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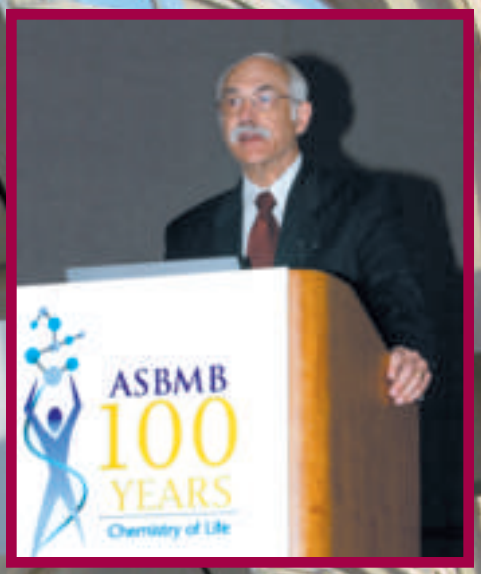
AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY



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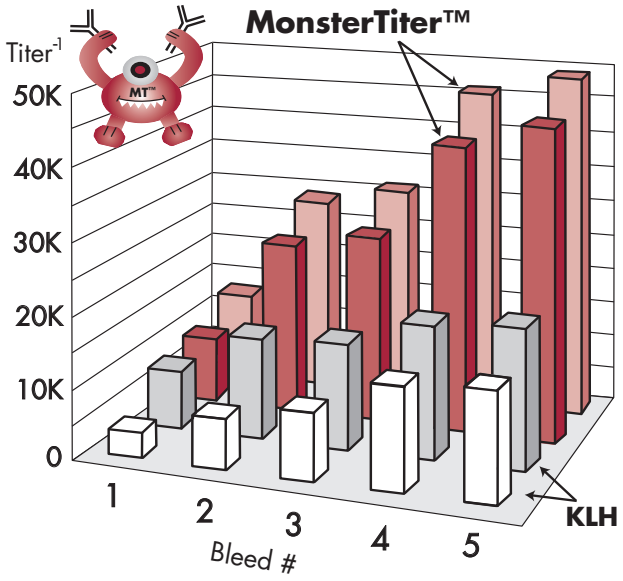

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ASBMB Today

AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

MAY 2005,
Volume 4, Issue 2

features

ON THE COVER:

12 2005 Annual Meeting

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2004 APEX AWARDS FOR PUBLICATION EXCELLENCE

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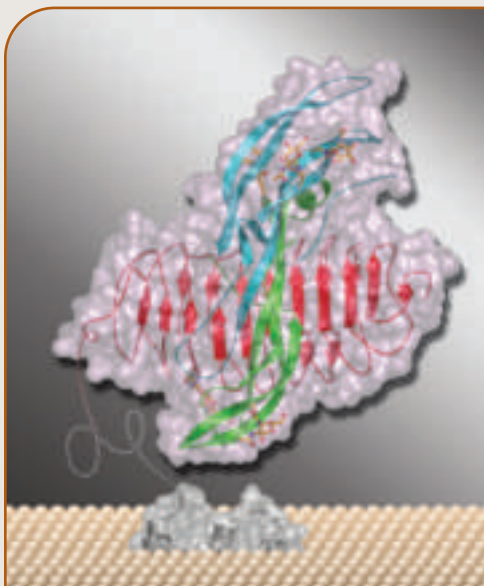

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Comments

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From the Desk of the President:

The Most Cited Life Science Journal in the World!

We have a lot to be proud of in the ***JBC***, not the least of which is that it is the most cited ***Journal*** in the life sciences in the world. There were over 384,000 citations to ***JBC*** articles in 2003, the quality of the ***Journal*** is well known, submissions to the ***Journal*** have risen to over 15,000 manuscripts per year, and for the online ***Journal*** about 160,000 hits (computer contacts with the *JBC* website) are recorded weekly. ***JBC*** was the first Online biomedical ***Journal*** (1995), manuscripts are accessible to everyone free online within a day after acceptance (since 1999), and all issues are freely available online back to the first issue of the ***Journal*** (October 1905). The 100th anniversary of the ***JBC*** is this year, 2005, while the Society (originally American Society of Biological Chemists) dates back to December 1906. It is only right that we are celebrating simultaneously the golden anniversary of the Society (now the ASBMB) and the ***Journal*** next year April 1–5, 2006, in San Francisco. There has been extensive overlap between the leaders of the Society and the Editors of the ***Journal***. For example, the first and third presidents of the Society, Russell H. Chittenden and Otto Folin, were on the original ***JBC*** editorial board. One of the two founding Editors of the ***Journal***, John J. Abel, was the second President of the Society. The other

JBC FOUNDING EDITORS John J. Abel (left) who was the second President of ASBMB and Christian A. Herter.

ASBMB PRESIDENTS Past, Present and Future: Bettie Sue Masters, Judith Bond, and Heidi Hamm who will take office as President-Elect on July 1.

Dr. Judith Bond

The Journal of Biological Chemistry

founding Editor was Christian A. Herter, an MD from NY who used his own funds to help the society survive in the early days; the Herter Fund was established upon his death in 1910, and still supports activities of the ***Journal*** such as the orientation session for new editorial board members. There have been several distinguished Editors along the way, including John Edsall (also a Past President of the Society) and William Stein. None are more distinguished than Herbert Tabor, our current Editor in Chief. Herb took the reigns as Editor

Robert Simoni (left), Executive Editor of JBC, and Herbert Tabor, Editor-in-Chief.

in 1971, and has led with vision and dedication for one-third of the 100 years! The leadership and management of the ***Journal*** are strong with Herb at the helm, Bob Simoni as Deputy Editor since 1998, Barbara Gordon as Director of Publications 1994-2004 (now Executive Director), and Nancy Rodnan, as our current Director of Publications.

A book on the history of our Society and the ***JBC*** is in the process of being written by Ralph Bradshaw, Chuck Hancock, and Bob Hill, three who have had a long history themselves with the Society and ***Journal***. Ralph is a past Associate Editor of ***JBC*** and Treasurer of the Society, and is currently Editor of ***Molecular and Cellular Proteomics***, a new journal published by the Society. Chuck was the Executive Director of the Society for 24 years, and just retired last year. Bob is a Past President and Treasurer of the Society, and is currently an Associate Editor of the ***JBC***. They are facing the challenge of pulling together our history for the Centennial with vigor and enthusiasm, and the work promises to be a gem; something many of us will cherish.

Judith Bond, President, ASBMB

ASBMB Executive Officer Barbara Gordon, President Judith Bond, and Director of Publications Nancy Rodnan.

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.

Jennifer R. Ball
University of Utah

Seth Brodie
State University of New York, Buffalo

Christian Dimaano
University of Utah

L. David Finger, Jr.
University of California, Los Angeles

LeAnn Godderz
University of Oklahoma Health Sciences Center

Francisco J. Herrera
Michigan State University

Mina Konigsberg
Universidad Autonoma Metropolitana

Janis Lee
University of Oklahoma Health Sciences Center

Samuel M. Pope
University of Cincinnati

Dustin Smith
University of Oklahoma Health Sciences Center

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

by Peter Farnham, CAE, ASBMB Public Affairs Officer

More Targeted Conflict of Interest Regulations

In a March 21 letter to ethics officials at the Department of Health and Human Services, ASBMB recommended that the department withdraw interim final rules on conflict of interest—put in place on February 3—and allow the National Institutes of Health to "develop a more targeted, balanced set of rules with flexible processes for managing perceived conflicts of interest." A description of the proposals appears in the March 2005 issue of ***ASBMB Today*** (p.6). The interim final rule can be found at: www.nih.gov/about/ethics_COI.htm

The letter, signed by ASBMB President Judith Bond, expresses the Society's "deep concerns" over the interim final rule. The concerns cover a half dozen subjects.

The rule is inflexible. The rule applies to all 17,500 NIH employees, not just those in a position to profit from their research interests or position at the NIH. The original allegations of widespread conflicts of interest at NIH were first raised in press reports in December 2003. However, no more than 100 employees were ever alleged to have been involved in conflicts of interest; further, the ***Washington Post*** reported in late February that since the initial allegations, as many as 80 of these individuals have been cleared of wrongdoing. Thus, the letter notes, "to apply such strict rules to all NIH employees when only a few dozen are still under investigation is clearly overreaching on the part of DHHS."

