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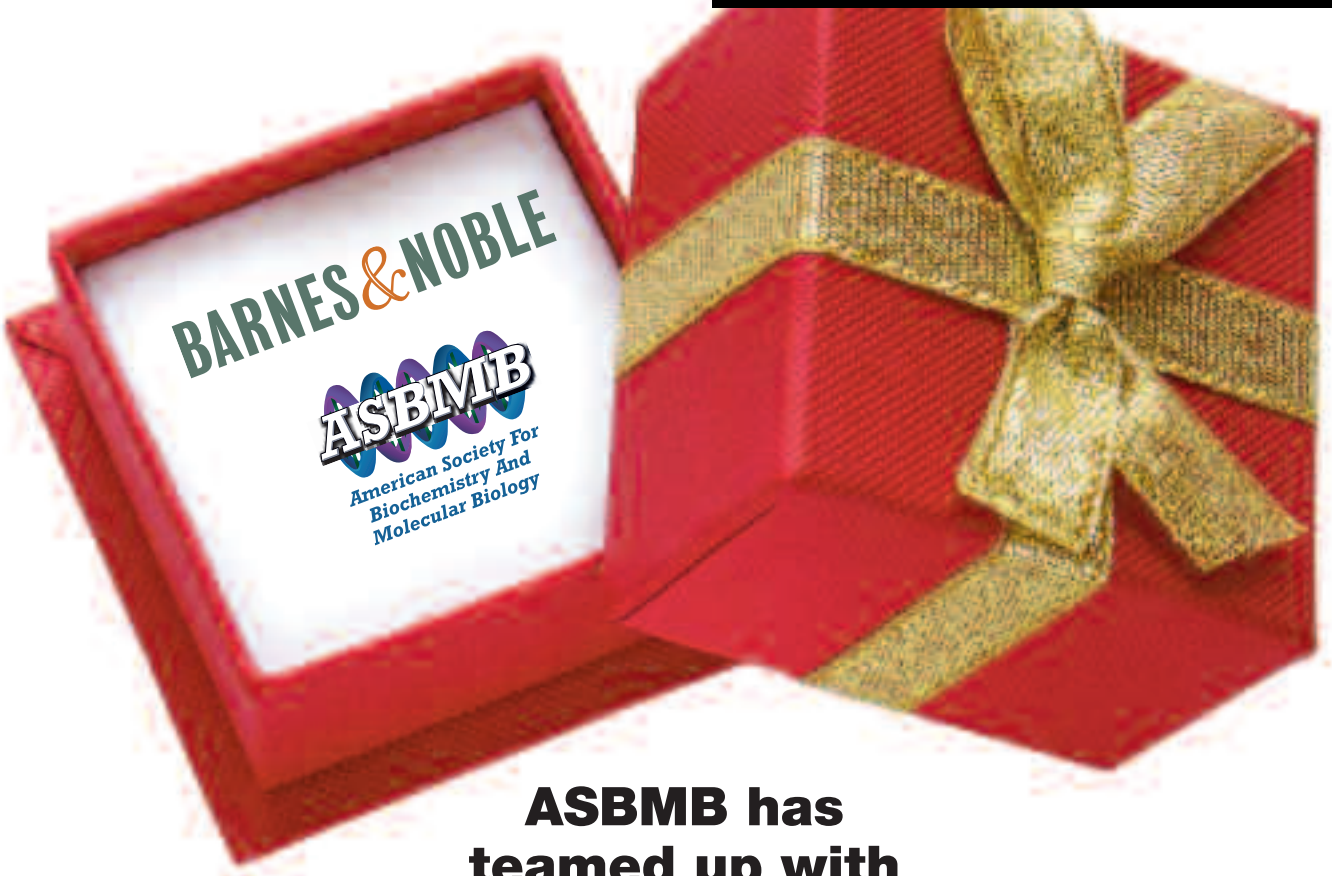

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ASBMB Today

AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

DECEMBER 2006
Volume 5, Issue 9

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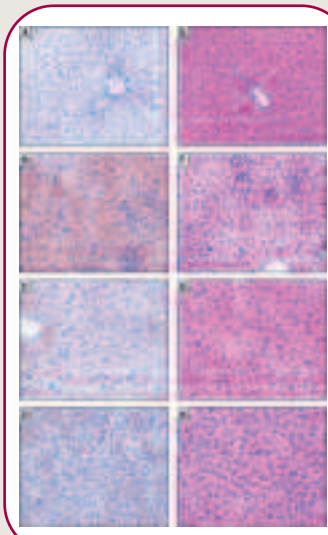

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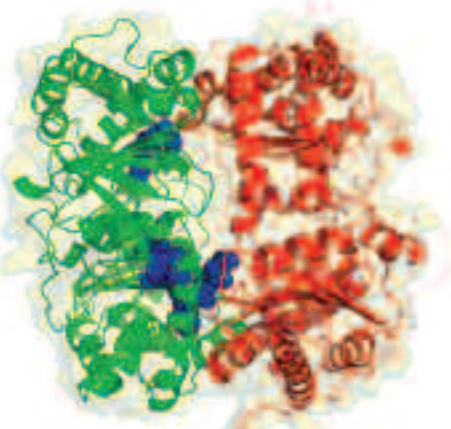

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NIH Responds to ASBMB Request;

The breakthroughs of science come from unexpected sources. There is substantial agreement that investigator-initiated research is the discovery engine that has brought the US biomedical research establishment to its preeminent position in the world and has increased our prestige in the world enormously. The US commands a predominant position in prizes such as the Nobel and the Lasker. One of the major goals of the leadership at ASBMB is to ensure that the NIH continues to appreciate and fund discovery science, the science that is driven by the best judgment and insight of individual investigators. The importance of unfettered investigation on making breakthrough discoveries is exemplified by the winners of this year's Nobel Prizes in Chemistry and Medicine.

As you have been repeatedly hearing from me, there has been an alarming trend toward NIH-solicited research during the period of the doubling of the NIH budget. For example, while the NIH budget increased 2.4-fold from 1996 to 2005 (from $11B to $28B), the number of competing R01s awarded increased by only 46% (4,959 in 1996 to 7,255 in 2004); there were only 6,275 competing awards made in 2005. The budgets of R01s increased by 69.2% (average $ per R01/29: $212.2k to $358.9) during this same time frame. The investigator-initiated R01s [that is, those not solicited by program announcements (PA) or requests for applications (RFA)] made up 89% of the total in 1996, but by 2003 they were only 83%, and in 2004, they dropped to 81%*. Thus, unfortunately, the NIH is driving more and more of the research to those areas that the NIH, itself, decides are appropriate for funding.

A new process that we have been watching carefully is the switch to electronic submission of NIH proposals. Starting in February, all R01 grants must be submitted electronically. We at ASBMB were alarmed to discover this past September that *all investigators will need to choose a program announcement or RFA to respond to, and there will no longer be a category for investigator-initiated research.*

In the past, the default pathway for a new application was investigator-initiated, and one had to specifically state if it was in response to an NIH-solicitation by including the PA or RFA number. Now, one MUST submit a PA number for any application.

Since that discovery, we have been working hard with Norka Ruiz Bravo, the Director of the Office of Extramural Research (OER) and NIH Deputy Director for Extramural Research, to convince her that investigator-initiated research is the bedrock of discovery research, and to change the system so fundamentally to remove this category is a grave error. Although she agreed with us that the lack of such a category was an oversight by the NIH, unfortunately, she was unable to change the process to add this category while the electronic submission procedures were being developed for the web. We worked hard to convince her that the process needed to be significantly modified to work around this problem, and now they have indeed changed

Dr. Heidi E. Hamm
ASBMB President

Keeps Door Open to Investigator-Initiated Research

the wording on the NIH website to add PA numbers that allow investigator-initiated research to be submitted.

