinai School	155,959,314	146,615,860	3,028,990
25	University of Chicago Pritzer School	153,751,372	137,973,565	5,167,185

Staying on the Path; One Atom at a Time

New percolation model may allow researchers to study biochemistry at the atomic level.

A report in the May 24 *Proceedings of the Royal Society of London. Series A: Mathematical and Physical Sciences* announces a mathematical model that will help researchers understand cell signaling and learn how single atoms travel along the circuitous pathways in a cell.

The model is a new approach to look at percolation-the flow of a liquid or small particle through a porous material. In the simulation, materials pass through fields of complex, three-dimensional shapes, a scenario that is closer to realworld environments than existing two-dimensional models and models incorporating simpler shapes.

The model was developed by Dr. Ann Marie Sastry and Dr. Yun-Bo Yi, both of the University of Michigan. The researchers will use their findings in a larger study that will deploy sensor proteins inside a cell where the nanoscale devices will track the paths of ions.

The model reveals how the sensors might interact with the miniscule ions that contribute to such diseases as stroke, cardiovascular disease and cancer. With the proper experimental design, the researchers may be able to watch fundamental chemical reactions, at the molecular level, as they occur in living cells.

In addition to biological applications, the simulation will help researchers develop new materials by revealing better ways to craft porous substances. By understanding the properties of these types of materials, researchers can enhance conductivity in batteries, flow paths in filters and numerous other percolation mechanisms.

Clusters of two, three and four permeable ellipsoids, generated from the percolation simulations of Yun-Bo Yi and Ann Marie Sastry. Credit: Yun-Bo Yi and Ann Marie Sastry, University of Michigan

Sastry won a 1997 NSF Presidential Early Career Award for Scientists and Engineers (PECASE), the highest honor bestowed by the United States government on scientists and engineers beginning their independent research careers. The NSF support from that award contributed to the development of the percolation model.

Support for the work was also provided by the Defense Advanced Research Projects Agency (DARPA) and the Office of Naval Research through the Synthetic Multifunctional Materials Program, managed by Leo Christodoulou of DARPA, and the W.M. Keck Foundation.

"With her PECASE award, Ann Marie Sastry has expanded her research focus from a single area in mechanical engineering, materials processing, into a broad exploration to uncover fundamental knowledge. She has demonstrated an ability to take advantage of support to move beyond her own initial training and move out to address societal needs," said Delcie Durham, Program Pirector in NSF's Division of Design, Manufacture and Industrial Innovation who oversaw Sastry's five-year award. "Because of her interests and abilities, Sastry has attracted a diverse team of students and guided them to address core areas within mechanical engineering. Sastry has expanded her research to address fundamental issues in mathematics, biology and energy."

The researchers will use their findings in a larger study that will deploy sensor proteins inside a cell where the nanoscale devices will track the paths of ions.

New Research at UNC Shows Ribosomes Do Not Function as Conventional Enzymes

Contrary to what some scientists have suggested, key intracellular particles known as ribosomes serve as mechanical matchmakers or readout devices rather than acting chemically to speed up reactions in the body the way enzymes do, University of North Carolina (UNC) at Chapel Hill researchers have discovered.

A report on the findings by Dr. Annette Sievers and Dr. Richard Wolfenden* of the UNC School of Medicine appears in the May 2004 issue of the *Proceedings of the National Academy of Sciences*.

"Enzymes, of which we have hundreds, participate chemically in the transformation of biological molecules by making and breaking bonds," said Wolfenden, Alumni Distinguished Professor of Biochemistry and Biophysics. "A hallmark of that direct chemical involvement is that their catalytic effects are extremely temperature dependent. The question was whether the ribosome acts as an enzyme, since there has been considerable interest in whether this particle does that."

Ribosomes are critical sites of protein synthesis, he said. Inside those particles, amino acids are laid down in proteins in the order specified by the genetic code. In general, enzymes, which are biological catalysts, facilitate a chemical transformation by lowering the energy barrier, said Dr. Sievers.

"In our present work we tested the contribution of enthalpy and entropy to lowering the activation energy barrier," she said. This was done by comparing the energy barrier of the reaction when the ribosome was present, and when the ribosome was not present. The reactions both with the ribosome present and without the ribosome have the same enthalpic activation barrier, the researchers found.

"The means by which the ribosome speeds up the chemical transformation is purely entropic in origin; the ribosome acts as a mechanical readout device, rather than speeding up the reaction in the way that conventional enzymes do," Dr. Sievers said.

The experiments will help scientists narrow their view of how ribosomes function and understand them better, Wolfenden said. This discovery has important implications for the design of inhibitors of protein synthesis and might ultimately furnish a new basis for drug design. It shows that the ribosome's effect is to introduce order into chaos.

*ASBMB member.

NAS Seeking Nominations For Science Awards

The National Academy of Sciences (NAS) is currently accepting nominations for three separate awards for excellence in scientific achievement. Nominations for all three awards will be accepted through September 10, 2004.

Richard Lounsbery Award
The Richard Lounsbery Award, a prize of $50,000, is presented to young (to 45 years of age) American and French scientists to recognize extraordinary scientific achievement in biology and medicine. The award is intended to stimulate research and to encourage reciprocal scientific exchanges between the United States and France.

NAS Award in Molecular Biology
The NAS Award in Molecular Biology, a prize of $25,000, is presented to a young scientist (35 to 45 years of age) for a recent, notable discovery in molecular biology.

Selman A. Waksman Award in Microbiology
The Selman A. Waksman Award in Microbiology, a prize of $5,000, presented for excellence in the field of microbiology.

For more information on these awards, contact:
National Academy of Sciences
Awards Program, Room NAS 285
500 Fifth Street, NW
Washington, D.C. 20001
Phone: 202-334-1602
Fax: 202-334-1682
E-mail: awards@nas.edu
Web: www.nas.edu/nas/awards

Views from ASBMB 2004

More to come in August!

First annual Herbert Tabor/Journal of Biochemistry Award, was presented to Robert Lefkowitz (center) by Bruce Thomas, President and CEO of Cadmus, at right. JBC Editor Tabor is at left.

Above: Over 70 posters were entered in the ASBMB Undergraduate Poster Competition and more than 200 in the Graduate Competition.