The NIH intramural staff may become scientifically isolated. ASBMB also expressed its concern about the stringent restrictions on intramural employee participation in the affairs of the Society. At least three current or former NIH employees have served the Society as President, and many others have served (or are currently serving) on our publications' editorial boards and on Society committees, in both compensated and uncompensated capacities. This participation has always been allowed heretofore; it now appears that much of it will not be. ASBMB recommends that specific, written exceptions to the rule be included so that intramural employees can serve in substantive capacities with their professional societies.

NIH scientists may be denied the right to receive ASBMB awards. The interim final rule includes restrictions on the type of awards NIH employees may receive. ASBMB offers six scientific awards, as well as a Public Service Award (named, ironically, after Howard K. Schachman, who served as NIH's liaison to the extramural scientific community for more than six years during the 1990s). The interim final rule now makes it problematic as to whether an NIH employee official can accept one of our awards. The rule requires NIH to establish a list of acceptable awards, and if an award is not listed, an NIH employee is not allowed to accept the award.

None of ASBMB's awards is on the NIH-approved list, even though the matter has been discussed with NIH ethics officials. As the letter notes, "ASBMB is not sure how to react to this. Frankly, we are reluctant to implement a policy that NIH employees are ineligible for ASBMB awards; on the other hand, to give an award to an NIH employee and have the employee be unable to accept it strikes us as an embarrassing situation for the NIH, the employee, and ASBMB."

The new policy on stock ownership is overly restrictive. ASBMB strongly recommends that restrictions be put in place regarding stock ownership for the small fraction of NIH employees who might be able to use their position to influence the value of a stock they may own. However, the interim final rule issues blanket prohibitions on stock ownership in whole classes of the private economy, and they apply not only to all NIH employees, but also their spouses and minor children. While DHHS has apparently moved back the date by which NIH employees and their families must divest themselves of offending investments, ASBMB notes that "the fundamental issue is the overly broad nature of the prohibition in the first place, not the date when divestiture is required."

The process under which the interim final rule was put in place is also subject to question. It is not clear under the terms of the Administrative Procedures Act that an interim final regulation should even have been issued. Only a few cases of alleged conflicts of interest are still being

Needed, ASBMB Advises DHHS

investigated, and since there has been no allegation that anyone was harmed by any actions taken by any of these individuals, there does not appear to have been an emergency situation involving danger to the public health that justified this action.

The rule is having a devastating effect on the morale of NIH employees. One knowledgeable observer told ***ASBMB Today*** that morale at NIH "has not only never been worse but it is unbelievably low." Longtime NIH employees who are not given to overstatement have used words like "draconian" to describe the interim final rule, and phrases like "the death of the intramural program" to describe its effect on the NIH as an institution.

Indeed, there is evidence that the predicted "brain drain" has already begun. Press reports indicate that at least three prominent scientists are planning to leave NIH in the next few months for jobs in academia or private industry. And, on March 30, the ***Washington Post*** reported that a prominent physician slated to become director of the National Institute of Environmental Health Sciences is now having second thoughts about accepting the job in light of the new regulations. He believes that the regulations will make recruitment very difficult, and noted in letters to Dr. Zerhouni and HHS secretary Mike Leavitt that the regulations were not in place when he accepted the position.

Two More-targeted Proposals Already Available

ASBMB recommends in its letter that the interim final rule be withdrawn and that more targeted proposals be put in place. There are two such proposals available for NIH consideration. An NIH Blue Ribbon Panel on Conflict of Interest Policies (chaired by Dr. Bruce Alberts, President of the National Academy of Sciences) issued a set of 18 recommendations in the winter of 2004 to address conflict of interest issues. These recommendations are more targeted, and correspondingly less likely to do long-term damage to NIH as an institution. The second set of proposals was developed by the NIH Assembly of Scientists, an on-campus group of intramural researchers. These proposals—in some cases involving stock ownership restrictions even more stringent than those in the interim final rule—are also more judicious and focused.

Dr. Raynard Kington, Deputy Director of NIH, has indicated that NIH and DHHS will be considering comments on the rule over the next year and will be prepared to make changes if necessary. So far, however, no one in Bethesda—or at the Humphrey building downtown—has blinked.

New Public Affairs Blog

ASBMB Public Affairs Officer Peter Farnham has begun to write a web log—"blog" for short—about public affairs matters affecting the Society and its members. "I thought it was time we started making use of the blogosphere," Farnham noted. "There are thousands of blogs out there now, providing news and views on a whole host of subjects. The blog I'm maintaining is another way to get public affairs information out to our members in a more timely manner than a monthly magazine or occasional mass e-mails."

The blog appears on the ASBMB homepage under the "What's New" column. It is called "PA News, Views, and Links." The subject matter is focused mostly on government affairs. It contains links to columns, press reports, and other media offerings about biomedical research. It also has links to government reports, hearing records, notices and other public information, as well as to ASBMB and FASEB commentary on public affairs events.

The blog is updated several times a week (sometimes daily) and is publicly available to anyone. "So check back often," Farnham urges ASBMB members, "and tell your friends. We'd also appreciate any comments or suggestions on how to make it more useful."

NAS Releases Report on 'Bridges to Independence'

by Peter Farnham, CAE, ASBMB Public Affairs Officer

On March 18, the National Academy of Sciences announced the conclusions of a new report to be released in May called Bridges to Independence: Fostering the Independence of New Investigators in Biomedical Research. The report proposes that the National Institutes of Health can foster independence among postdoctoral scholars, entry-level faculty, staff scientists, and other new investigators in biomedical research by improving their training and giving them more resources to pursue their own projects, says the new NAS report. Presenting the report were NIH Director Elias Zerhouni, HHMI President, Committee Chair Thomas Cech, and NAS President Bruce Alberts.

"Science would benefit from a system that actively encourages new investigators to try out novel ideas and approaches," said Dr. Cech. "Now is the time for action. Our report offers a plan to help ensure the continued vitality of the biomedical research enterprise and its work force."

Among the report's recommendations: Individuals should not be allowed to work as postdoctoral researchers for more than five years, regardless of the type of award or grant they work under. If postdocs continue to work in the same laboratory after reaching the five-year limit, the continuation should be treated as a change in career track, accompanied by promotion to a "staff scientist" position with employee benefits and appropriate levels of responsibility.

NIH should move some of the resources for postdoctoral support from R01 grants to training grants and individual awards that aid postdoctoral work, to encourage postdoctoral creativity.

NIH should create a new independent-research award that enables postdocs to identify, explore, and control their own projects under the mentorship of senior investigators. The new awards should be portable, allowing selected postdocs to use them anywhere, and large enough to cover their salaries and job benefits.

Recognizing the importance of non-U.S. citizens to biomedical research, the report recommends that either U.S. citizenship requirements for training grants be dropped, permitting researchers who are not U.S. citizens or permanent residents to compete for the funds, or equivalent avenues of support should be made available to these scholars.

NIH should replace K22 "career transition" awards with a new agency-wide grant program that backs innovative research by scientists who are moving into their first jobs as independent investigators.

NIH should create a New Investigator R01 award that would require a discussion of previous experience instead of preliminary data. The awards should have the same requirements across the agency, as well as budgets similar to other R01 grants. In addition, they should have a five-year term, giving researchers time to establish laboratories, train personnel, and collect data without having to worry about immediately finding more research dollars.

A prepublication copy of the report can be viewed at: books.nap.edu/catalog/11249.html.

NIH Directors Blast Bush's Stem Cell Policy

By John D. Thompson, Editor

The Bush Administration policy for funding research on human embryonic stem cells is hindering NIH's lead in this emerging scientific field according to NIH institute directors.

In letters submitted at an April 6 hearing of the Senate Appropriations Labor/HHS Subcommittee, which Sen. Arlen Specter (R-Penn.) chairs, the NIH chiefs warned that NIH will fall behind other nations due to restrictions on the number of hESC lines available.

National Institute on Deafness and Other Communication Disorders Director James Battey wrote, "It is clear that the state of the science is evolving very rapidly and limitations of the President's policy become more apparent."

National Institute of Child Health and Human Development Director Duane Alexander, noted that scientists have complained about "inadequate quantity and quality" in the stem cells that are available.

Specter pressed NIH Director Elias Zerhouni to explain why excess frozen embryos from ***in vitro*** fertilization clinics are not being used for federally funded research.

Zerhouni responded, "The issue is not a scientific issue as you well know. The policy is based on a moral and ethical line."