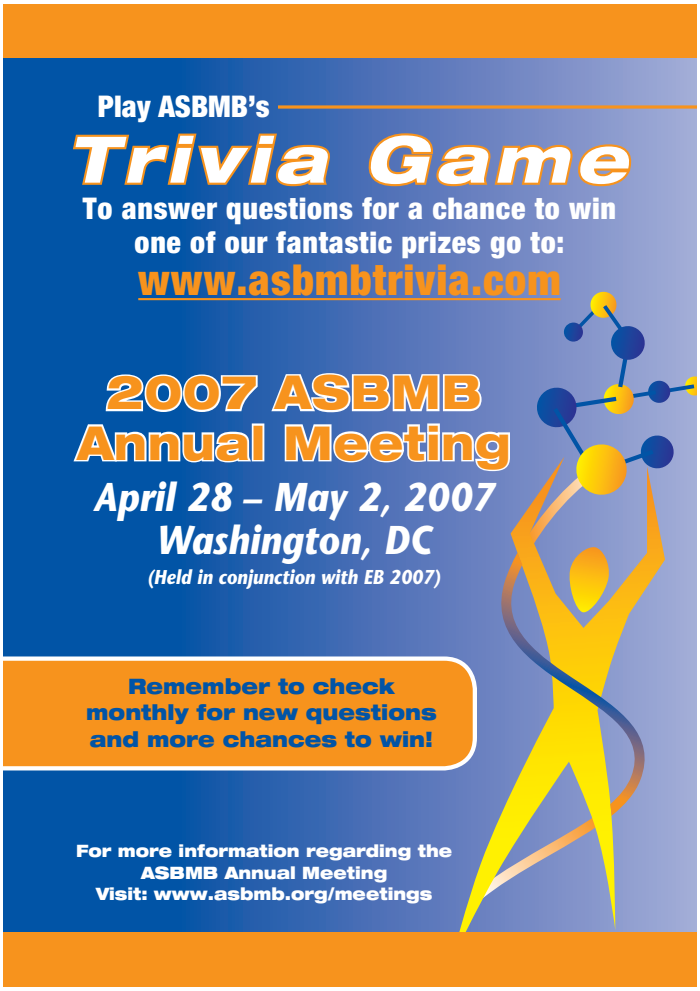
The following wording was added: "An important procedural change with electronic submission of grant applications is that all applications must be submitted in response to a Funding Opportunity Announcement (FOA)*. NIH and other HHS Agencies plan to develop omnibus Parent announcements by early November, 2006, for our most widely used grant mechanism, the research project grant (the R01), for use by applicants who wish to submit what were formerly termed "unsolicited" applications. Responding to such an omnibus or umbrella Parent FOA ensures that the correct application package is used and enables NIH to receive the application from Grants.gov. This process in no way diminishes the interest of NIH Institutes and Centers in investigator-initiated, unsolicited research grant applications. Parent announcements are NIH-wide, but some NIH institutes may limit their participation, so check the announcement's statement of interest."

Now, when you go to the NIH Grants and Funding Opportunities website, and then to the OER home page, and then to the Funding Opportunities and Notices web page, scroll down to "Browse Active Funding Opportunities" and you will find "Parent Announcements (unsolicited applications)". There, you will find the Parent R01, with the announcement number PA-07-070. This announcement number can be used to download the electronic forms from grants.gov. However, beware that going to grants.gov and searching with the keyword search for Parent Announcements, investigator-initiated R01, or such words nets you 621 opportunities. It is a daunting task to delve through all of these. To avoid this situation, you must put this announcement number into the "Search by Funding Opportunity Number", and it will be the only PA that is found.

To help you to navigate this process, there is a new issue of *NIH Extramural Nexus*, a special edition dedicated to the upcoming R01 electronic submission in February 2007 (http://grants.nih.gov/grants/partners/1106Nexus.htm).

The mechanics of the electronic submission is quite different from the previous paper form, and will certainly take longer than usual, at least the first time you do it. The first thing you will need to do to download an electronic form is to respond to a Funding Opportunity Announcement, or FOA. Please, don't wait to the last minute! Hopefully, the Research Office (Sponsored Programs or Grants Management) at your University will be informed and capable of helping you in navigating the electronic submission process. You may wish to contact them now to determine if they are prepared for this new mechanism of NIH submission.

*There is ample documentation of this, on the NIH website, as well as on ASBMB's public affairs web page.



by Peter Farnham, CAE, ASBMB Public Affairs Officer

Democrats Take Over Congress; Outlook

"Probably better," is how one long-time congressional observer characterized the outlook for science in the next Congress, which will be controlled by the Democrats for the first time in 12 years as the result of the November 7 election.

The Democratic majority in the House is 29 seats as of this writing, with five races still undecided. The election sent a clear message; not one incumbent House Democrat running for reelection was defeated.

Iraq was the single largest issue working against the GOP; President Bush's unpopularity was also a factor. Various scandals figured in a half dozen other House races.

Republicans who suffered most tended to be moderates in the northeast and the Midwest, many of whom were staunch supporters of science and biomedical research. Typical was the defeat of Rep. Jim Leach (R-IA), a long-time GOP maverick very much at odds with the conservative wing of the Republican Party for most of his career. Leach lost narrowly to a Democrat who portrayed him as an "enabler" of unpopular White House policies. Very few Republican congressmen now remain in all of New England, and the seats that flipped will be difficult for the GOP to reclaim in future elections.

New Leaders—New Approaches?

The presumptive new Speaker of the House is Rep. Nancy Pelosi (D-CA), the first female Speaker in history (she is also a former co-chair of the Congressional Biomedical Research Caucus). The new Majority Whip is Rep. Steny Hoyer (D-MD), a longtime member of the House Labor/HHS Appropriations Subcommittee.

The new chairman of the L/HHS Subcommittee will probably be Rep. Dave Obey (D-WI), another House veteran with years of experience in appropriations (he will also probably serve as chair of the full Appropriations Committee). The committee will have a lot of work to do in January; the outgoing GOP majority will not pass the 10 remaining appropriations bills before the new Congress convenes, thus giving the Democrats $460 billion in unpassed bills to deal with as soon as the new Congress reconvenes.

The new chairman of the Energy and Commerce Committee (which oversees NIH), will be Rep. John Dingell (D-MI), who during the 80s and 90s presided over numerous investigations of issues associated with biomedical research, including excessive university indirect cost charges, and misconduct in science

Regarding the NIH reauthorization bill. The outgoing chairman of the committee, Rep. Joe Barton (R-TX) produced a bill that many in the biomedical community endorsed (including ASBMB and FASEB). Democrats endorsed the Barton bill overwhelmingly (it passed the House in September with only a handful of "no" votes), but several changes in a new version are likely next year.

Rep. Henry Waxman (D-CA) will probably chair the House Government Operations Committee, and he can be expected to vigorously pursue a wide range of investigations of supposed Bush administration malfeasance. For example, he is one of the few Members of Congress to publicly decry "politicization of science" in areas such as global warming, reproductive health, and stem cell policy.

Members of the ASBMB Public Affairs Advisory Committee met with outgoing Rep. Sherwood Boehlert (R-NY) long-time chair of the House Science Committee, on November 14, to present him with the Society's Howard K. Schachman Public Service Award. From left to right: Robert Wells, Executive Director Barbara Gordon, Boehlert, Judith Bond, and Thomas Smith

for Science "Probably Better"

The outlook for the treatment of science in the House is perhaps better in the next couple of years than it has been, but it remains to be seen if the new majority will assign a high priority to funding it. Competition for scarce Federal funds will likely be even more intense than it has been in the last couple of years.

On to the Senate...