ASBMB's Past-President Bettie Sue Masters was surprised with birthday cake during reception at Annual Meeting.

Minority Affairs Committee meeting was attended by Phillip Ortiz, Thomas Landefeld, Gail Pinder of ASBMB staff, Juliette Bell, and Jacquelyn Roberts of FASEB.

ASBMB booth was active site on the exhibit floor.

In One Era

A Message from the New President of the ASBMB

– *Judith S. Bond*

It is with pleasure and anticipation that I assume the presidency of our Society in July 2004. Because the President serves a two-year term, I will be the last president of the first century of the Society and the first president of the Society's second century. What an honor it is to serve in these transitional years! It will be a time to celebrate our history, growth and member accomplishments, to plan strategies for the second century, and to move ahead into the future with newly defined goals. There are already many activities being planned for our centennial celebration in San Francisco in April 2006, initiated under the outstanding leadership of Bettie Sue Masters.

The Society underwent an important transition this year when Chuck Hancock retired as Executive Director after 24 years of exceptional service. After a thorough and extensive search, Barbara Gordon was chosen to be our Executive Director, and assumed that position in April 2004. Many of you know Barbara because she as been associated with the ASBMB for 32 years; in the capacity of Assistant to the Editor of *The Journal of Biological Chemistry (JBC)* since 1987, Director of Publications since 1994, and Deputy Executive Officer since 1996. Barbara is uniquely qualified to take the helm as Executive Director because of her extensive experience with ASBMB publications, meetings, council and committee work. Her energy, understanding of the organization, and commitment to the Society are exemplary. The Society did not lose a beat in the transition to new staff leadership. Barbara has already hired Joan Geiling to fill a vacancy in meetings management, a science writer,

Out the Other

Nicole Kresge, and is in the process of identifying a person to replace herself as Director of Publications. Barbara and her staff of 20 in the ASBMB office are crucial to our Society's success and the implementation of the new goals that we set during the coming years.

We have much to be proud of in our Society, such as the quality of our publications, our leadership role in online publications, the professional success of our members, the outreach of our members to the next generation of scientists, and our advocacy efforts to inform decision makers of the importance of our science. Our Society's mission is:

"Promoting understanding of the molecular nature of life processes"

We represent the discipline of Biochemistry and the technologies of Molecular Biology, which are fundamental to all the life sciences, and define the universal language of the life sciences. It is clear that what we do as biochemists and molecular biologists overlaps and benefits other branches of science. Our Society must adapt to the environment in the age of interdisciplinary and multidisciplinary science, and be true to the mission of promoting understanding of the molecular nature of life processes. We are committed to promulgating advances, bringing in new people and ideas, and communicating our message to the public, leaders, and the next generation of scientists. Our members have inquisitiveness about the molecules that make up living systems, their regulation, function and interactions. We represent a basic science that is driven by curiosity, sometimes considered 'untargeted,' and one that spans a multitude of systems from the prokaryotic, archea and eukaryotic world, and from small molecules to multicomponent complex "omes" (e.g., genome, proteome, lipidome, glycome, metabonome).

Our flagship journal, *The JBC*, has very clearly defined its scope, and advises authors that: "Manuscripts failing to deal with biological processes at the biochemical or molecular level are usually inappropriate for *The Journal*. In the absence of novelty and significance, medical relevance or pharmacological potential will not be considered sufficient justification for publication." Thus, the Society through the Journal stresses biochemical and molecular biological insights and mechanisms, not the translation of these underlying insights into medical, pharmacological, or agricultural advances.

Basic science is essential to the foundation of many practical advances, but this is not always obvious to the public and policy makers. In my own field of proteases and their substrates, I can think of many examples in which basic science has led to unanticipated commercial developments. One example of this is the development of inhibitors to the HIV protease for the treatment of AIDS. I recall an international meeting in the 1980s on aspartic proteases (endopeptidases that depend on an aspartic residue for their catalytic activity). At that meeting, many of my colleagues were expressing concern that it was increasingly difficult to obtain funding to investigate the mechanisms and regulation of aspartic proteases (enzymes such as cathepsin D and E). Only a very small subset of investigators was interested in this subgroup of enzymes, and there were no obvious immediate utilities. Not long after that meeting, the world became aware of AIDS and HIV, a virus that depends on an aspartic protease to replicate, and the rapid and uncontrolled spread of the disease in many parts of the world. It was because of the great wealth of basic science knowledge on the structure and function of these enzymes that scientists could move rapidly to develop inhibitors of the AIDS virus protease, and capitalize on the difference of this protease to the mammalian aspartic proteases. This is just one example of how basic science can lead to treatment of a disease.

Over the course of my professional career, I have observed many examples of how science progresses, and how technology, communication, collaboration and curiosity drives science. My personal scientific contributions illustrate this.

In the early 1980s meprins, zinc endopeptidases, were discovered in my laboratory when a colleague from England, Robert Beynon, came to work

Two presidents:ASBMB's Judith Bond and Pennsylvania State University President Graham Spanier.

with me at the Medical College of Virginia of Virginia Commonwealth University. I had met Rob at an international conference on proteases, and through discussions we realized that we had common interests in cell-associated proteases and protein degradation. Meprins were discovered as azocasein-degrading proteases of the rodent kidney because of my interest in the regulation of proteases in diabetic mice, and Rob's use of azocasein as a good substrate for proteinases that act at neutral and basic pH values.