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ASBMB Members Honored by

Four ASBMB members were among 17 individuals selected by the National Academy of Sciences (NAS) for awards in recognition of their outstanding scientific achievements. The awards were to be presented May 2 at a ceremony in Washington, DC, during the Academy's 142nd annual meeting. The awards and the ASBMB members receiving them are:

The Richard Lounsbery Award, a medal and a prize of $50,000 awarded annually in recognition of extraordinary scientific achievement in biology and medicine, alternating between young American and French scientists, was received by John Kuriyan, Investigator, Howard Hughes Medical Institute, and Chancellor's Professor, Department of Molecular and Cell Biology, University of California, Berkeley. Dr. Kuriyan was chosen "for his critical role in revealing the structural mechanisms underlying processivity in DNA replication and the regulation of tyrosine kinases and their interacting target proteins." The award was established by Vera Lounsbery in memory of her husband and has been presented since 1979.

Dr. John Kuriyan

The NAS Award in Chemical Sciences, a medal and prize of $15,000 awarded annually for innovative research in the chemical sciences that, in the broadest sense, contributes to the better understanding of the natural sciences and to the benefit of humanity, was presented to Thomas C. Bruice, Research Professor in Chemistry and Biochemistry, Department of Chemistry and Biochemistry, University of California, Santa Barbara. Dr. Bruice was chosen "for his leading role in the development of bioorganic chemistry, and especially for deep and lasting contributions to the understanding of enzyme mechanisms." The award, supported by The Merck Company Foundation, has been presented since 1979.

Dr. Thomas Bruice

In the last 10 years, the Bruice group has been involved in research directed to the design of antisense and antigene agents. Progress has been reported in 52 manuscripts. The most important result is finding that one of the microgonotropens can pass through a human cell wall, enter the nucleus, and bind to a particular DNA sequence. This prevents TF attachment and gene expression, resulting in the loss of ability to synthesize a protein.

The NAS Award for Chemistry in Service to Society, a prize of $20,000 awarded every two years for contributions to chemistry, either in fundamental science or its application, that clearly satisfy a societal need, went to Marvin H. Caruthers, Distinguished Professor, Department of Chemistry and Biochemistry, University of Colorado, Boulder. Dr. Caruthers was chosen "for his invention and development of chemical reagents and methods currently used for the automated synthe-

Dr. Marvin Caruthers

National Academy of Sciences

sis of DNA oligonucleotides (i.e., the "gene machine")." The award, established by E. I. du Pont de Nemours & Co. and given this year for contributions made in academia, has been presented since 1991.

More recently, Dr. Caruthers and his research group have pioneered the development of a new, two-step DNA synthesis approach that is expected to be extremely useful in preparing both DNA chips and large amounts of DNA. The group also has developed new methods for RNA synthesis in recent years.

The Selman A. Waksman Award in Microbiology, a prize of $5,000 given every two years in recognition of excellence in the field of microbiology, went to Lucy Shapiro, Director, Beckman Center, and D. K. Ludwig Professor of Cancer Research, Stanford University School of Medicine. Dr. Shapiro was chosen "for her pioneering work revealing the bacterial cell as an integrated system with transcriptional circuitry interwoven with the 3-D deployment of regulatory and morphological proteins." The award is supported by the Foundation for Microbiology and has been presented since 1968.

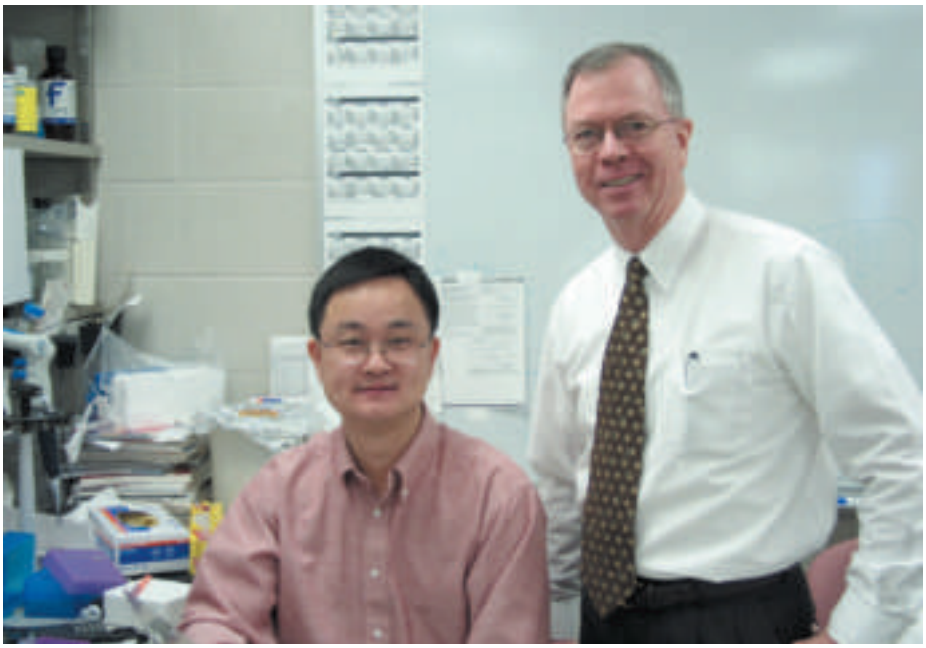
Dr. Lucy Shapiro

"We take a systems approach to decipher the regulatory circuitry that controls the bacterial cell cycle," says Dr. Shapiro. "To do so, we integrate the transcriptional networks with spatially and temporarily regulated phosphorylation cascades and proteolytic events to coordinate cell differentiation and asymmetric cell division."

Key Cellular Process in Prostate, Other Cancers May

Mayo Clinic researchers are the first to identify an interaction between two cellular proteins, Skp2 and FOXO1, that is important for the growth and survival of cancer cells. Researchers also show that this interaction can be chemically reversed to stop cancer tumor growth and may lead to new and better cancer treatments.

Their report appeared as an electronic advance article of *PNAS, The Proceedings of the National Academy of Sciences*. The research was performed on human cells in the laboratory and was found effective against human cancer cells. Researchers say it will be at least a year before the discovery can be applied in a human clinical trial.



Urology Researcher Haojie Huang who performed the study (at left) and Co-Investigator Donald J. Tindall.

The Findings

For the first time, the Mayo Clinic research group provides laboratory evidence to describe a new mechanism by which cells lose the protection of tumor suppressors, and therefore become vulnerable to cancerous cell growth. In particular, they show that Skp2 is the cellular player that interacts with FOXO1 by tagging it for destruction. This degradation of FOXO1 caused by high levels of Skp2, in turn, abolishes the ability of FOXO1 to suppress tumors. The result of their experiment indicates that human prostate cancer grows without the protection of the tumor suppressor protein FOXO1. Importantly, they also show that this loss of function can be reversed, even in the presence of high levels of Skp2, by using chemicals that inhibit protein destruction, and thus block Skp2's action against FOXO1.

Significance of the Finding

"The major finding of our studies is that the tumor suppression function of FOXO1 is abolished due to Skp2-mediated protein degradation," said Urology Researcher Haojie Huang who performed the study. Co-Investigator Donald J. Tindall,* Professor in the Mayo Clinic's Department of Biochemistry and Molecular Biology, added, "We've discovered a viable therapeutic target in human cancers, especially those with high levels of Skp2."

The Mayo Clinic researchers' findings suggest a promising new treatment target at which drug designers can aim new therapies for prostate cancer, as well as a number of other human cancers in which elevated levels of Skp2 have already been documented. These include cancers of the breast, lymphatic leukemia, small cell lung cancer and certain cancers of the mouth and colorectal cancer.