The Democrats managed to wrest control of the Senate from the GOP as well, although with a slim, 51-49 majority. Democratic control rests on keeping Independent (and newly reelected) Senator Joe Lieberman (I-CT) happy enough to continue to caucus with the Democrats. If he were to decide to become a Republican, or begin to caucus with them, the GOP would regain control of the Senate in a 50-50 split, with Vice President Cheney casting any needed tie-breaking vote.

Several strong opponents of stem cell research were defeated, including Senators Rick Santorum (R-PA) and Jim Talent (R-MO). Talent's narrow defeat has been tied to the passage of a pro-stem cell ballot initiative (that ASBMB supported). Talent's opponent supported the initiative. However, there is still not a veto-proof majority for any pro-stem cell legislation—which the President would undoubtedly veto—that might emerge from the next Congress.

The chairmanship of the L/HHS subcommittee will switch to Senator Tom Harkin (D-IA) from Senator Arlen Specter (R-PA), but this does not represent much of a change as far as NIH is concerned, since the two senators have both supported NIH for many years and enjoy a close working relationship.

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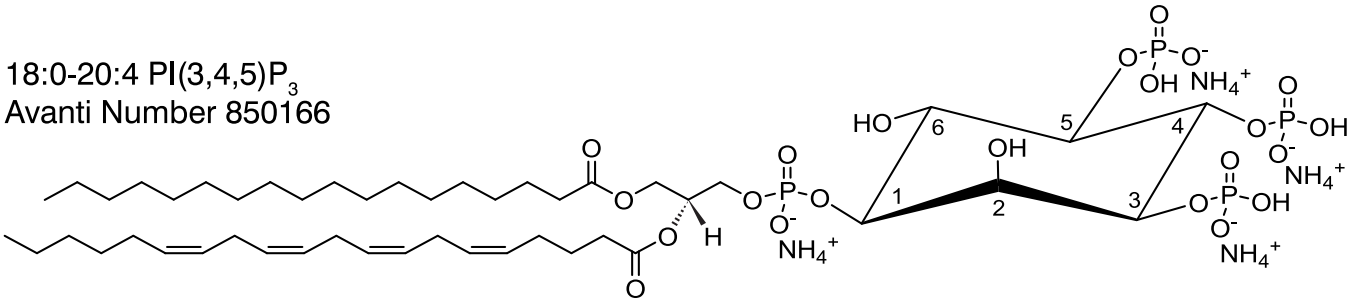

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Biosecurity Board Recommendations May Affect Future Biomedical Research

By Carrie D. Wolinetz, Ph.D., FASEB Office of Public Affairs

The National Science Advisory Board on Biosecurity (NSABB) is beginning to generate and share products that could ultimately impact federally funded scientists. NSABB was formed in early 2005 to develop federal regulations and review processes related to dual use biological research. The term 'dual use' refers to research whose purpose is benign or beneficial, but whose misuse could cause harm. Concern about dual use research was raised following a 2004 report by the National Academies titled, Biotechnology Research in an Age of Terrorism: Confronting the Dual Use Dilemma? Officially administered through the National Institutes of Health's (NIH) Office of Biotechnology Activities, NSABB comprises 25 voting members with expertise in science, biosecurity, biodefense, pharmaceuticals, and / or law, as well as 18 ex-officio members representing various federal departments and agencies.

Over the course of the past two years, NSABB has been meeting biannually and conducting its work primarily through working groups. The groups have been developing criteria for identifying and evaluating dual use research, generating communication strategies related to dual use research, exploring the use of codes of conduct for life sciences, and beginning to outline a regulatory scheme for control of dual use research. More recent working group projects include outreach to the international research and policy community and the regulation of synthetic genomics. NSABB has been actively seeking engagement with the broader scientific community on these issues, setting up meetings with stakeholders and participating in domestic and international scientific and professional conferences. Their meetings are open to the public, webcast live and all meeting materials and agenda items are available online at the NSABB website: www.biosecurityboard.gov.

Among the NSABB draft products currently available for viewing on their website are the criteria for identifying dual use research and evaluating whether it is of concern and in need of further review. This review process is the subject of the NSABB working group on oversight, which is developing an oversight and review framework similar to that of IACUCs, IRBs or the RAC. In addition, NSABB has published considerations for developing a code of conduct for life sciences, which they see as a guideline for use by scientific societies or institutions. The synthetic genomics group has just issued a report recommending potential modifications to the select agents rules, as well as proposed restrictions or regulations on suppliers of synthetic DNA. Directed at both publishers and scientists, the communications working group has put forward several products and reports related to publishing research with dual use implications. Among NSABB's charges, as a federal advisory body, is to serve as a national level of review and advice for the dissemination of research results. Their first foray into this function was the review of the publication of the reconstructed 1918 influenza virus in September 2005.

Why should biomedical researchers pay attention to NSABB's activities? NIH has made it very clear that when NSABB's products and recommendations are final, they plan to implement many of them as requisite for federal funding. Given the interagency nature of NSABB, it may be likely other federal science agencies will follow suit. For example, the synthetic genomics working group has suggested a number of ways suppliers of synthetic DNA might prevent aiding the construction or reconstruction of a pathogenic organism, including referencing the select agents taxonomy and keeping detailed records. They have also recommended that federal grantees be required to obtain synthetic DNA only from those suppliers complying with these rules. Although many of the NSABB's recommendations are thoughtful, proactive, and even sound policy, it is without doubt that if implemented, they will affect life scientists. FASEB has been following the activities of NSABB very closely and in June, FASEB President Leo Furcht, M.D. participated in a roundtable discussion to provide input on NSABB's criteria for identifying dual use research . NSABB plans on publishing all of its recommendations and products, when final, in the federal register for public comment. In the meantime, however, nearly all of their documents are freely available online for review and members of NSABB seem eager to receive feedback from the scientific community.

NIMH Research Seeks to Find How Antidepressants May Be Associated with Suicide

The National Institute of Mental Health (NIMH), part of the National Institutes of Health (NIH), is funding five new research projects that will shed light on antidepressant medications, notably selective serotonin reuptake inhibitors (SSRIs) and their association with suicidal thoughts and actions.

Studies have shown that most individuals suffering from moderate and severe depression, even those with suicidal thoughts, can substantially benefit from antidepressant medication treatment. However, use of SSRIs in children and adolescents has become controversial. In 2005, the U.S. Food and Drug Administration (FDA) adopted a "black box" warning, the most serious type of warning in prescription drug labeling, for all SSRIs. The notice alerts doctors and patients of the potential for SSRIs to prompt suicidal thinking in children and adolescents and urges diligent clinical monitoring of individuals of all ages taking the medications. This can be particularly challenging because it is difficult for patients, their family members, and practitioners to determine whether suicidal thoughts may be related to the depression, the medication, or both.

"These new, multi-year projects will clarify the connection between SSRI use and suicidality," said NIMH director Thomas Insel. "They will help determine why and how SSRIs may trigger suicidal thinking and behavior in some people but not others, and may lead to new tools that will help us screen for those who are most vulnerable."

The projects are:

Kelly Kelleher, M.D., of the Columbus Children's Hospital and the Ohio State University, and Joel Greenhouse, Ph.D., of Carnegie Mellon University, will build on data initially collected by the FDA to analyze antidepressant medication use and suicidal behavior among youth, adults, and older adults. Kelleher will use new and more sensitive statistical approaches to integrate data from numerous other studies—both randomized and non-experimental—to paint a more complete picture of the relationship between antidepressant medication use and suicidal thoughts or actions.

Marcia Valenstein, M.D., of the University of Michigan, will examine the records of 994,000 individuals from the U.S. Department of Veterans Affairs National Registry for Depression, Medicare records, and the National Death Index to determine what relationships exist between the use of antidepressants and suicide attempts and/or deaths and the use of any concurrent medications or treatments. The study will help determine the relative effectiveness of different depression treatments in reducing suicidal thoughts and actions.