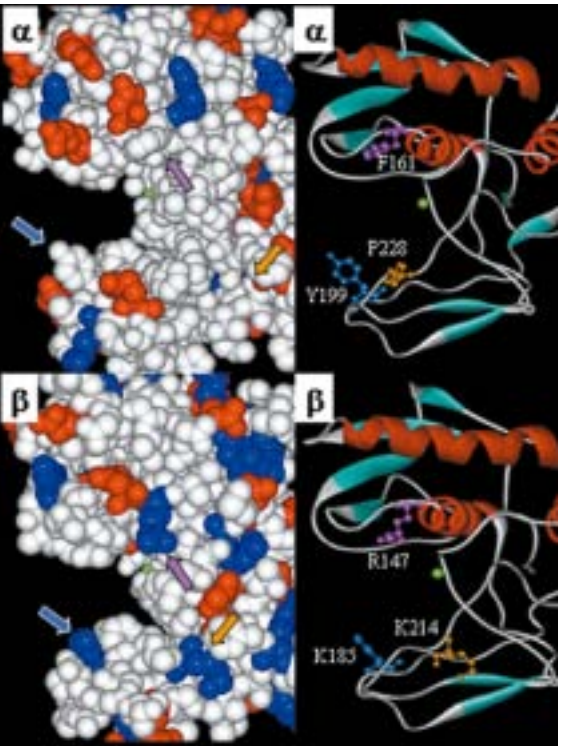
When we discovered a very high proteolytic activity in Balb/c mouse kidney using this substrate, and could not find evidence for this activity in the literature, it was curiosity that led to purifying and characterizing the membrane-associated enzyme. A few years after the discovery of meprins, we found that some inbred strains of mice (the Strong C strain of mice, such as C3H/He and CBA mice) had very low levels of kidney azocasein-degrading activity. This observation resulted in a collaboration with a mouse geneticist, Chella David, who recognized that one of the genes for meprins was linked to the histocompatibility complex on mouse chromosome 17. It was communication and collaboration, again, that led to this insight.

Through other collaborations the genes for the α and ß subunits of meprins were mapped in the mouse and human genomes, and the enzymes were visualized as brush border enzymes using electron microscopy. In the late 1980s and early 1990s, my trainees, colleagues (including Erwin Sterchi) and I applied the technologies of molecular biology and cloned and sequenced the mouse and human meprin subunits. Using the rapidly expanding information in protein databases, we discovered that meprins were members of an evolutionary family that we named "the astacin family of metalloproteinases." Astacin, a crayfish enzyme, is one of the smallest members of this family, and to date is the only member of this family that has been crystallized.

Meprins are quite complex multidomain, multimeric enzymes that are highly glycosylated. There are membrane-bound and secreted forms that tend to self-associate and form some of the largest proteolytic complexes seen in living systems, 1 to 6 MDa. Meprins are capable of hydrolyzing biologically active peptides such as bradykinin, gastrin, and angiotensin, cytokines and chemokines such as MCP-1 and osteopontin, and proteins such as fibronectin, collagen IV, and gelatin. Through collaboration we have constructed homology models of meprin active sites and determined amino acids critical to the different proteolytic activities of the subunits.

More recently we and others have found that meprins are upregulated in certain cancer cells and in leucocytes during intestinal inflammation. One of the subunits has been suggested as a candidate gene for diabetic nephropathy, and the other subunit implicated in ulcerative colitus. Meprins are also implicated in tumor cell metastasis, and thus we are beginning to ask how they can be down-regulated and inhibited. The basic science has led to science that has potential targets for disease, and perhaps this will lead to translational research, from bench to bedside.

My story illustrates too that we as individuals wear many hats and can be identified with many different types of research during the course of a career, as independent scientists, members of a team, or through collaboration. Members of our Society are not only biochemists and molecular biologists, but also pharmacologists, immunologists, microbiologists, geneticists, bioinformatics specialists, developmental biologists, physicians, plant physiologists to name a few. We have in common an interest in promoting the understanding of the molecular nature of life processes, but we use many different approaches and sys-



Critical amino acid differences within the active site of meprin a and ß metalloproteinases for substrate and peptide bond specificity. The top panels are homology models in space filling (left) and ribbon (right) representations of the protease domain of mouse meprin a based on the crystal structure of crayfish astacin. For the space filling representations acidic residues, Asp and Glu, are red, basic residues Lys and Arg, are blue; all other residues are white. The zinc located in the center of the active site is green. For the ribbon representation α-helices are red and ß-sheets are cyan. The bottom panels contain the corresponding representations for mouse meprin ß. Active site electrostatic differences are denoted by arrows in space filling models and are numbered in ribbon representations. (from J Biol Chem 278:42545-42550)

Bond Laboratory Group: Seated (from left to right): Susan Senchak, Sanjita Banerjee, Bond, Xiaoli Han; Standing (left to right): John Bylander, Renee Dusheck, Bill Patrie, Ryan Gailey, Gail Matters

tems to accomplish our aims and advance science.

This brings me to the topic of how our Society intends to grow and develop, and to address some of the issues and challenges we face. The leadership of the Society intends to undertake strategic planning in the fall of 2004, and to set the agenda for the coming years. However, let me briefly mention issues that I see confronting us as a Society. They generally fall under: publications, membership, meetings, public advocacy, education.

Publications: The first and most important issue is maintaining and improving the quality and impact of our journals. This is a topic that Editors and Associate Editors of our Journals, along with our Publications Committee will be addressing. In addition, it is important that we build on the strength of our publications and our leadership in online, accessible publication. *The JBC* was the first biomedical journal to publish online in 1995. All *JBC* articles are now accessible online back to the first issue in 1905, and articles are freely accessible the day they are accepted for publication. We are in the transition from total print to total online publication, and there are significant questions as to how the journal will be sustainably financed and archived once there are no print journals. The Society also made a decision several years ago, to publish a new journal (*Molecular and Cellular Proteomics*), to acquire the *Journal of Lipid Research*, and to publish *Biochemistry and Molecular Biology Education* (*BAMBED*) in collaboration with the International Union of Biochemistry and Molecular Biology. The new journals are establishing a constituency and their own niche, and will also need to find the right formula for financial sustainability.

Membership: The Society has increased its membership to 12,000 at about 10% per year for the last few years. It will be important to determine how we wish to grow, and particularly how to recruit the next generation of scientists and diverse populations. A survey of the membership several years ago indicated that the great majority our members are at American academic institutions. Many of the new scientists are engaged in diverse enterprises such as biotechnology companies, industrial companies, government agencies and foreign institutions. As the authors of manuscripts in our journals are increasingly international, there is the possibility of increasing numbers of foreign members of our Society. Do we want to encourage membership of other groups not traditionally members of our society, such as college and high school teachers?

Meetings: The Society currently sponsors the annual meeting (usually but not always with the FASEB) and small meetings. Because there are so many meetings available to scientists, the question becomes what role should the Society play in sponsoring meetings. Meetings are important for our mission and developing a community of scientists. But the Society will have to determine what type of meetings best serve our members and fulfill our mission.