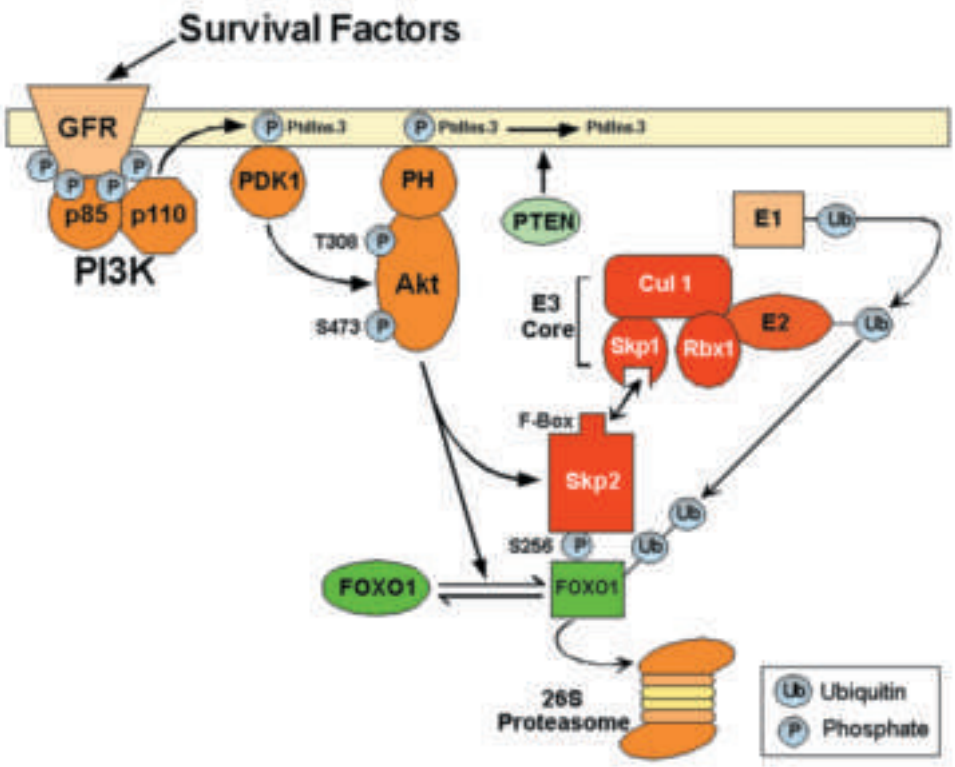
Prostate cancer is the second most common cause of cancer in men (skin cancer is first) and the second leading cause of cancer death in American men, exceeded only by lung cancer. In 2005, the American Cancer Society estimates 232,000 new cases will be diagnosed. While one in six men will be diagnosed with prostate cancer in his lifetime,

Lead to Better Treatment

only one in 33 will die of it. Because of the widespread disability and death that prostate cancer causes, finding new strategies to develop better treatments is an important public health goal.

Background

The Mayo Clinic researchers wanted to understand the relationship between a group of proteins known as tumor suppressors that belong to the FOXO1 family, and the Skp2 protein.



Regulatory signaling pathways that gauge the ubiquitin-dependent degradation of FOXO1 protein. Binding of growth factor receptors (GFR) to their cognate ligands, such as survival factors, results in the activation of phosphatidylinositol 3-kinase (PI3K) and phosphorylation of lipid phosphatidylinositol at the D3 position (PtdIns-3). This process in non-malignant cells is counterbalanced primarily by the lipid phosphatase function of the tumor suppressor gene PTEN. Recruitment of Akt and PDK1 kinases by their binding to the phosphatidylinositol triphosphate PI(3,4,5)P3 via the pleckstrin homology (PH) domain results in the phosphorylation of Akt. Activated Akt phosphorylates the FOXO1 protein at serine-256 and induces increased expression of Skp2, a key component of Skp1/Cullin1/F-box protein (SCF) E3 ligase complex. Elevated levels of Skp2 and phosphorylation of FOXO1 at serine-256 are two key events that are required for the ubiquitination and degradation of FOXO1. Therefore, it can be speculated that amplification of PI3K and Akt, loss of PTEN, and overexpression of Skp2 often seen in a wide range of tumor types may lead to the degradation and loss of tumor suppressor function of FOXO1.

When tumor suppressors fail, the result is abnormal cell growth that can eventually transform healthy cells into cancerous cells. In particular, the Mayo Clinic team wanted to find out what disables FOXO1 tumor suppressor, and how it works, in hopes of reversing the process to find a new cancer therapy strategy.

The team knew from previous research:

- FOXO1 possesses tumor suppressor functions. Its tumor suppression works two ways: by curbing cell reproduction and by inducing cells to kill themselves — especially cancer cells.
- Some tumor suppressors lose their effectiveness through a means known as the "ubiquitin pathway." This pathway is a cellular strategy for attaching an identifying marker to the tumor suppressor that targets it for destruction.
- Skp2 is known to target several tumor suppressors for destruction.
- FOXO1 is suited to being targeted for destruction via the ubiquitin pathway.

The researchers noted that high levels of Skp2 were associated with low levels of FOXO1 in many human cancer cells, including prostate cancer — and then combined the lines of evidence outlined above to design experiments to answer the specific question: Do elevated levels of Skp2 drive down and disable FOXO1, thus resulting in loss of its tumor suppression ability? The answer is yes .

**ASBMB member*

Annual

Co-organizers of the 2005 Annual Meeting Dennis Voelker, and Cecile Rochette-Egly.

The 2005 Annual Meeting of the American Society of Biochemistry and Molecular Biology opened April 1 before an audience of almost 3,000—about one out of every four of those registered for EB 2005—in attendance for the Herbert Tabor/JBC Lecture. Presenting the lecture were Michael S. Brown and Joseph L. Goldstein, both from the University of Texas Southwestern Medical Center, Dallas, who shared this award as well as the 1985 Nobel Prize for Medicine.

Dr. Goldstein, who opened the lecture, brought laughter from the audience when he recounted how his first submission of a paper to the *Journal of Biological Chemistry,* was initially rejected but after some revision accepted for publication. Since then, he and Dr. Brown have published more than 400 scientific papers.

Professor Goldstein and his colleague Professor Brown have worked together for the last 30 years on the genetics and regulation of cholesterol metabolism. Their discovery of the LDL receptor as the major molecule regulating cholesterol metabolism and its genetic disruption in the human disease familial hypercholesterolemia have been recognized by their receipt of numerous awards, including the Albert D. Lasker Award in Basic Medical Research (1985), Nobel Prize in Physiology or Medicine (1985), and the U.S. National Medal of Science (1988). More recently, their discovery of the SREBP family of membrane-bound transcription factors and the elucidation of the proteolytic pathway by which the SREBPs become activated to regulate lipid metabolism were recognized by the receipt of the Albany Medical Prize in Biomedical Sciences in 2003.

San Diego 2005

Meeting Opens to Full House

Meeting photos by California Convention Photography

The Brown Goldstein Laboratory is at the heart of UT Southwestern's approach to research. Their findings have led to the development of statin drugs, cholesterol-lowering compounds that are used by 16 million Americans and are the most widely prescribed medications in the United States.

Also addressing the ASBMB Meeting was FASEB Excellence in Science Award Winner Anita Roberts, Principal Investigator in the Laboratory of Cell Regulation and Carcinogenesis at the National Cancer Institute. Dr. Roberts outlined the exciting events leading to the discovery of TGF-, in the early 1980s . She journeyed through some of the key discoveries related to the biological roles of TGF-, and discussed recent work in her laboratory and the laboratories of others defining the complex role of TGF-, and its signaling pathways in fibrotic disease and in cancer. She also discussed the promise that comes from the development of a myriad of approaches now directed at controlling the sometimes contradictory effects of TGF-, with the hopes that these can contribute to new clinical modalities.

Protecting Vessels at Risk of Atherosclerosis

Atherosclerosis is more likely to occur in vessels with turbulent blood flow than in vessels with a smoother, more steady flow says ASBMB-Amgen Award recipient Dr. Barry Forman, Principal Investigator of the Beckman Research Institute of the City of Hope National Medical Center and the Gonda Diabetes Center, and the scientist who first explained why this should be true. Vessels with a regular blood flow are protected with what Dr. Forman calls a lock and key. The endothelial cells that line the inner walls of all blood vessels produce large receptor proteins, the "lock," but only vessels with a smooth blood flow produce ligands, small molecules that bind to the large receptor protein—the "key"—and inhibit the earliest stage of atherosclerosis, recruiting monocytes to build up plaque.

In his ASBMB-AMGEN Award lecture at the ASBMB Meeting, Dr. Forman described new experiments in which he has been able to trick the endothelial cells in blood vessels with turbulent blood flow into turning on the same genes that protect blood vessels exposed to smooth blood flow. The trick, he says, was to activate the receptors by adding synthetic drugs to the cells exposed to turbulent flow, thereby causing the cells to display the protective gene expression pattern.

"This is very exciting work," said Dr. Forman, "because it offers the first

understanding of how blood flow forces can regulate transcription through a lipid intermediate and it suggests a rationale for the pharmacological treatment of atherosclerosis, a disease that kills as many Americans each year as all forms of cancer combined."