Wayne Goodman, M.D., of the University of Florida, will investigate if and how SSRIs may induce in some young people an "activation syndrome"—a set of symptoms such as irritability, agitation, and mood swings that may lead to suicidal thoughts or actions. He will study this potential syndrome among pediatric patients diagnosed with obsessive compulsive disorder. By focusing on patients with a disorder that is less likely to be associated with suicidality, he will be able to better assess whether SSRIs are related to an actual activation syndrome and whether suicidality is a component of the syndrome. The study will improve recognition and understanding of the syndrome and help identify interventions that will reduce the risk of suicide.

Sebastian Schneeweiss, M.D., of Brigham and Women's Hospital, will assess critical issues surrounding the safety of antidepressant medication use by comparing several large datasets of SSRI users. He will measure rates of suicidality, identify social and demographic factors that may be associated with SSRI use and suicidality, and examine the impact of FDA actions on use of SSRIs. The study aims to develop and better target prescribing and risk management strategies.

Prudence Winslow Fisher, Ph.D., of the New York State Psychiatric Institute, will develop better and more reliable ways of monitoring for adverse reactions to the use of antidepressant medication. The study's long term goal is to construct a standardized computer tool for adolescents and parents that could be used to screen for suicidality associated with the use of antidepressant medications.

In addition to these new projects, NIMH is funding other studies that aim to find the best treatments for individuals suffering from depression, and reduce or prevent suicidal behavior. Studies focused on youth depression and suicidal behavior include the Treatment for Adolescents with Depression study, the Treatment of SSRI-Resistant Depression in Adolescents, and the Treatment of Adolescent Suicide Attempters.

Scientists Reverse Friedreich's Ataxia Defect in Cell Culture

In a study published in the October issue of *Nature Chemical Biology,* researchers tested a variety of compounds that inhibited a class of enzymes known as histone deacetylases in a cell line derived from blood cells from a Friedreich's ataxia sufferer. One of these inhibitors had the effect of reactivating the frataxin gene, which is silenced in those with the disease.

The researchers then went on to improve on this molecule by synthesis of novel derivatives, identifying compounds that would reactivate the frataxin gene in blood cells taken from 13 Friedreich's ataxia patients. In fact, one of the compounds the researchers tested produced what amounted to full reactivation of the frataxin gene in 100 percent of cells tested.

About one of every 20,000 to 50,000 people in the United States has Friedreich's ataxia, which is caused by a genetic defect that prevents adequate production of the protein frataxin. In neuronal and muscle cells, frataxin is essential for proper functioning of mitochondria. Low levels of the protein lead to degeneration of nerve tissue in the spinal cord and nerves controlling muscle movement in the arms and legs.

The genetic defect involves numerous extra repeats of a GAA-TTC triplet pattern in a person's DNA that prevent expression of the frataxin gene. Where normal cells contain 6 to 34 repeats, Friedreich's ataxia sufferers can have as many as 1,700. The more triplets a person's DNA contains, the earlier symptoms appear and the greater their severity.

Only individuals who carry the Friedreich's ataxia defect on both of their paired alleles, i.e. who are homozygous for the trait, suffer from the condition. Those individuals who are heterozygous, with only one defective allele, produce about half the normal level of frataxin but do not suffer disease symptoms. This suggests that a treatment for Friedreich's ataxia need not raise frataxin production all the way to normal levels to be effective.

Joel Gottesfeld, Ph.D., a professor in the Scripps Research Department of Molecular Biology and leader of the project, notes that the repeats causing Friedreich's ataxia are in a region of the gene that does not code for the protein frataxin, so reversing gene silencing may be all that is needed to treat the disease.

Researchers are still working to understand the reasons the triplet repeats prevent transcription of the frataxin gene. One idea suggested by the paper's authors is that the triplets cause an unusual DNA structure that attracts proteins such as histone deacetylases (HDACs), removing critical acetyl groups from the histones, packaging the histones in an inactive form called heterochromatin and ultimately leading to silencing of the frataxin gene.

Based on this theory, Gottesfeld and his colleagues began looking for compounds that might block the HDACs with the goal of reactivating frataxin production. The researchers were able to draw from a range of commercially available products because many HDAC inhibitors have been developed as tools for molecular biology research and as potential cancer treatments.

Experiments revealed that one HDAC inhibitor, called BML-210, did in fact reverse the heterochromatin formation in cultured lymphocytes from Friedreich's ataxia patients and increased the production of frataxin messenger RNA (mRNA), although not sufficiently to bring protein production to normal.

Next, the researchers chemically modified BML-210 to produce a variety of analogs whose effects on the cells were then tested. One class of analogs produced a two- to three-fold increase in frataxin transcription amounting to full reactivation of the frataxin gene in

Continued on next page

Dr. Joel M. Gottesfeld

ASBMB member Joel M. Gottesfeld is Professor in the Department of Molecular Biology at The Scripps Research Institute in La Jolla, California. He received his B.A. in Biochemistry from the University of California, Berkeley in 1971, and his M.Sc. in Biochemistry from Merton College, Oxford University in 1973. He then earned his Ph.D. in Biochemistry from the California Institute of Technology in 1975. Gottesfeld joined the Division of Cellular Biology at The Scripps Research Institute as an Assistant Member in 1978. He then became a member of the Department of Molecular Biology in 1984. Gottesfeld left Scripps in 1989 to become Chief of the Division of Developmental Biology at the Medical Biology Institute in La Jolla, but returned to the Scripps in 1992. Research in the Gottesfeld laboratory concerns the protein-DNA interactions involved in regulation of gene expression in mammalian cells and the development of small molecules to regulate gene expression at will. His current research focuses on the development of Py-Im polyamides as new therapeutics for human diseases, including cancer, neurodegenerative diseases, and infectious diseases. Gottesfeld is also an Associate Editor for the *Journal of Biological Chemistry.*

Researchers Uncover Critical Player in Cell Communication

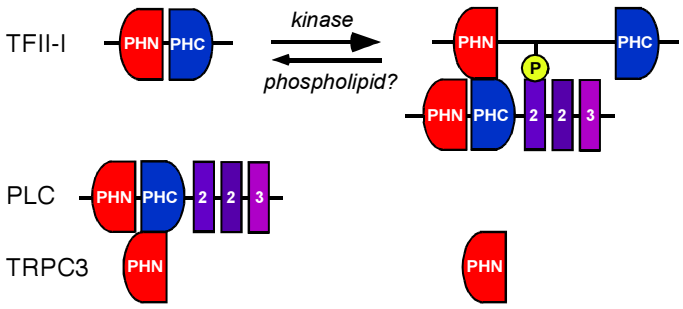
Johns Hopkins researchers have teased out the function of a protein implicated in Williams-Beuren syndrome, a rare cognitive disorder associated with overly social behavior and lack of spatial awareness. Called TFII-I, the protein, which has long been known to help control a cell's genes, also controls how much calcium a cell takes in. The study was published in the October 6 issue of *Science*.

"While the previously described function of TFII-I very well also could contribute to the cognitive defects of Williams-Beuren syndrome, its role controlling calcium makes much more sense," says Stephen Desiderio, M.D., Ph.D., a professor of molecular biology and genetics and director of the Institute of Basic Biomedical Sciences at Hopkins. And, says Desiderio, others have shown that defects in a cell's ability to take in calcium can lead to other neurological and behavioral conditions.

Williams-Beuren syndrome occurs in roughly one in 25,000 births and is caused by a deletion of a small section of chromosome 7 that contains several genes, including the gene that encodes the TFII-I protein.