Public Advocacy: There are multiple issues of interest to our members in the public arena these days, including funding issues (especially governmental), regulatory issues (cloning, stem cell, animal rights, compliance), and evidence-based decision-making. Our Society will no doubt want to continue to inform governmental leaders about issues that directly affect us, and work with other agencies such as the FASEB. What mechanisms are most effective?

Education: The Education and Professional Development Committee has made great strides in setting up networks with undergraduate faculty and students for curriculum development and for interactions with our Society. How do we want to expand on this? Do we want to reach down to elementary and high school education, as well as support career development for graduate students and postdoctoral fellows?

This is a healthy Society. We have a clear mission, are in a financially sound position, and are growing in membership. In my positions as a Chair of a Biochemistry and Molecular Biology Department, an Associate Editor of the JBC, and an active researcher, I have a personal interest in all the major activities of the Society and want to see the Society flourish. I promise to work diligently with the Council, Staff, Editors, and Committees of the Society to take us into the next century of the Society with a clear vision. We will develop a strategic plan this fall, and implement the plan over the coming years. Together we can do so much more than we can do as individuals.

Insulin-Producing Pancreatic Cells

Howard Hughes Medical Institute (HHMI) researchers at Harvard University have discovered that insulin-producing beta cells in the pancreas that are attacked in type 1 diabetes are replenished through duplication of existing cells rather than through differentiation of adult stem cells.

Although the experiments, which were done using mice, do not rule out the possibility that there are adult stem cells in the pancreas, the researchers say that they do suggest strongly that embryonic stem cells or mature beta cells may be the only way to generate beta cells for use in cell replacement therapies to treat diabetes.

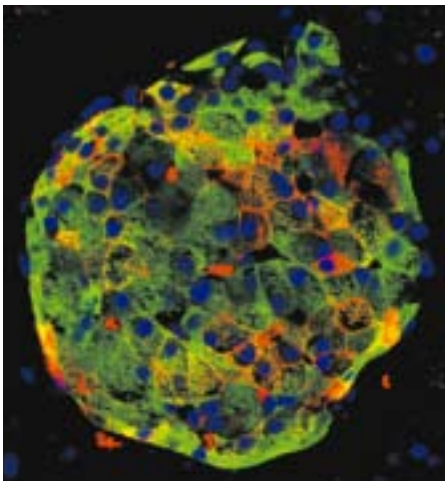
The research team, which was led by HHMI Investigator Douglas A. Melton* at Harvard University, reported its findings in a research article published in the May 6, 2004, issue of the journal Nature. Melton's co-authors include Yuval Dor, Juliana Brown and Olga I. Martinez, all of Harvard.

In cell culture, embryonic stem (ES) cells retain the properties of undifferentiated embryonic cells. ES cells have the capacity to make all cell types found in an adult organism. One of the most hotly debated questions in biology is whether adult stem cells, which have been isolated from blood, skin, brain and other organs, have the same developmental capacity as ES cells.

Researchers have known for some time that ES cells can give rise to pancreatic beta cells during development. "But the more interesting question for us has been what happens in mature pancreatic tissue to both maintain the pancreas and to regenerate it," said Dr. Melton. "Previous studies have suggested that there are sources of adult stem cells that might give rise to beta cells. However, those studies had largely depended on histological `snapshots' of tissues." Those snapshots can only suggest the "geographic" origin of new beta cells and not the identity of the cells from which they arise, he noted.

Dr. Melton and his colleagues knew that they could finally put such questions to rest if they could tag beta cells in such a way that that they could determine unequivocally whether the new cells were made from existing beta cells or from a different reservoir of stem cells. For these studies, they devised a "genetic lineage tracing" technique that involved engineering a mouse whose beta cells contained a telltale genetic marker that could be switched on by administering the drug tamoxifen to the mice.

The logic behind the technique is relatively straightforward: When the researchers administer a pulse of tamoxifen to the adult mice, Cre recombinase is induced transiently and removes a "stop" sequence from an alkaline phosphatase reporter gene, allowing it to be expressed. They can easily follow the marker to determine whether it is inherited by subsequent generations of beta cells. If it is inherited, then the cells expressing the marker are the offspring of pre-existing beta cells.



©2004 Yuval Dor, HHMI at Harvard University

A pancreatic islet, in which a subset of beta cells have been marked in red to trace their genetic lineage. Insulin appears as green and DNA has been stained blue.

When the researchers applied their technique to the mice, they discovered that all the new beta cells they examined — whether arising in the usual process of renewal or during regeneration following partial removal of the pancreas—were generated from pre-existing beta cells. According to Dr. Melton, the finding highlights a largely unappreciated capability of beta cells.

Replenished by Duplication

"No one has really paid much attention to the replicative capacity of the beta cell," he said. "And this work shows the cells to have a significant proliferative capacity that could be clinically useful."

According to Dr. Melton, the findings might have implications for developing treatments for type 1 diabetes, a disease that destroys beta cells. "If such people have residual beta cells, these findings suggest that a useful clinical direction would be to find a way to boost the proliferative capacity of those beta cells, to restore insulin production in such patients.

"On the other hand, if type 1 diabetics don't have any beta cells left, then these findings suggest that the only source of new beta cells is probably going to be embryonic stem cells, because there don't appear to be adult stem cells involved in regeneration."

He emphasized that although the results by his group cannot rule out the existence of beta-cell-producing adult stem cells, "they raise the bar on trying to demonstrate their existence. In these experiments, we find no evidence for the existence of adult pancreatic stem cells."

The genetic lineage tracing technique devised by the group is a tool that can now be used to trace the origin of cells involved in the maintenance and repair of other types of tissue. Dr. Melton and his colleagues are now using this technique to determine the origin of new cells in lung tissue, and they believe it should be possible to apply the technique to understand the origin of cancer cells in tumors or to understand the role of stem cells in such malignancies.

** ASBMB member*

A New Spin on

Three centuries after a pioneering Dutch microbiologist first observed the spiral-shaped oral pathogen *Treponema denticola*, scientists have deciphered the bacterium's entire DNA sequence and used comparative genomics to cast new light on other spirochete microbes.