Altering Steroid Receptor Genes Creates Fat Burning Muscles

The Salk Institute scientist who earlier discovered that enhancing the function of a single protein produced a mouse with an innate resistance to weight gain and the ability to run a mile without stopping has found new evidence that this protein and a related protein play central roles in the body's complex journey to obesity and offer a new and specific metabolic approach to the treatment of obesity related disease such as Syndrome X (insulin resistance, hyperlipidemia and atherosclerosis).

Dr. Ronald M. Evans, an HHMI Investigator at The Salk Institute's Gene Expression Laboratory, presented two new studies in ASBMB sessions. His studies focus on genes for two of the nuclear hormone receptors that control broad aspects of body physiology, including serving as molecular sensors for numerous fat soluble hormones, Vitamins A and D, and dietary lipids.

The first study focused on the gene for PPARd, a master regulator that controls the ability of cells to burn fat. When the "delta switch" is turned on in adipose tissue, local metabolism is activated resulting in increased calorie burning. Increasing PPARd activity in muscle produces the "marathon mouse," characterized by super-ability for long distance running. Marathon mice contain altered muscle composition, which doubles its physical endurance, enabling it to run an hour longer than a normal mouse. Marathon mice contain increased levels of slow twitch (type I) muscle fiber, which confers innate resistance to weight gain, even in the absence of exercise.

In other work Dr. Evans found that activation of PPARd suppresses the inflammatory response in the artery, dramatically slowing down lesion progression. Combining the results of this new study with the original "marathon mouse" findings suggests that PPARd drugs could be effective in controlling atherosclerosis by limiting inflammation and at the same time promoting improved physical performance.

New Technique Finds Molecules Needed for Cancer Metastasis

Tufts University researchers have identified several proteins on the surface of cancer cells that contribute to the cells' ability to metastasize. When the researchers destroyed these particu-

MAC Symposia Focus on Mentoring Young Students and World Health

This year, for the first time in its history, the ASBMB Minority Affairs Committee (MAC) sponsored two symposia at the Annual Meeting. The first symposium was an issues-based one, dealing with mentoring young scientists, while the second was a scientific symposium on world health and malnutrition.

The issues-based symposium, Mentoring Young Scientists, focused on the critical role mentoring plays in nurturing young scientists and the responsibilities that faculty members have to their students. MAC Chair Juliette Bell opened the session by saying, "A mentor is like a tattoo, once you get it, it's always there." Throughout their talks, the session speakers continued to stress the importance and permanence of mentors while they addressed issues such as how to choose a mentor and ways to take advantage of mentoring opportunities and increase one's success as a scientist.

Juliette Bell

The second MAC symposium, World Health: Malnutrition, focused not only on how nutrient deficiency is affecting health worldwide, but also how over-nutrition and obesity are culprits in declining health. The speakers discussed the physical and mental effects of various vitamin, mineral, and nutrient deficiencies and abundances and gave examples of how they are affecting life-span and susceptibility to disease throughout the world. Several programs and policies that addressed these problems were also reviewed.

The MAC also held a very successful lunchtime Minority Scientist Mixer. Approximately 60 minority students and faculty members attended the event and took advantage of the opportunity to get to know each other as well as several of the speakers from both MAC symposia. Appearances by both ASBMB President Judy Bond and Presidenmt-Elect Heidi Hamm also provided attendees an opportunity to meet with the Society's current and future Presidents.

Several of the PowerPoint presentations from both symposia will be available on the MAC website at http://www.asbmb.org/asbmb/site.nsf/Main/Diversity?OpenDocument.

The ASBMB booth was a busy spot on the exhibition floor. Anna Sullivan of Cadmus is seen here describing the benefits of ASBMB membership to meeting attendees.

lar proteins, the cancerous cells show a significant decrease in their ability to invade healthy cells, a finding that provides a new target for badly needed drugs. Although most cancer deaths occur from metastasis, not from the original cancer itself, no drug treatments are currently available specifically to prevent the spread of the cancer from the original site to other organs. The team also has discovered new roles related to the spread of cancer in two molecules known for other, non-cancer activities.

Dr. Daniel Jay, who presented the study, reported that the findings were made possible because he and his colleagues have developed a new Fluorform-Assisted Light Inactivation technology (FALI). The researchers were able to destroy a specific protein, sparing all others attached to the cell as well as the cell itself, by targeting an antibody to that specific cell. They tag the antibody with a dye that absorbs a specific wavelength of light. When the light is turned on (earlier technology required lasers; the new FALI technology needs only the light of a slide projector), the light energy absorbed by the dye in the antibody generates free radicals that destroy the specific protein bound by that antibody.

For more about the Annual Meeting see the June issue of ASBMB Today.

ASBMB Honors . . .

HERBERT TABOR/JBC LECTURESHIP RECIPIENTS *Dr. Joseph Goldstein (second from left) and Dr. Michael Brown (second from right) of University of Texas Southwestern Medical Center—Dallas are seen here with Professor Daniel Steinberg, University of California, San Diego at left, ASBMB President Judith Bond, and Journal of Biological Chemistry Editor Herbert Tabor.*

FRITZ LIPMANN AWARD *was presented to Dr. Christopher T. Walsh (right) of the Harvard Medical School by Dennis Voelker, Co-Organizer of the 2005 ASBMB Meeting.*

Dr. Anita Roberts, Principal Investigator in the Laboratory of Cell Regulation and Carcinogenesis at the National Cancer Institute, received the ***FASEB EXCELLENCE IN SCIENCE AWARD*** *from FASEB CEO and Executive Director Frederick Rickles.*

*AMGEN Biology Director Bei Shan (right) presented **ASBMB-AMGEN AWARD** to Barry Forman, Principal Investigator of the Beckman Research Institute, City of Hope National Medical Center and the Gonda Diabetes Center.*

*Jack E. Dixon, Professor and Dean of Scientific Affairs at the University of California, San Diego School of Medicine, received the **2005 ASBMB-MERCK AWARD** from Professor Minor J. Coon, University of Michigan Medical Center.*

*Dr. Minor J. Coon presented the **WILLIAM C. ROSE AWARD** to Dr. Frederick Guengerich, Vanderbilt University Medical School.*

Dr. Ruth Duffy, Associate Principal Scientist in Schering-Plough's Cardiovascular and Metabolic Disease Discovery Group in Kenilworth, New Jersey, presented the Schering-Plough Research Institute Award to Brian Strahl, Assistant Professor, Department of Biochemistry and Biophysics, University of North Carolina School of Medicine.

***THE AVANTI AWARD IN LIPIDS** was presented to William Dowhan, John S. Dunn Professor of Biochemistry at the University of Texas Medical Center in Houston, by Avanti's Walter Shaw at left, and at right Christian R. Raetz, Professor and Chair of the Department of Biochemistry, Duke University Medical Center.*

A Blueprint for Possible

Researchers now have a much better picture of how follicle-stimulating hormone (FSH), one of the most frequently used fertility drugs, works, and with it, ideas for creating a new generation of oral medications to treat infertility.

The exquisite detail of the molecular images produced by Wayne A. Hendrickson,* Howard Hughes Medical Institute (HHMI) Investigator and University Professor, Columbia University College of Physicians and Surgeons, and colleague Dr. Qing Fan, also of Columbia, begins to tell for the first time how the FSH hormone attaches to a key segment of its receptor on the cell surface. The binding of the hormone to its receptor then stimulates the maturation of ovarian follicles in women or sperm production in men.

Insights gleaned from this structure could aid in the development of improved fertility drugs or contraceptives for both men and women. Hendrickson and Fan reported the details of the structure in an article published in the January 20, 2005, issue of the journal ***Nature***.

"Although the nature of FSH and other glycoprotein hormones has been known for more than 30 years, there is still no orally active therapeutic drug," wrote Dr. James A. Dias of the Wadsworth Center in Albany, New York, in a commentary in the journal ***Nature***. "But such a drug might one day be developed, thanks to the findings presented by Fan and Hendrickson."

Researchers are equally excited by the architectural blueprint of FSH and its receptor because it may help unravel the structural framework of a trio of other hormones, notably, luteinizing hormone (LH), chorionic gonadotropin (CG), and thyroid-stimulating hormone (TSH).

Receptors such as FSH are switches that are situated in the cell membrane. When triggered by a molecular signal, such as a hormone, the switches activate specific cellular processes. In the case of FSH, activation stimulates egg and sperm production in reproductive cells.