The discovery came after Desiderio and his team used biochemical bait to fish for candidate proteins that bind to TFII-I. The fishing expedition returned one protein known to control when and how much calcium a cell takes in.

"The partner we found in the fishing experiment and the abundance of TFII-I outside the cell nucleus led us to suspect that this protein must be doing more than regulating gene expression," says Desiderio.



A model for antagonism between PLC-gamma and TFII-I in which TFII-I fluctuates between "open" and "closed" states.

"The finding was stunning to us because calcium is one of the most important messengers in cells," says Desiderio, "and both it and TFII-I are in every cell. That affirmed our suspicion that TFII-I could be doing something important with calcium signaling."

In one experiment, the Hopkins team knocked down the amount of TFII-I in lab-grown cells and looked for changes in calcium flow under a high power microscope using a dye that glows when it comes in contact with calcium. The researchers realized that when they depleted the cells of TFII-I, the cell responded by installing more calcium channels on their surfaces.

"There's good evidence suggesting that the frequency and intensity of this ebb and flow of calcium can determine a cell's response to external cues," says Desiderio. "TFII-I may be a universal player in communication between cells, in the brain, the immune system, and elsewhere."

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an astonishing 100 percent of cells from 13 Friedreich's ataxia sufferers.

Importantly, the team's HDAC inhibitors have also proven uniformly non-toxic to the lymphocytes and do not significantly affect cell growth rates. Ongoing animal studies also have not revealed any toxicity. If the results of animal testing remain positive, said Gottesfeld, the HDAC inhibitors could enter human trials as a Friedreich's ataxia treatment in as soon as 18 months' time.

ASBMB member Stephen Desiderio is Director of the Johns Hopkins Institute for Basic Biomedical Sciences (IBBS). He received his B.A. from Haverford College in 1974 and completed his M.D. and Ph.D. degrees at the Johns Hopkins University School of Medicine in 1981. He joined the faculty of the Johns Hopkins University School of Medicine in 1984 and became a Howard Hughes Medical Institute Investigator in 2000. He became Director of the Program in Immunology of the Johns Hopkins Institute for Cell Engineering in 2002 and was named Director of IBBS in 2003.

Desiderio is the recipient of numerous awards and honors, including the 1993 Professors' Award for Excellence in Teaching from the Johns Hopkins University School of Medicine and the Michael A. Shanoff Research Award. He has authored or co-authored works in more than 54 publications. He currently studies the immune system and mechanisms that govern assembly of antigen receptor genes. His laboratory has begun to use new tools of genetics and genomics to describe and dissect immune responses that are genetically hardwired, or stereotypic, such as the onset of inflammation.

Dr. Stephen Desiderio

Structure of Enzyme Offers Treatment Clues for Diabetes, Alzheimers

Researchers from the University of Chicago and Argonne National Laboratory have deciphered the three-dimensional structure of insulin-degrading enzyme, a promising target for new drugs because it breaks down not only insulin but also the amyloid-beta protein, which has been linked to the cognitive decline of Alzheimer disease.

In the October 19 issue of *Nature*, the researchers described the structures of insulin-degrading enzyme (IDE) in complex with four of the proteins it digests: insulin, amyloid-beta, amylin, and glucagon. The structures suggest ways to develop drugs that could either speed up or slow down this ubiquitous enzyme's activity.

"The structure of insulin-degrading enzyme tells us a lot about how it works, which is somewhat unorthodox," said Wei-Jen Tang, Ph.D., associate professor in the Ben May Institute for Cancer Research at the University of Chicago and director of the study. "Understanding how it works gives us clues about how to design drugs either to inhibit or activate it.

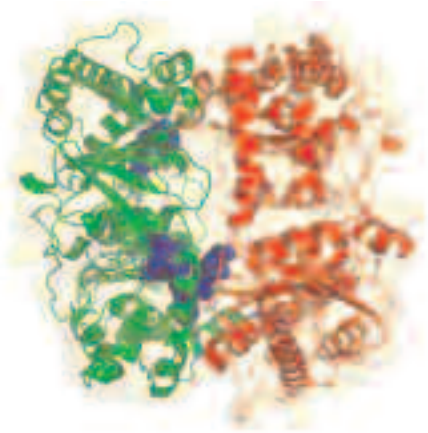
"By introducing small, targeted mutations, we have already been able to increase the enzyme's activity by as much as 40-fold," he said. "That gives us a blueprint for the next step, trying to devise a drug that would produce a similar effect."

Using the Advanced Photon Source at Argonne National Laboratory, Tang and colleagues were able to solve the structures of this enzyme in complex with insulin and with amyloid-beta, as well as amylin and glucagon. These high resolution crystal structures open the door to the rational design of pharmacological modulators of this important protease.

The enzyme, Tang's team reports, resembles the video game character "Pac-Man," with two bowl-shaped halves joined by a hinge at one end and held closed, most of the time, by a latch of hydrogen bonds on the other end. When the bowls come together, like a shut mouth, they enclose a chamber, shaped like a triangular prism, with a base that measures 35 x 34 x 30 angstroms and a height of 36 angstroms, large enough to contain relatively small peptides, such as insulin or amyloid-beta, which have fewer than 50 amino acids.

Although it can cleave larger molecules, the proteins IDE degrades most readily fit neatly within this chamber. Negative electrical charges on their outer surfaces help to align them with the positive charges on one inner surface of the chamber. Once they are in place, the enzyme slices them multiple times into tiny pieces, which are then discarded.

Although the enzyme's structure is similar to Pac-Man, its behavior differs. Pac-Man keeps his mouth wide open to gobble up anything in his path. With IDE the mouth is usually closed. The hydrogen bond latch that holds the jaws together protects its active, or catalytic, site.



Structure of human insulin-degrading enzyme (IDE) in complex with beta-amyloid.

IDE resembles the video game character "Pac-Man," with two bowl-shaped halves joined by a hinge at one end and held closed, most of the time, by a latch of hydrogen bonds on the other end.

But in a series of experiments, Tang and colleagues were able to make small mutations of IDE that altered only the latch, disrupting the alignment of contacts that normally keep the enzyme closed. Three of these altered versions of wide open IDE proved to be 30 to 40

Continued on next page

Dr. Wei-Jen Tang

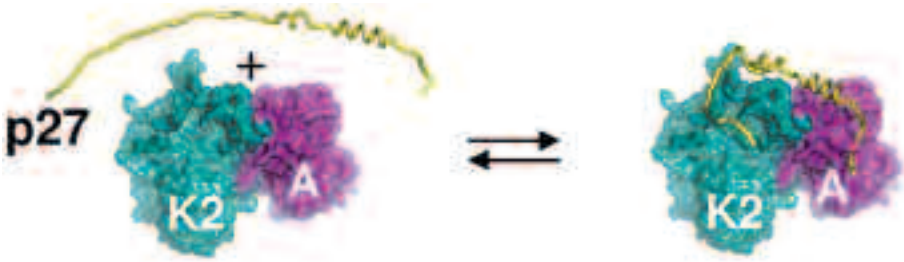
ASBMB member Wei-Jen Tang is an Associate Professor at the Ben May Institute for Cancer Research at the University of Chicago. He received his B.S. in Zoology at the National Taiwan University in 1982. After two years of service in the Republic of China's Air Force, his earned his Ph.D. in Biological Sciences at the University of Texas at Austin in 1988. He became an Instructor at the University of Texas Southwestern Medical School in 1991 and was promoted to Assistant Professor in 1993. He joined the faculty of the University of Chicago in 1994.

Tang has authored or co-authored works in more than 50 publications, and holds two patents. He is the recipient of many honors and awards including the 1999 American Heart Association Established Investigator Award. His laboratory currently focuses on elucidating the molecular basis of cell communication by analyzing the interaction between prokaryotic and eukaryotic cells. His current research deals with the biology of bacterial adenylyl cyclase toxins, proteins that secreted by human bacterial pathogens.