The study by scientists at The Institute for Genomic Research (TIGR) and collaborators at Baylor College of Medicine and the University of Texas Health Science Center at Houston found profound differences between the gene content of *T. denticola*, which is associated with periodontal (gum) disease, and of other spirochetes that cause syphilis and Lyme disease.

"This highlights the power of comparative genomics to help us understand how related pathogens can cause completely different diseases," says Ian Paulsen, who led the sequencing along with fellow TIGR researcher Rekha Seshadri. Dr. Paulsen says the *T. denticola* genome "provides an excellent point of reference to study the biology of spirochetes."

The paper appeared in the April 13, 2004, issue of *Proceedings of the National Academy of Sciences (PNAS)*. The study was supported by the National Institute of Dental and Craniofacial Research (NIDCR), which is part of NIH.

The researchers found that *T. denticola* has more than twice as many genes as the spirochete that causes syphilis, *T. pallidum*, and that there is virtually no conservation of gene order (synteny) between the genomes of the two related microbes. The authors say that indicates that the two spirochetes' divergence from a common ancestor "was an ancient event" in contrast to the more recent divergence of many other groups of bacteria from their ancestral relatives.

The genome study is expected to help scientists find out more about how oral pathogens interact in dental plaque to cause gum disease. *T. denticola* tends to aggregate in such subgingival plaque with Porphyromonas gingivalis, a bacterium that is associated with periodontitis, a gum disease that affects an estimated 200 million Americans. Having the complete genomes of both microbes will help researches study their interactions and possibly provide molecular clues to find targets for drugs to treat gum disease.

TIGR scientists and collaborators sequenced the genome of *P. gingivalis* last year and are now deciphering the genomes of six other oral-cavity bacteria and conducting a "meta-genomic" assay of mouth microbes. Of the estimated 500 microbial species in the human mouth, only about 150 species have been cultured in laboratories.

"The genome sequence reveals mechanisms used by *T. denticola* to colonize and survive in the complex environment of oral biofilms," says Dr. Seshadri, the study's first author. TIGR's collaborators in the PNAS study included Dr. Steven J. Norris at the University of Texas Health Science Center at Houston and Dr. George M. Weinstock* at Baylor College of Medicine's Department of Molecular and Human Genetics.

In the PNAS paper, researchers reported that the genome of *T. denticola* "reflects its adaptations for colonization and survival" with other bacteria in plaque. Compared to

ASBMB Welcomes New Ph.D.s

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

Gregory J. Carven
Massachusetts Institute of Technology

Gustavo A. Nader
University of Illinois at Chicago

Jennifer Palenchar
University of Delaware

Peter R. Panizzi
Vanderbilt University School of Medicine

Anna Seibert
State University of New York Buffalo

Zarixia Zavala-Ruiz
Massachusetts Institute of Technology

In our June issue, **Shawn Sweeney** was incorrectly listed as receiving a Ph.D. from University of Texas, A&M University. The degree was from Thomas Jefferson University.

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

Spirochetes

other spirochetes (including an estimated 60 other treponomal species or phylotypes found in dental plaque), *T. denticola* is relatively easy to cultivate and manipulate genetically, making it an excellent model for spirochete research.

Spirochetes are distinguished by their spiral shapes and their ability to corkscrew their way through gel-like tissues, causing a number of different diseases. The father of microbiology, Antonie van Leeuwenhoek, had first sketched an oral spirochete—later named *T. denticola*—after viewing it through his primitive microscope in the 1670s. Even after three centuries, however, spirochetes are poorly understood in contrast to many other major types of bacteria.

So far, TIGR has sequenced the complete genomes of three spirochetes: *T. denticola*, *T. pallidum*, which causes syphilis; and *Borellia burgdorferei*, which causes Lyme disease. The genome of a fourth spirochete, *Leptospira interrogans*, which causes Leptosporisis, was sequenced at the Chinese National Human Genome Center.

TIGR's comparative analysis found that about half of *T. denticola*'s 2,786 genes are not present in the other three sequenced spirochetes. The 618 genes that all four spirochetes have in common include some that are not found in other microbes whose genomes have been sequenced.

Claire M. Fraser,* TIGR President, says the sequence data "provide a new starting point" for exploring the molecular differences that may explain why and how *T. denticola* and *T. pallidum* cause such different diseases: "This study has revealed new insights into spirochete-specific biology as well as the evolutionary forces that have shaped these genomes."

* ASBMB member

by John D. Thompson, Editor

Report Finds Brighter Prospects For Biotech in the U.S., Asia

After some four years of an up-and-down relationship with investors, the biotech business in the United States—and possible Asia, too—is back in the good graces of the investment community.

The Ernst & Young accounting and consulting firm reports that the 1,437 biotech companies in the U.S. raked in $14.4 billion in new investment money last year. That, according to the report released last month, is some 66 percent more than investors put into biotech in 2002. That helped raise the industry's market capitalization by more than 50 percent to almost $300 billion by the end of 2003. During that year, seven U.S. biotechs carried out initial public offerings (IPOs), and Scott Morrison, head of U.S. Life Sciences at Ernst & Young, expects as many as 30 such companies to have gone public by the end of this year.

Why this return to favor in the investment community? As usual, money follows money. The total revenue of publicly-owned biotech firms hit almost $36 billion last year, and Ernst & Young predicts that at this rate the publicly-owned biotechs actually be in the black by 2008. These firms, the consultants note, have already produced several billion-dollar pharmaceutical blockbusters and are on the road to delivering more. Last year 25 biotech drugs won FDA approval, and another 300 are in the final stages of the approval process.

Some of this productivity reflects deals with major pharmaceutical companies which need to pump life into sluggish development pipelines, as well as a trend on the part of the biotechs to refocus their business strategy.

Meanwhile, the fledging biotech industry in Asia is on a rapid growth curve. Ernst & Young estimates that there are some 660 biotech companies in the Asia-Pacific region, the bulk of them in Australia, China, India, Japan, and Singapore. The total is small compared to that in the U.S., but the Asians are beginning to establish themselves as rivals in such niches as drug screening biotech-drug manufacturing.

In contrast, the picture in Europe is on he bleak side. Venture financing dropped by 10 percent last year, and Ernst & Young predicts that the Europeans will continue to fall behind the U.S. unless they learn how to get more drugs to the market faster. In *The Economist's* words, "There is an urgent need for consolidation to build critical mass" in order to gain a competitive edge.