HHMI Investigator Wayne Hendrickson and colleague Dr. Qing Fan,

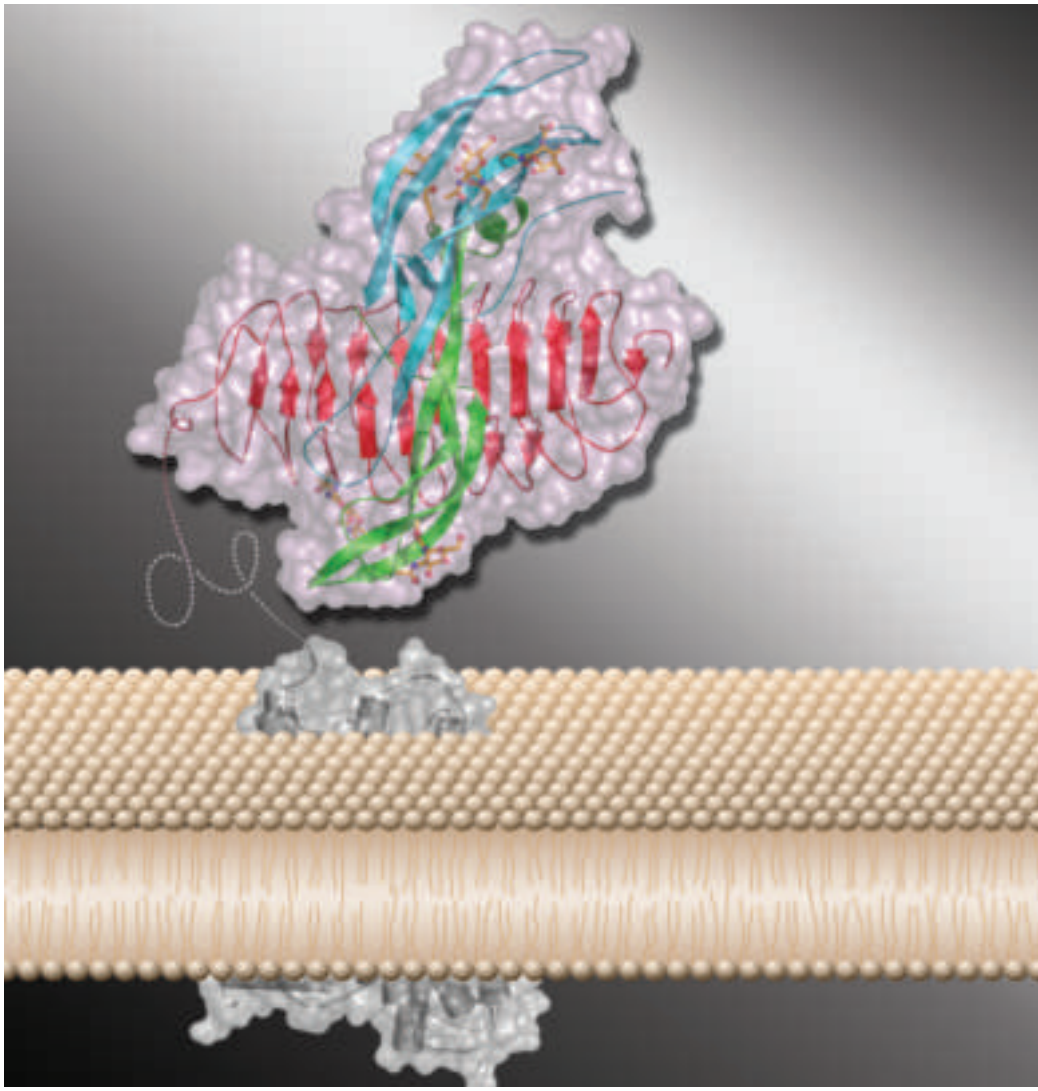
Until now, researchers did not understand key details about how FSH interacts with its receptor, largely because the complex had never been crystallized and examined at the molecular level. Thus, Qing Fan set out to produce crystals of the complex to use in determining its structure using x-ray crystallography. The diffraction patterns that result are then analyzed using computers to deduce the structure of the molecule under study.

Producing the crystals was a considerable challenge, said Dr. Hendrickson because FSH and its receptor are glycoproteins with numerous sugar molecules attached to the protein backbone. The presence of sugar molecules complicates both the crystallization of the protein and its production in microorganisms normally used as "factories" for such molecules. Dr. Fan concentrated on crystallizing the FSH molecule while it was attached to a truncated binding portion of its receptor. She also removed some of the sugars on the complexed molecules to aid crystallization.

Dr. Fan engineered the cells to produce the FSH-receptor complex together, rather than trying to make the two molecules separately and combine them, said Dr. Hendrickson. "We reasoned that we might have a better shot at obtaining the complex if we co-produced them and tried to form the complex directly."

The resulting x-ray crystallographic structure yielded important insights into the FSH-receptor complex. "We found that the binding segment of the FSH receptor takes the shape of a slightly curved tube, and it binds FSH in what we describe as a `handclasp,'" Dr. Hendrickson explained. "It's an extensive interaction, as if you take one hand and clasp the other." A peculiarity of the interface between FSH and the receptor, he noted, is that the handclasp covers a broad area, with each protein having large charged surfaces that interacts with the other.

New Fertility Drugs



Surface and ribbon representation showing the crystal structure of human FSH bound to the extracellular hormone-binding domain of its receptor (FSHR-HB). FSH alpha- and beta-subunits are in green and cyan, respectively. FSHR-HB is in red. A seven-helix transmembrane domain (gray, modeled on the structure of rhodopsin) anchors the receptor in the membrane. Upon receptor binding, FSH undergoes a concerted conformational change that affects the protruding loops, which may in turn play a direct role in activation through the receptor transmembrane domain. Image: Courtesy Qing Fan and Wayne A. Hendrickson.

The structure offers new information about how FSH is able to interact with its receptor so specifically and not with other highly similar receptors. It was known that the "alpha" subunit of such glycoprotein hormones—FSH, LH, CG and TSH—is common among the hormones, and that only the "beta" subunit is specific to a hormone. However, Hendrickson and Fan found that both the alpha and beta subunits work in concert to create specificity of interaction.

"If you take at face value the idea that the specificity of interaction is caused only by the beta subunit, it's hard to understand how they both contribute," said Dr. Hendrickson. "But the value of our three-dimensional structures is that they show that specificity is conferred by a strip of the hormone's beta subunit sandwiched between pieces of alpha, all of which are in contact with the receptor molecule."

Fan and Hendrickson also found that the hormone undergoes a conformational change during its interaction with its receptor—an insight that could provide a valuable clue to how FSH and other related hormones switch on signaling activity in the target cell.

"This paper provides many quite specific hypotheses that we can now test as we work to understand the process of receptor activation," said Dr. Hendrickson. Thus, he said, further efforts in his laboratory will include producing the entire receptors for such glycoprotein hormones, to explore their signaling mechanisms when triggered by the hormones.

Dr. Hendrickson is keenly aware that his group's studies could have important clinical implications. "FSH is already being used to stimulate ovulation in women who are infertile and to enhance spermatogenesis in men," he explained. "Knowing the details of the hormone-receptor structure could enable modifications to FSH used in treatment to make it more potent and longer-lived in the bloodstream. One could also imagine the possibility of designing small-molecule contraceptive compounds that would bind to the receptor and prevent hormone binding."

ASBMB member

Humans and Mice Share Large-Scale Patterns of Genome Structure

In the most detailed large-scale study to date of the proteins that package DNA, researchers have mapped a family of switches that turn genes on and off. Their findings may help scientists understand regulatory mechanisms underlying cancer and human development.

The research team includes first author Bradley Bernstein, recipient of a Howard Hughes Medical Institute physician postdoctoral fellowship who works in the Harvard University laboratory of HHMI Investigator Stuart L. Schreiber.* Other co-authors are from the Broad Institute of MIT and Harvard, and Affymetrix. Their findings were published in the January 28, 2005 issue of ***Cell***.

Co-lead authors Dr. Michael Kamal (left) and Dr. Bradley Bernstein

"Now that the human genome has been sequenced, it is vital to learn how the genome is translated to make living cells and organisms, and how we can use that information to improve human health," said Dr. Bernstein, an Instructor of Pathology at Brigham & Women's Hospital and Harvard Medical School.

Many scientists believe changes in the regulatory scaffolding surrounding the genome may be as important as changes in the genome itself in causing diseases such as cancer.