First Major Study of Mammalian "Disorderly" Proteins

Investigators at St. Jude Children's Research Hospital turned up the heat on "disorderly" proteins and confirmed that most of these unruly molecules perform critical functions in the cell. The St. Jude team completed the first large scale collection, investigation, and classification of these so-called intrinsically unstructured proteins (IUPs), a large group of molecules that play vital roles in the daily activities of cells.

The new technique for collecting and identifying IUPs is important because although scientists have been aware of the existence of flexible proteins for many years, they have only recently realized that these molecules play major biological roles in the cell, according to Richard Kriwacki, Ph.D., an associate member of the St. Jude Department of Structural Biology. Moreover, he said, previous work by other researchers suggested that a large proportion of IUPs in mammalian cells play key roles in transmitting signals and coordinating biochemical and genetic activities that keep the cell alive and functioning. Kriwacki is senior author of a report on this work that appears in the October issue of *Journal of Proteome Research*.



IUPs play diverse roles in cells by folding upon binding to their regulatory targets.

"Until now there was no way to separate IUPs in large numbers from the more structured proteins and confirm their roles in the cell," Kriwacki said. "Our new technique selectively concentrates the IUPs that are involved in regulating functions in the cell and transmitting signals within them."

Unlike the classic description of proteins described in science textbooks, IUPs are not completely locked into rigid, three-dimensional shapes that determine their function in the cell. Instead, IUPs have varying amounts of flexibility within their sometimes spaghetti-like structures that is critical for function. For example, one protein named p27 initially looks like a Slinky™ toy. However, when p27 goes to work, it puts a vise-like grip on an enzyme that otherwise would promote uncontrolled cell division.

The St. Jude team developed a technique that uses heat to isolate IUPs in large, purified quantities from extracts of NIH3T3 fibroblasts. The IUPs were resistant to the heat, unlike more structured proteins, which fell apart. Based on these studies, the investigators were able to classify all proteins into one of three categories: IUPs, intrinsically folded proteins (IFPs, i.e. fully folded into specific shapes), or mixed ordered or disordered proteins (MPs), which have both structured and unstructured parts.

"This work further illustrates that the disorderliness of IUPs isn't just a curiosity," said Charles Galea, Ph.D., a postdoctoral fellow in Kriwacki's lab. "This characteristic is a fundamental part of how these proteins work. So determining their exact nature, including the parts that are disordered, is an important part of understanding how they work. This is especially important in the case of IUPs linked to cancer and other diseases."

Dr. Richard Kriwacki

ASBMB member Richard Kriwacki, Ph.D., is an assistant member in the St. Jude Children's Research Hospital Structural Biology Department. He joined the St. Jude staff in 1997 after performing postdoctoral studies at The Scripps Research Institute and receiving graduate training at Yale University.

Kriwacki's laboratory applies structural, biophysical, and cell biology techniques to understand the relationships between protein structure and biological function. Emphasis is placed on studies of proteins within tumor suppressor pathways, especially those involved in regulating the cell division cycle, because their genes are frequently targeted by mutations in cancer.

times more active than the normal version of the enzyme.

"This suggests that the rate limiting step may be the speed at which the enzyme can reopen and then clamp down on a new morsel rather than the time it takes to chew something up," said Tang. "This makes us think that if we can slightly alter its shape, we can substantially boost its activity."

The researchers are now searching for small molecules that can duplicate the effects of those mutations, shifting the balance toward the open rather than the closed state. "Such compounds," the authors note, "might facilitate the clearance of amyloid-beta and other pathologically relevant IDE substrates."

Biomedical Careers in Industry:

By Robert A. Copeland, Ph.D., Vice President, Enzymology & Mechanistic Pharmacology, GlaxoSmithKline Pharmaceuticals

The desire to find practical solutions to problems of commercial interest has fueled key discoveries in the biochemical sciences from early civilizations to the present. Throughout history, practical applications of biological chemistry have contributed in myriad ways to improving the human condition. In modern times, industrial applications of biomedical sciences, perhaps most notably within the pharmaceutical industry, have contributed greatly to extending and enhancing human life through the discovery, development and commercialization of medicines, diagnostics and medical devices.

Hence, innovation, creativity and the desire to apply these skills in a focused and contemporaneous way to societal problems has been, and continues, to be the hallmarks of industrial biomedical science. A scientific career in industry can be extremely rewarding for those who wish to see the potential fruits of their labors translate into meaningful impact on humanity within their own lifetime. A growing number of young scientists are emerging from their academic training with the realization that their professional aspirations can be best met through a career in industry. Although many bright and talented students have come to this realization, few of them have any familiarity with how science is conducted within an industrial setting and what skills are most valued by their potential employers. This month and next month I will attempt to address these issues in a two-part series on biomedical careers in industry. All of my industrial experience has been in the pharmaceutical industry and I will focus my comments on this industry. I suspect, however, that many of the statements I am about to make apply equally well to other biomedical industries as well.

Transitioning from Academic to Industrial Science

Everyone who enters the biomedical industry comes out of an academic setting where there are specific goals and approaches to how science is done. The goals and approaches in industry are distinct, and can seem quite foreign to the newcomer; it is thus worthwhile to consider how these two settings differ.

One of the most obvious differences is in the degree of focus that is applied to biological questions within the two settings. While academic researchers tend to ask questions of broad interest, the industrial researcher must take a more practical view, focusing attention almost exclusively on questions of pathobiology that have a direct clinical utility. To exemplify this consider the activity of target validation within the pharmaceutical industry. The goal here is to determine whether the activity of a particular biomolecule (usually a protein) is critical to a specific disease process and whether targeting this biomolecule for drug intervention will have the desired effect on the disease. This activity requires the combined efforts of scientists from multiple disciplines including biochemistry, molecular biology, genetics, cellular and animal biology and perhaps medicinal chemistry. One can invest many months or even years in understanding the detailed role of a putative target in, for example, cell signaling. Along the way one may uncover fascinating aspects of the cell biology associated with a particular biomolecule, but may also discover that it is not an appropriate target for drug discovery. At such a point, an academically trained scientist may be tempted to explore further the interesting biochemistry and biology of the molecule, to add to the general knowledge base. The industrial scientist, however, must immediately abandon further work on such a target, as to prolong efforts on the target would be counterproductive to the goal of bringing new medicines to patients in need. The industrial scientist is likely to publish his/her finding so that others, perhaps in academics, can pursue the basic science, but would then quickly move on to other activities. This example illustrates another distinction between academic and industrial research: project lifetimes are much more finite in the industrial setting. It is not uncommon for an academic scientist to pursue a major research project or at least a common research theme for a significant portion of their career. In contrast, projects in industry are of more limited duration, defined either by successful transition to the market or by suspension for pragmatic reasons, as just described. Pharmaceutical research is expensive; current estimates of the typical cost of going from target identification to a marketed drug are in the range of 900 million U.S. dollars. Hence, if a project is not going to yield a usable drug, it is in the researcher's and the company's best interest to discover this and terminate the project as early as possible. For this reason, scientists in industry are often challenged to come up with what are commonly referred to as "killer experiments" - designed to test rigorously the suitability of a scientific approach for progression. Failure to meet predetermined outcomes in such experiments would lead to termination (i.e., "killing") of the project.

For young investigators in academic settings (e.g. assistant professors) there is usually a strong incentive to work as an independent researcher and to avoid significant collaborative research. This is because collaborative research

A Few Tips for the Newcomer (Part 1)

projects make it difficult for tenure committees to assess the significance of the individual investigator's contributions. In stark contrast, essentially all research in the industrial sector is done as collaborative, matrix teams. This is necessitated by the complexity of drug discovery, requiring the concerted efforts of talented scientists from multiple disciplines from molecular biologists and biochemists to clinicians. Thus, newcomers to the pharmaceutical industry must adapt to this style of interactive and interdependent science.