Importing a Fight With Boston's

This month, Boston is set to become the largest city in the U.S. to make it easy for public employees to buy imported pharmaceuticals. Boston's move coincides with a proposed bill in the Massachusetts Legislature that would permit the state's residents to seek federal permission for a website with links to Canadian internet pharmacies. However, this has drawn criticism from biotechnology executives. They say importing cheaper drugs will eat into profit and divert funding from fledgling drug companies.

With many drugs selling for 20 to 80 percent less in Canada due largely to government price controls there, several U.S. cities already import drugs for residents or employees even though the FDA considers such programs illegal. Springfield, Massachusetts, has has had such a program for a year, reportedly saving taxpayers $2 million; and Montgomery, Alabama, and Burlington, Vermont, also have import programs.

A statewide importation plan in Illinois is on hold pending a change in the FDA's stance, but Minnesota and Wisconsin have already set up websites that guide residents to approved Canadian pharmacies, and Rhode Island's state website links to Wisconsin's.

Massachusetts is home to more than 280 biotechnology companies–three times as many as 10 years ago–with the vast majority concentrated in Boston and Cambridge, where start-ups such as Genzyme Corp. and Biogen Inc. have grown to become some of the industry's largest and most profitable firms. Drug giant Novartis AG moved its research headquarters to Cambridge, the city across the Charles River from Boston

Biotech Leaders Express Concerns At Industry's Annual Meeting

While the newly released Ernst & Young Report sees bright prospects for biotech in the U.S. and Asia, industry leaders at last month's Biotechnology Industry Organization annual meeting expressed concerns about public support for biotech, investor pressure for short-term profits, and increased competition with large pharmaceutical companies.

The consenasus of four top executives who spoke at the meeting, was that the industry needs to become more open and willing to educate the public about biotech."We're doing a terrible job of communication," said Chireon CEO Howard Pien. He also pointed to challenges to innovation, the possibility of generic biologics, and restrictions on stem cell research.

"We tend to be too scientific and clinical," said James C. Mullen, Biogen Idec's CEO, who urged the industry's leaders to increase their presence in the public debate about biotech. "It's got to be a discussion that brings the science, but marries it to other issues, such as cultural values."

Dennis M. Fenton, Executive Vice President of Amgen, said his greatest concern for the industry is the push for lower prices by government and health insurers that might diminish patient choice. "We're moving to an environment where drugs must not only be safe and effective, but also cost effective," he stated. Fenton also noted the industry's failure to sell many products in markets beyond the wealthy nations of Europe and the United States.

Arthur D. Levinson, Chairman and CEO of Genentech, said the increasing costs of developing drugs may bring biotech firms into direct competition with large pharmaceutical companies looking to biotechnology for new products. He also cited the problem of convincing investors to look beyond the next quarter's financial results and stand by their investments over the long run. Genentech, he noted, had struggled to win investor support to increase research funding that has since paid off in major product approvals.

Biotech Industry

that is home to Harvard University and the Massachusetts Institute of Technology.

Boston Mayor Thomas M. Menino claims that his city can be both a biotechnology powerhouse and an importer of prescription drugs from Canada. However, Massachusetts Governor Mitt Romney (R) and state House Speaker Thomas M. Finneran (D) have both expressed reservations about the impact of importation on the drug industry.

Industry experts have warned that the investment capital that fuels biotech companies' research and development is likely to dwindle if the importation movement accelerates. As the goal of importation is to drive down prices paid by Americans for pharmaceuticals, they say, such plans cut into the potential profit of a successful new drug.

Are the Belgians Coming?

Earlier this year it was the French worrying about a foriegn invasion, when Switzerland's Novartis was trying to buy France's Aventis. Now biotech industry watchers in the UK are concerned about a Belgian invasion thanks to UCB's £1.5 billion ($2.7 billion) bid for Britain's second largest Biotech company, Celltech.

Celltech, which had sales of £353 million ($635 million) last year has an anti-arthritis drug due to go on the market in 2007, which it looks for to add another £600 million ($1,080 million) in sales. Celltech's board is said to be in favor of the Belgian offer, as well it might since it already has licensed marketing rights for the new drug to UCB. Some of the British media, however, have depicted the potential acquisition as a crushing loss with a rising star of the nation's biotech industry being captured by a foreign firm.

That view, however, seems to overlook the fact that a third of the equity in Britain's Celltech is in American hands, namely California's Capital Group and American-owned but Bermuda-based Fidelity.

by John D. Thompson, Editor

Legal Battle Looming Over Generics Issues

The biotech industry, Congress, and the FDA are on the verge of a three-cornered battle over the approval process for generic drugs developed through biotechnology rather than the traditional chemistry-based process.

At issue is the approval process for these drugs, called "generic biologics." The generic equivalents of traditional drugs have been approved as being identical to the original product, and consequently not requiring costly clinical tests in order to gain approval. However, the process of manufacturing biologics creates difficulty in demonstrating scientifically that the active molecules in the biologic product are identical to those in the original. The FDA has said that it will consider approving biologics while reserving the right to require data from clinical tests, but at the same time it is looking to set a more definitive policy. This has been confirmed in congressional testimony by Acting Commissioner Lester Crawford, who said the agency was preparing to release such guidelines

The FDA's move toward setting procedures for the approval of generic biologics has become the subject of industry concern for some time, as it seems to make clinical testing a likely requirement for approval. Last year, the Biotechnology Industry Organization (BIO) filed a challenge to the FDA's legal authority and scientific feasibility of the agency approving biologics under its current procedures. Then, on April 8 of this year, Genentech filed a petition aimed at preventing the FDA from issuing the expected guidelines. Genentech claimed that any such document would necessarily involve the illegal use of proprietary data the company had submitted to the FDA in seeking approval for Genentech products. It charges that FDA approval of generic versions as being compatible with the company's products, would inevitably involve the disclosure of Genentech's manufacturing processes. Subsequent to that filing, Crawford said that the proposed guidelines would only pertain to data in the public domain.

Meanwhile, Senate Judiciary Committee Chair Orrin Hatch (R-Utah) and other influential members of Congress are said to be interested in easing the way for approval of generic biologics. As of this writing, legislation had yet to be submitted, however Congress appears likely to move along a similar track to that of the FDA.