This regulatory structure, chromatin, is a key regulator of gene expression in healthy and diseased cells, Bernstein said. Chromatin is composed of DNA spooled around bundles of histone proteins, and resembles a chain of beads which is then compressed into a working chromosome. Chemical tags placed on the histones alter the way chromatin is organized, thus allowing the right combination of genes to be turned on.

The researchers analyzed the chromatin structure of the two shortest human chromosomes, numbers 21 and 22, containing about two percent of the human genome. They also sampled additional regions in both the human and mouse genomes, finding similar patterns along equivalent chromosomal regions, even where the underlying DNA sequences are different.

Bernstein and Schreiber began to develop the analytical techniques several years earlier, working with the smaller yeast genome. To investigate the much larger human genome, they collaborated with Affymetrix. They isolated the DNA regions with certain major methyl and acetyl tags, and used new microarray technology to identify the underlying genetic sequences associated with the tagged chromatin. Next, they teamed up with Michael Kamal, the co-first author of the paper, Eric Lander, and their Broad Institute colleagues, for the daunting computational analysis required to interpret the resulting data.

In most cases, the mapped tags coincided with the transcription starting points of active genes, as had been seen earlier in the yeast. Unexpectedly, they also found tags idling over regions near genes. They think these sites have important regulatory functions, because the methylation patterns are similar in comparable portions of the mouse genome.

Most exciting to Dr. Bernstein is the unusual density of histone tags spread over the regions of genome containing the HOX genes, which are key regulators of development.

"In most of the genome, we see short stretches associated with activated histones," he stated. "However, in the HOX regions, we see huge stretches of genome, many thousands of base pairs in length, that are completely covered by tags." They speculate that these unique chromatin structures could be activating sets of HOX genes for specific developmental programs.

"The human genome still has many surprises lurking within it," said Lander, Director of the Broad Institute and senior author on the study. "One of the most important is the mystery of how genes are turned on. The ability to take global views of chromatin in human cells holds tremendous promise for unraveling this mystery."

***ASBMB member**

Finding Yields Insight Into Stem Cells, Cancer; Opens Door to Possible Drug Discovery

New research by investigators at Duke University Medical Center has provided insight into a fundamental cellular control mechanism that governs tissue regeneration, stem cell renewal and cancer growth. In humans, malfunctions in the pathway have been implicated in skin and brain cancers, as well as certain developmental defects, according to the researchers.

The team found that the protein beta-arrestin2, earlier linked to a variety of inhibitory functions, also plays a critical role in activating the so-called hedgehog (Hh) signaling pathway, which plays a central role in early development and normal cell proliferation. When left unchecked, uncontrolled cell growth spurred by the hedgehog pathway can lead to the development of cancerous tumors.

The researchers reported their findings in the Dec. 24, 2004, issue of Science.

"Studies have found a wide breadth of functions for beta-arrestins, but none had revealed a role for these proteins in development," said James B. Duke Professor Marc Caron,* a researcher in the Duke Institute for Genome Sciences and Policy and senior author of the study. "The involvement of beta-arrestin2 in the hedgehog signaling pathway provides a previously unappreciated paradigm for its role in promoting growth, differentiation, and malignancies."

The finding in zebrafish could lead to new drugs that block the growth of tumors by disrupting the beta-arrestin2 protein's normal function, the researchers said. In other cases, drugs that activate beta-arrestin2 might also drive the proliferation of therapeutic stem cells, they added.

Dr. Marc Caron

Hh proteins play a central role in cell proliferation and embryonic patterning. In humans, inhibitory mutations in the pathway result in developmental defects such as holoprosencephaly—an often fatal condition characterized by abnormal brain development and facial deformities. In contrast, mutations that spur overactivity of the pathway lead to basal cell carcinoma, the most common form of skin cancer, and medulloblastoma, an aggressive form of brain cancer. About one in five childhood brain tumors are medulloblastomas.

The researchers injected zebrafish embryos with a chemical that specifically blocked the function of beta-arrestin2. Humans and zebrafish, both vertebrates, share fundamental developmental pathways, the researchers said. Zebrafish embryos are an ideal model for study because their transparency allows researchers to easily observe their early development.

> ***"Drugs that disrupt the function of beta-arrestin2 might also offer an alternative approach to cancer therapy."***
>
> **— Dr. Marc Caron**

The injected embryos, which lacked almost all beta-arrestin2 protein, exhibited characteristics earlier linked to defects in the Hh signaling pathway, including curved bodies, underdeveloped heads and abnormal muscle development. Furthermore, injected embryos exhibited reduced activity of other genes that respond to Hh activity compared to normal embryos, suggesting that loss of beta-arrestin2 blocked their activity. Injection of other substances that activate the Hh pathway restored normal development in embryos lacking beta-arrestin2.

"It appears that beta-arrestin2 is a positive force in Hh signaling in living organisms," Dr. Caron said. "The current finding opens up new avenues for study of normal developmental regulation and the manner in which abnormalities in that regulation can lead to cancer. Drugs that disrupt the function of beta-arrestin2 might also offer an alternative approach to cancer therapy."

Another experimental system developed by the researchers—which includes cells with fluorescently tagged beta-arrestin2—might offer a useful tool for identifying drug compounds that either disrupt or promote the protein's activity, said Dr. Gregory Fralish of Duke, co-author of the study. Beta-arrestin2 normally concentrates at the periphery of cells as it binds to activated receptors nestled in the cell membrane, including a component of the Hh pathway known as Smoothened, he explained. Quantifying changes in the amount of fluorescent beta-arrestin2 at the cell surface in the presence of other compounds would therefore identify those that modify Hh pathway activity—compounds of potential therapeutic use.

***ASBMB member**

by John D. Thompson, Editor

To Publish or Not to Publish, That is the Question

Those attending the March 2005 Clinical Trial Congress in Philadelphia heard plenty of discussion, but no consensus about the question of whether to publish or to not publish the results of their clinical trials.

Industry leaders in a panel on trial registries at the conference expressed different views. Some said they did not fear the disclosure of unpublished trials. Their companies are already selectively releasing some data on their own websites and to the federal government. However, most expressed concern about the proliferation of clinical trials worldwide.

Ronald Krall, Senior VP of Worldwide Development at Glaxo Smith Kline (GSK), expressed concern that confidence in the industry is in short supply at the moment, despite the precaution and thought that goes into clinical research. He noted one poll which found that "60 percent of those responding were not very or not at all sure that drug companies publish timely information on side effects. As the respondents were older, the doubts were higher. Yet they are the ones that use more of the drugs that we produce."

Krall acknowledged that people who participate in clinical trials "expect that the results will be available." GSK, he said, will publish most trials that meet nonbonding International Conference on Harmonization (ICH) guidelines about hypothesis-testing studies. The information to be published at the GSK website includes type of trial, rationale, methods, study design, patient population demographics, primary and secondary endpoints, adverse events, and references to published citations in the peer-reviewed medical literature. That would seem to meet most of the requests from journal editors. However, GSK will not be publishing trial results.

Speaking for Eli Lilly, Global Medical Director Per Cantor, said, "We will post trials within the year after completion of the trial." He noted, however, "There may be situations where we cannot meet the one-year deadline."

Laurence Hirsch, Merck's Executive Director of Medical Communications, said Merck prefers to participate in a scientific dialogue with physicians using the peer-reviewed literature. "We do not have a Merck clinical trial registry," said Hirsch. "We don't have a trial results database on Merck.com. The company's thinking at this point is that it is not intending to go down that road."

Biomolecular Computer Can Operate Billion Programs

A new version of a biomolecular computer composed entirely of DNA molecules and enzymes and developed at the Technion-Israel Institute of Technology can perform as many as a billion different programs simultaneously. Previous biomolecular computers, such as one built by a joint team from Technion and the Weizmann Institute of Science three years ago, were limited to just 765 simultaneous programs.

This new computer is autonomous and it processes calculations from beginning to end without any human assistance.

"A final innovation is the incorporation of a gold-coated chip, which allows simple, real-time readout of the results," said lead researcher Professor Ehud Keinan of the Technion Faculty of Chemistry. He explained that results produced by current biomolecular computers can only be analyzed by using elaborate techniques that include separating and sorting molecules according to size and the use of radioactive materials. The development of Technion's biomolecular computer was reported in the March 2005 *Journal of the American Chemical Society*.