A final contrast between academic and industrial science is the ultimate product of the efforts in these two sectors. In academics the ultimate product of research is information, most typically disseminated in the form of scholarly publications and lectures. In industry the ultimate product of research is a tangible entity, such as a new medicine in the case of the pharmaceutical industry. What about the information gleaned along the path to product marketing? As with our academic colleagues, we industrial scientists share this information with the general scientific community in the form of scholarly publications, lectures and patents. However, where these media for information sharing are the key products of academic research, they are viewed as byproducts – important byproducts, but byproducts nonetheless - of industrial research.

Skills Valued by Industrial Employers

As a young scientist nears completion of their academic training it is common to begin thinking about how best to present oneself to potential employers. A question that frequently arises at this point is what are the skills and talents that are most valued by potential employers and that may portend career success in the industrial sector. There is no generic answer to this type of question. Every company and every individual hiring manager will have different perspectives on this issue. I can only answer this question from the perspective of a supervisor and hiring manager, in terms of what I personally find of most value in potential employees. Below I describe some of the attributes that I look for in job candidates.

Be a scientist, not a technologist. Everyone coming out of their academic training will have honed their skills in specific types of technologies. Employers expect you to be a master of your craft. However, it is a fundamental mistake to market yourself on the basis of a collection of specific techniques that you are trained in. Rather, what is most valued is someone who demonstrates good scientific problem solving abilities. This involves being able to: identify important scientific problems, define a cogent plan for experimentally approaching the problem, collect and analyze data appropriately, test hypotheses objectively, draw clear and thoughtful conclusions and be able to effectively communicate these conclusions and their impact in the broader context of a drug discovery project to fellow scientists and laypeople.

Demonstrate quantitative skills. While there are many important techniques in biological sciences that yield qualitative results, the greatest value is usually gained from quantitative data. Hence, researchers who can analyze and interpret data in quantitative terms, using appropriate mathematical models, are highly sought after. I believe this to be universally true in all science, but it is especially important to industrial science. Phenomenological observations may be a good starting point for an investigation, but it is only when one can define a phenomenon quantitatively that one can truly begin to understand the nature of the observations. In the pharmaceutical industry quantitative data is needed at every step in discovery and development. Drug-target affinity, cellular and in vivo dose-response analysis must all be expressed in quantitative terms; synthetic steps must be quantified in terms of reactant stoichiometry and yields; drug formulation must be precisely described; and pharmacokinetics, toxicokinetcs and pharmacodynamics must all be defined in a quantitative fashion.

Communicate effectively. I cannot stress enough the importance placed on effective oral and written communication skills. These are absolutely critical to success in any field of science. It doesn't matter how brilliant a theoretician, nor how skilled an experimentalist you are if you cannot communicate your ideas, results and conclusions to your peers and others. Hence, hone these skills throughout your academic training. Write and speak as often as you can. Seek out and accept constructive criticism from mentors, colleagues and others whose skills you admire. If English is not your first language, don't expect prospective employers to take this into account; it is up to you to be a competitive job candidate. Therefore, look for extra help during your academic training.

Be a team player. As I've described above, industrial science is a team sport. People who can effectively network and collaborate in the context of project matrix teams will be most successful in industry. Those who need all the glory and therefore try to work in isolation are doomed to failure in this setting. Drug discovery is just too complicated for any one person to master. It is only through

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ASBMB 2007 Enzymes: Mechanism and Design

Organizer: Dorothee Kern

The enormous rate acceleration and specificity of enzymes has fascinated scientists for many decades. While classical enzymology has provided detailed insight into the chemical nature of these catalyzed reactions, structural biology elevated our understanding to a new level. Recently, the role of protein dynamics for enzyme catalysis has gained increasing interest. New biophysical methods such as NMR spectroscopy, single molecule experiments, mass spectrometry as well as development of sophisticated computational approaches to this problem provide powerful tools to investigate this question. The unique features of macromolecules to sample conformational states, a necessity for function, is being presented in a separate, but coordinated theme, Macromolecular Structure and Dynamics).

The Enzymes Theme at the 2007 ASBMB meeting in Washington will offer a comprehensive picture of our current understanding of enzyme mechanisms based on all the above mentioned approaches. Thanks to the diverse group of speakers we will see the beauty of combining different experimental approaches and computation to tackle the secrets of enzymes. Open questions will be identified that need to be addressed in the future.

The session entitled Structural Enzymology will highlight the incredible impact of x-ray crystallography to the current understanding of enzyme mechanisms. Dr. Karen Allen (Boston University) will illustrate how knowledge of atomic resolution of a number of intermediates in an enzymatic cycle reveals chemical details of enzyme catalysis. Dr. Perry Frey (University of Wisconsin) will shed light into the energetics of an enzyme-catalyzed reaction. Dr. Dagmar Ringe (Brandeis University) will talk about the mechanism of pyridoxal phosphate, one of the most universally used cofactors in nature, and how mechanism-based inhibitors for this enzyme class function.

Dr. Peter Wright (The Scripps Research Institute) will chair the session The Role of Dynamics in Enzyme Catalysis and discuss dynamic NMR experiments and classic enzyme kinetics to describe the energy landscape of the enzyme dihydofolate reductase (DFHR). Dr. Gordon Hammes (Duke University) will follow with single molecule studies on DFHR. Dr. Dorothee Kern (HHMI/Brandeis University) will explore the dynamic personality of enzymes by "watching" them during turnover. Through combining crystallography, NMR, computation and single molecule FRET experiments she investigates the hierarchy in time scale of dynamics. Dr. Judith Klinman (University of Berkeley) will present exciting results on hydrogen tunneling that give insight into the role of dynamics in enzyme catalysis.

The session on Computational Studies of Mechanistic and Dynamical Aspects of Enzyme Reactions, chaired by Dr. Sharon Hammes-Schiffer (Pennsylvania State University) will emphasize the power of computation in our efforts to understand how enzymes accomplish their incredible catalytic efficiencies. Dr. Hammes-Schiffer will illustrate that by comparing computational results on hydrogen tunneling with experimental data. Dr. Kenneth Merz (University of Florida) and Dr. Jiali Gao (University of Minnesota) will present a similar theme. This session will demonstrate state of the art methodology in computation and the strength of these methods of detecting correlated motions and characterizing pathways.

Dr. Dorothee Kern inserting an NMR sample in a 600 MHz NMR spectrometer.

The session on Enzyme Design will exemplify our current understanding of enzyme mechanism by rational design of enzymes. Stephen Mayo (HHMI/California Institute of Technology) will present recent successes in computational enzyme design. Dr. Kendall N. Houk (University of California, Los Angeles) will focus on the heart of an enzyme, the active site. He will show results from active site designs based on Quantum Mechanical calculations. Dr. Homme W. Hellinga (Duke University Medical Center) will implement a number of different functions in a protein using a common scaffold as a starting point for rational design.

From Genome to Epigenome – Modification and Repair

Organizer: Gregory Verdine, Harvard University

Tremendous strides have been made in recent years toward understanding what may be called "the secret life of the genome," the spectacular enzyme-catalyzed operations that alter the covalent structure of DNA to remodel its information content and enable it to withstand the sometimes harsh environment of the cell. Scientists at the leading edge of this revolution in our understanding of genomic husbandry will convene at the 2007 ASBMB Meeting, April 28 – May 2 in Washington, DC, to provide an account of their latest findings in this fast-moving area. This Theme, organized by Greg Verdine of Harvard University and the Dana-Farber Cancer Institute and entitled From Genome to Epigenome – Modification and Repair, consists of four sessions, each covering an important topic in genome modification.