Another factor, though, could be public concern over the rising cost of medication. Conceivably this could lead to a less restrictive policy for the approval of generic biologics. That in turn might bring small- and medium-size biotech companies into the field as competition for the established players.

Upstate Awarded National Cancer Institute Grant In Collaboration With University of Virginia

Upstate, in collaboration with the University of Virginia Health Science Center, has been granted a Phase I STTR (Small Business Technology Transfer) award in the amount of $207,522 by the National Cancer Institute. The grant is to fund initial experiments to develop novel small molecule inhibitors of histone acetyltransferase enzymes (HATs), important regulators of genome function.

Abberant HAT function is common in several types of cancer, and the development of inhibitors to HATs could lead to future progress in cancer therapeutics. Cell signaling, Upstate's core business, is a common theme in cancer research and drug discovery.

The STTR award mandates that work be conducted jointly with a business performing at least 40 percent of the work and a non-profit research institution performing at least 30 percent. Under the grant structure, positive peer reviewed results at the end of Phase I (next year) could lead to an additional grant approval for Phase II and a dramatic increase in funding.

"We are extremely pleased to have this opportunity to work with the University of Virginia Health Science Center on this project. This type of research can lead to the development of novel cancer treatment protocols," said James Bone, Ph.D., a Research and Development Manager for Upstate.

Upstate, a supplier of cell signaling products, technology, platforms and services, is headquartered in Charlottesville, Virginia, and has centers in Lake Placid, New York, and Dundee and Cambridge in the UK.

New UK Center to Focus on Stem Cell Research

A new £16.5 million ($30 million U.S.) stem cell center in Cambridge that was founded by the UK government last month will be committed to fundamental research on both human embryonic and adult stem cells as a step toward studying therapeutic applications.

The new center will be directed by Roger Pedersen, Professor of Regenerative Medicine at Cambridge University, who said that more than half of the research will be on embryonic stem cells.

"This funding comes at a critical juncture in the development of the stem cell field, as the UK builds strength and momentum to take the lead in the international stem cell research effort," he added. "Thousands of people live with the effects of juvenile diabetes, even though they take insulin, and existing therapies for Parkinson's disease, Alzheimer's and multiple sclerosis, also fall far short of a cure. The new Medical Research Council (MRC) Center will help scientists bridge the gap between fundamental stem cell research and clinical application, speeding the delivery of treatments for diseases, many of which are currently incurable, from the lab to the clinic."

In the U.S., Christopher Reeve, Chairman of the Christopher Reeve Paralysis Foundation, commented, "I am delighted to hear from Roger Pedersen that the Medical Research Council will be providing support for a stem cell research center in Cambridge, bringing a world-class team of scientists together under one roof. I believe that research on embryonic stem cells must be taken forward with the utmost urgency, as it is our greatest hope for curing conditions such as spinal cord injury, diabetes and Parkinson's disease that are beyond the reach of current therapies. Stem cell research should lead to the kinds of medical advances that one day will be compared to the development of penicillin, the polio vaccine and the heart transplant."

The United Kingdom has recently passed several milestones in stem cell research. The world's first stem cell bank was formally opened in Hertfordshire in May, with the deposition of two cell lines. In the same month, the Newcastle Centre for Life applied to the Human Fertilization and Embryology Authority for a license to undertake research involving somatic cell nuclear transfer.

Dr. Pedersen, who was drawn to Cambridge from California by the freedom to work on human embryonic stem cells, predicted that his new center will attract a top stem cell researchers from the U.S. who are dissatisfied with the failure of the government to support human embryonic stem cell research. He told *The Scientist* that the stability of the UK's policy on stem cell research will prove more attractive than the potential volatility of U.S. policy which is subject to change depending on which party controls Congress and the White House. There is, he said, no guarantee that any change for the better will not be undone by a future administration.

The UK ProLife Party urged the new center to concentrate on animal, rather than human, embryonic stem cells. "There are still fundamental problems to be solved in animal models, in particular how to control growth of stem cells and stop them forming tumors," a ProLife spokesperson told *The Scientist*.

Pedersen, however, pointed out that while much of the center's early research will be fundamental, it will also address issues of clinical interest already identified by other laboratories, and this requires human stem cells. "We are already starting along that pathway, for example, asking how we make insulin-producing cells for the pancreas," he said.

Calendar of Scientific Meetings

AUGUST 2004

12th International Conference on Second Messengers and Phospoproteins

August 3–7 • Montreal, Canada
Contact: smp2004@eventsintl.com
Website: http://www.secondmessengers2004.ca

FASEB Conference: Transcriptional Regulation During Cell Growth, Differentiation, and Development

August 14–19 • Saxtons River, Vermont
Co-organizers: Barbara Graves and John Tamkun
Go to http://src.faseb.org to fill out online application.
Student travel awards available.

Macromolecular Organization & Cell Function

August 15–20 • Queen's College, Oxford, UK
Ph: 401-783-4011; Email: grc@grc.org
Website: http://www.grc.uri.edu/programs/2004/macromol.htm

EuroScience Open Forum 2004: Highlighting Science, Technology & Innovation in Europe

August 25–28 • Stockholm
Contact: Gabriella Norlin, Project Leader
Phone: +46 8 546 44 154; Fax: +46 8 546 44 155
Email: gabriella.norlin@esof2004.org
Postal address: Swedish Research Council
SE-103 78 Stockholm, Sweden

International Congress on Biocatalysis 2004

August 29–September 1 • University of Technology, Hamburg, Germany
Contact: Gerlinde Loebkens; FON +49-40-76618012
FAX +49-40-76618018; e-mail: loebkens@tutech.de
Website: www.biocat2004.de

8th International Symposium on the Maillard Reaction

August 28–September 1 • Charleston, South Carolina
For detailed information about the meeting, including abstract submission, a call for papers and deadlines.
Website: http://Maillard.chem.sc.edu
Email: Maillard@mail.chem.sc.edu

5th Meeting on Methods in Protein Structure Analysis

August 29-September 2 • University of Washington, Seattle
Ph: 206-706-8118; Email: mpsa2004@u.washington.edu
Website: http://depts.washington.edu/biowww/mpsa2004/