One of the most promising applications for such autonomous molecular computers would be the encryption of images on a chip containing the equivalent of 41 million pixels, so that deciphering them would be impossible to those without access to a secret key comprised of several short DNA molecules and several enzymes. By comparison, the highest quality image from a professional grade, 6-megapixel digital camera is comprised of "just" 6 million pixels.

Keinan and his team will now focus their efforts on creating more sophisticated biomolecular computers, including ones whose final outputs are actual biological functions. This would make possible the encryption methods, as well as disease detection and treatment.

Canadian Research Group Opens Throttle on Systems Biology

Researchers at the Blueprint Initiative, a research program in the Samuel Lunenfeld Research Institute of Toronto's Mount Sinai Hospital, and the University of Toronto's Edward S. Rogers Sr. Department of Electrical and Computer Engineering have developed a hardware-based method for accelerating data analysis that comes with a dramatically lower price tag than conventional cluster-based approaches. The innovation was described in a paper in the March 30, 2005 issue of *Rapid Communications in Mass Spectrometry.*

"Our goal in this project has been a longstanding one—to get a search of the three billion base pairs of the human genome sped up so that it can be done in less than one second and fit the solution inside a single desktop computer," explained Dr. Christopher Hogue, co-author and Blueprint principal investigator. "With this system, we can now keep up with the tremendous amount of data coming from proteomics and link mass spectrometry data to the Human Genome."

The scale of data produced and analyses performed in most large labs is too much for conventional PC memory, so scientists have traditionally responded by parallelizing their search jobs or analytical methods across a processor cluster. The costs associated with cluster acquisition and maintenance, however, are high, and inherent communication delays in cluster systems mean that when someone doubles the demand on the cluster, they have to more than double the size of the cluster to get the same level of performance.

Because many of these tasks involve simple repeatable operations, custom hardware is a practical solution, the Toronto team turned to Field-Programmable Gate Arrays (FPGAs), programmable hardware that can be designed to maximize the memory bandwidth searching and work much more efficiently than a sequential microprocessor-based program.

"The real power of this system comes from our parallel design. This FPGA design uses a large number of transistors, which on an FPGA are organized into logic units called Lookup Tables (LUTs)," Dr. Hogue says. "This hardware design uses 20 times more LUTS than most other published FPGA solutions in bioinformatics. It achieves its speed using data pipelining so that searching, analysis and results scoring are continuously computed."

FPGA Systems Become Commodity Components

"With a single FPGA and using full tandem MS spectra, we are able to query the human genome and identify target proteins in 1.6 seconds," says Dr. Jonathan Rose, co-author and University of Toronto Professor. "To achieve the same price/performance would require a conventional 64-processor cluster costing about $80,000 with a fulltime employee maintaining the system."

Dr. Hogue added: "It is conceivable that FPGA accelerator boards can be as cheap, ubiquitous and high-performing as high-end video graphics boards."

Recommendations on Alzheimer's Drugs Called Blow to Patients, Research

Draft recommendations on medicines to treat Alzheimer's disease, published in March by the UK's National Institute for Clinical Excellence (NICE), are a devastating blow to patients and will act as a significant deterrent to companies undertaking further research in this area, according to the Association of the British Pharmaceutical Industry (ABPI). The trade association also stated that the proposed recommendations would put the UK out of step with the rest of Europe, where the medicines are available in all countries where they have a license.

"NICE's draft recommendations put small cost savings before the benefit that these medicines can bring to so many people who have Alzheimer's—and to their family, friends, and carers," said Dr. Richard Barker, Director General of the ABPI. "It also sends a discouraging message to pharmaceutical companies that are putting major research work into discovering new, innovative medicines to help people with Alzheimer's and other forms of dementia. How can companies justify investing huge sums in research and development—it costs on average about £550 million to develop a new medicine—if such decisions can be made to withhold medicines from patients despite their benefits? We call upon NICE to reconsider this heartless and damaging decision in the interests of both current patients."

Calendar of Scientific Meetings

JUNE 2005

7th Annual Plant Sciences Institute Symposium; Meristems 2005

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

2005 International Workshop on Ataxia Telangiectasia, ATM and the DNA Damage Response

June 8-11 • Hotel Villa Carlotta, Belgirate, Lake Maggiore, Italy.
The meeting will feature sessions on ATM and related proteins, sequence alterations in ATM and ATR pathways and their consequences; cellular responses to single strand breaks and related phenotypes; DNA damage response in the nervous system; therapeutic strategies.
Contact: domenico.delia@istitutotumori.mi.it
Website: www.atworkshop.com

International Society For Stem Cell Research 3rd Annual Meeting

June 23–25 • San Francisco Marriott
Abstract Submission closes February 25.
Submission for oral and poster presentations will be via the ISSCR website. Ph: 847/509-1944; Fax: 847/480-9282
Email: isscr@isscr.org; Website: www.isscr.org

Glycoproteomics—Protein Modifications for Versatile Functions

June 28–30 • Dubrovnik,Croatia
For information: Email: glauc@pharma.hr; Ph: 385 1 4818 757
Website: bmb.pharma.hr/glyco2005/

JULY 2005

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

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

7th International Symposium on Biocatalysis and Biotransformations

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

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

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

Pathobiology of Cancer

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

BioScience2005—From Genes to Systems

July 17–21 • Glasgow, UK
Poster abstract deadline: April 15, 2005, Early registration deadline: May 23, 2005, For more information: BioScience2005, Biochemical Society, c/o Commerce Way, Colchester, Essex CO2 8HP
Ph: +44 (0)1206 796351; Fx : +44 (0)1206 798650
Email: info@BioScience2005.org; www.BioScience2005.org

Gordon Research Conference on Molecular & Cellular Biology of Lipids

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

AUGUST 2005

Ninth International Congress on Amino Acids and Proteins

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

2005 International Gap Junction Conference

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

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

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

SEPTEMBER 2005

Second World Congress on Synthetic Receptors

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

Strategies for Engineered Negligible Senescence (SENS), 2nd Conference

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

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

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

International Conference on Enzyme Technology RELATENZ 2005

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

American Society for Bone and Mineral Research (ASBMR) 27th Annual Meeting

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

OCTOBER 2005

Supramolecular Chemistry

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

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

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

NOVEMBER 2005

International Workshop on Biosensors for Food Safety and Environmental Monitoring

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

DECEMBER 2005

Xth PABMB Congress: Panamerican Association for Biochemistry and Molecular Biology

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

ASBMB 2006

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

ASBMB/JBC Centennial Celebration

Honoring 100 Years of Achievements and Contributions to Science

Thematic Meetings

MOLECULAR STRUCTURE

Macromolecular Structure and Dynamics
Andrej Sali, UCSF

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

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

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

GENOME DYNAMICS

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

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

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

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

CELL SIGNALING

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

Signaling in Growth and Development
Michael B. Yaffe, MIT

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

MEMBRANE BIOGENESIS

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

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

EDUCATION AND PROFESSIONAL DEVELOPMENT SYMPOSIA

J. Ellis Bell, University of Richmond

MINORITY AFFAIRS SYMPOSIA

Juliette Bell, Fayetteville State University

2006 Program Co-Chairs

George M. Carman, Rutgers University

Laurie S. Kaguni, Michigan State University

Special Events

Centennial Opening Celebration

An Evening with the San Francisco Symphony

A Taste of San Francisco

Award Lectures

Herbert Tabor/Journal of Biological Chemistry Lectureship

ASBMB Amgen Award

ASBMB Award of Exemplary Contributions to Education

ASBMB-Merck Award

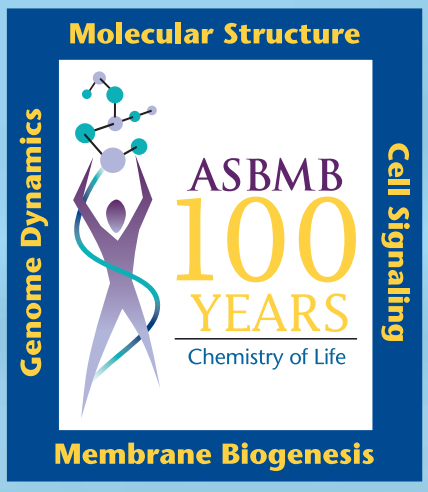
Avanti Award in Lipids

Herbert A. Sober Lectureship

Howard K. Schachman Public Service Award

Schering-Plough Research Institute Award

William C. Rose Award



www.asbmb.org/meetings