SEPTEMBER 2004

Relaxin 2004: Fourth International Conference on Relaxin and Related Peptides

September 5-10 • Grand Teton National Park, Jackson Hole, WY
This conference will present recent advances on the chemistry, physiology, and pharmacology of relaxin, related peptides, and their receptors.
Email: relaxin-2004@ad.uiuc.edu
Website: http://www.life.uiuc.edu/relaxin2004/

Stem Cell Biology: Development and Plasticity

September 16-19 • Scheman Continuing Education Building Iowa State University, Ames, Iowa.
Abstracts due July 16, 2004; Registration deadline: August 16, 2004
Student Travel Grant Applications due July 16, 2004
Contact: Growth Factor and Signal Transduction Conferences Symposium Office
Ph: 515-294-7978; Fx: 515-294-2244; Email: gfst@iastate.edu
Website: http://www.bb.iastate.edu/-gfstlhomepg.htmi

Cellular and Molecular Basis of Regeneration EuroConference on the Molecular Pathways Leading to Regeneration

September 18–23 • San Feliu de Guixols, Spain
Contact: European Science Foundation, EURESCO Office
Ph: +33(0)3 88 76 71 35; Fx: +33 (0)3 88 36 69 87
Email: euresco@esf.org; Website: http://www.esf.org/euresco

OCTOBER 2004

Cytokines in Cancer and Immunity: Joint Conference of ICS and ISICR

October 21-25 • San Juan, Puerto Rico
An exceptional meeting bringing together leading investigators in cytokine biology, cancer and immunology.
Keynote speakers: Michael Karin and Tak Mak.
Abstract deadline: June 11, 2004
Email: info@cytokines2004.org; Fax: 706 228-4685
Website: www.cytokines2004.org

An ASBMB Sponsored Symposium: Redox Signaling in Biology and Disease

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

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

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

NOVEMBER 2004

4th International Congress on Autoimmunity

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

American Association of Pharmaceutical Scientists AAPS Annual Meeting and Exposition

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

First Latin-American Protein Society Meeting

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

Second National Meeting of the American Society for Matrix Biology

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

DECEMBER 2004

American Society for Cell Biology, 44th Annual Meeting

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

Department Heads Take Note:

ASBMB Offers Free Membership to New Ph.D.s

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

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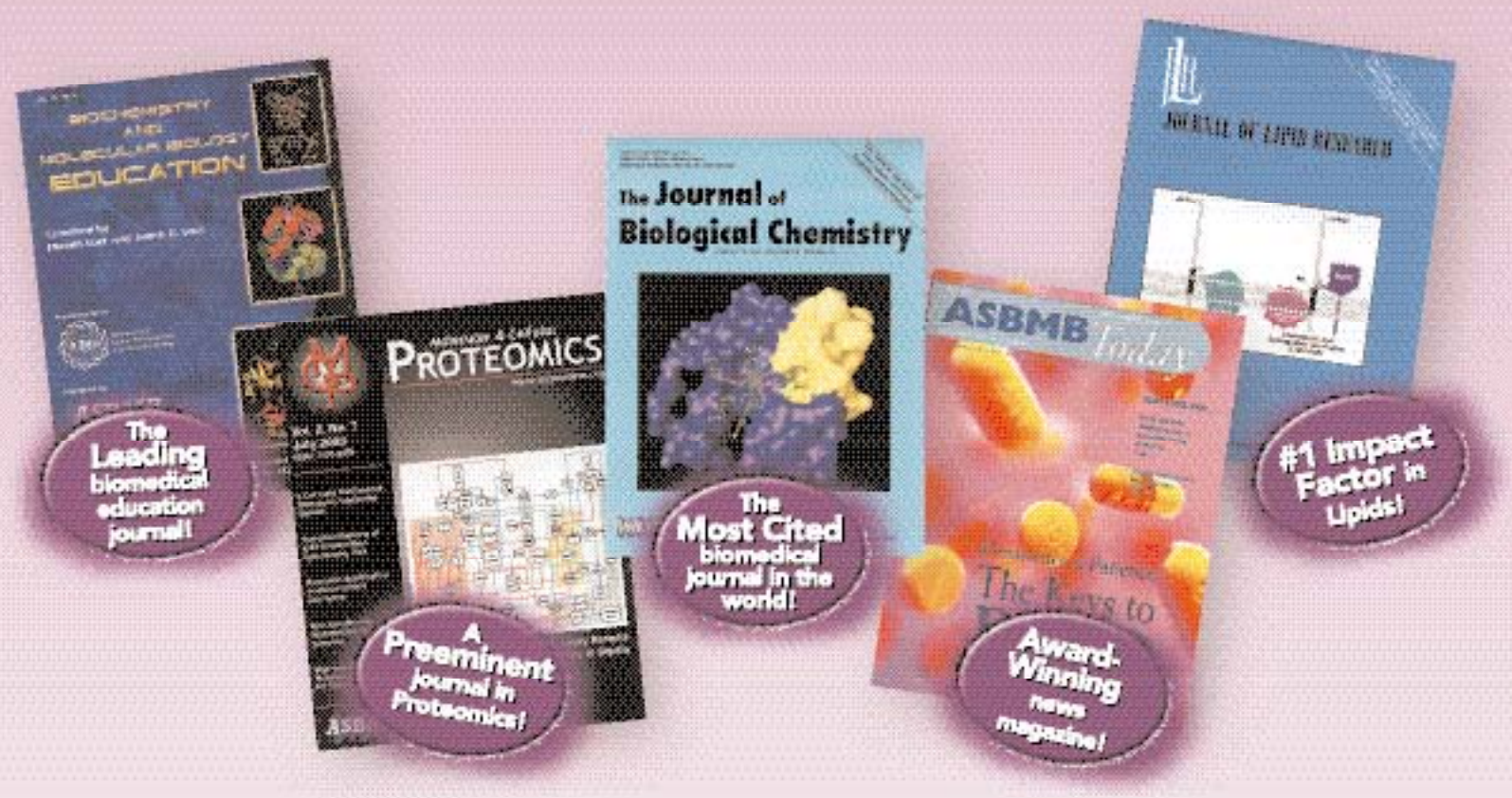

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