The first session, Recombining and Modifying DNA, was organized and will be chaired by David Schatz of Yale university. The talk of David Schatz will focus on the use of FRET to examine the structure of the synaptic complex formed by the RAG1/RAG2 proteins during V(D)J recombination. Greg Van Duyne of the Howard Hughes Medical Institute and the University of Pennsylvania School of Medicine will discuss recent insights into the asymmetric nature of the Cre-loxP site-specific recombination reaction. William Reznikoff of the University of Madison-Wisconsin will discuss structure and function studies on transposition catalyzed by Tn5 transposase.

Dr. Greg Verdine

The second session, Making and Re-Making DNA, was organized and will be chaired by Lorena Beese of Duke University Medical Center. Lorena Beese will discuss insights into DNA replication and repair. Graham Walker of MIT will cover recent developments in understanding the process of translesion DNA synthesis. Greg Verdine will recount the efforts of his lab to understand how DNA glycosyases locate rare damaged bases embedded in a vast excess of undamaged DNA.

The third session, Telomeres and Telomerase, was organized and will be chaired by Kathleen Collins of the University of California, Berkeley. In this session, Elizabeth Blackburn of the University of California, San Francisco will talk about new developments in studies of telomeres and their maintenance mechanisms. Kathy Collins' talk will describe requirements for telomerase ribonucleoprotein assembly and activity in the cellular context. Carol Greider will explain their study regarding how short telomeres limit the division of both cancer cells and stem cells and the role that this shortening plays in human disease.

The fourth and final session, Methylating and De-methylating DNA, was organized and will be chaired by Tim Bestor of Columbia University College of Physicians and Surgeons. In this session, Tomas Lindahl of Cancer Research UK will discuss biochemical and cellular studies aimed at understanding human proteins responsible for the repair of aberrantly methylated DNA. Tim Bestor will talk about methylation of aspartic acid tRNA by a protein that by sequence and structure must be a DNA methyltransferase. Bob Fischer of the University of California, Berkeley will discuss how the DEMETER (DME) DNA glycosylase establishes gene imprinting by demethylating maternal alleles in Arabidopsis.

Careers continued ...

Continued from page 13

team efforts that new medicines can be successfully discovered and developed.

Think holistically. As a member of a project matrix team, you will have primary responsibility for one aspect of the project, or for the application of one scientific discipline (e.g., biochemistry or molecular biology). Again, you are expected to be a master of your specific discipline, but that is not enough. Successful researchers in the pharmaceutical industry are those who commit to understanding a project in its entirety. This does not mean that one must be an expert in every discipline. Rather it means making a commitment to learning enough about each aspect of a project team so that one can be an effective collaborator with one's colleagues from different disciplines, and can best put one's own research in the correct context of the project team objectives.

In part 2 of this series we will discuss some frequent misconceptions about industry and some more general advice for career fulfillment.

Susan Taylor to Receive William C. Rose Award

Former ASBMB President Susan Taylor of the Department of Chemistry and Biochemistry and an HHMI Investigator at the University of California, San Diego, has been selected to receive the William C. Rose Award. The Award recognizes outstanding contributions to biochemical and molecular biological research and a demonstrated commitment to the training of younger scientists, as epitomized by the late Dr. William C. Rose. The Award consists of a plaque, stipend, and transportation to the 2007 Meeting to present a lecture. Recent recipients of this award were: W. L. Smith in 2006, Frederick P. Guengerich in 2005, Sunney I. Chanin 2004, Jack E. Dixon in 2003, and in 2002 Gordon Hammes.

Taylor is one of the most preeminent scientists in the world studying the structure and function of protein kinases, a large family of signaling proteins representing 2% of the human genome, and involved in many crucial cellular processes including growth, metabolism, differentiation and apoptosis. Disregulation of this family of molecules underlies a number of diseases, especially cancer. Susan was the first to crystallize a protein kinase, the cAMP-dependent protein kinase, which revolutionized our understanding of the body plan of protein kinases as a family. This classic work has shed light on the evolution, function, and dynamics of protein kinases. She has been for the past 20 years the leading figure this important field. She published the first crystal structure of the cAMP-dependent protein kinase in 1991, and there followed a highly productive period in which she illuminated the allosteric regulation, dynamics, catalytic mechanism and energetics, and recognition of substrates, modifiers, activators and other binding partner proteins.

Taylor's broad interests and collaborative style are evident in her activism in making the implications of her structural insights as broadly available as possible to the scientific community. She worked hard with others in the field to create the Protein Kinase Resource (http://pk[.sdsc.edu/html/index.shtml) which houses a rich compendium of information about protein kinases, and tools for structural and computational analyses. Anyone who has been involved in such broad, community-minded endeavors knows that they are labors of love, and they require just the skills that Taylor has of imparting her enthusiasm and ambition to others, organizing meetings and working groups, and always passing along most of the credit to her collaborators.

Her interest in ways to foster widespread collaboration between disparate disciplines that intersect around molecular structure, led to her active involvement in biomolecular computing in collaboration with the San Diego Supercomputer Center, where she is a Senior Fellow. Taylor plays important leadership roles in biomolecular structural visualization and bioinformatics. She also worked hard with Helen Berman on a project that revolutionized the usability of the Protein Data Bank (PDB). In her local environment, in the UCSD and San Diego area, she is a bridge- builder, consortium-builder and collaborative force. In addition, she is a superb recruiter for UCSD and the larger local scientific community.

Dr. Susan Taylor

Taylor has played innumerable national and international activist roles that are well-known to FASEB and its member societies. She was an early advocate for increasing involvement of young people in scientific organizations. During her Presidency of ASBMB, she spearheaded membership drives among young people and helped to create the ASBMB Fall Symposia that showcased their talent. She has worked tirelessly to advocate for increased funding for science with FASEB and the Joint Steering Committee (JSC) for Public Policy. She excels at searching out, nurturing, and mentoring young talent, and has served on many panels such as the David and Lucile Packard Fellowships Advisory Panel, the Burroughs Wellcome Fund Advisory Committee for Interfaces in Science Program (2004, Co-Chair), as well as many others. Not surprisingly, she is a wonderful mentor to graduate students and postdoctoral fellows, many of whom are by now accomplished scientists holding academic positions allover the world.

Christopher Burge to Receive Schering-Plough Award

Dr. Christopher Burge of the Department of Biology at Massachusetts Institute of Technology will receive the Schering-Plough Research Institute Award at the ASSBMB Annual Meeting, April 28 – May 2 in Washington, DC. The Schering-Plough Award recognizes outstanding research contributions to biochemistry and molecular biology. The recipient must have no more than ten years post-doctoral experience, and the nominees and nominators need not be ASBMB members. The Award consists of a plaque, stipend, and transportation and expenses to present a lecture at the 2007 Meeting. Previous recipients of this award were J.M. Berger in 2006, Brian Strahl in 2005, Pehr A. B. Harbury in 2004, Catherine Drennan in 2003, and in 2002 John D. York.

Burge did his graduate work at Stanford in Computational Biology with Sam Karlin where he developed a widely acclaimed computational program, Genscan, to identify gene sequences. This and other software Burge has produced have been described as probably second only to BLAST in how widely they are used by genome analysts. After Burge completed two years of postdoctoral research, he became MIT/Merck Bioinformatics Fellow in the Department of Biology.

The nearly unique aspect of Chris' research is the integration of strengths in computational science and statistics with a strong personal interest in biology. This interdisciplinary program makes his research particularly fresh and exciting. Chris is now recognized as a leader in his field of research and his reputation will grow exponentially in the coming years.

One nominator wrote, "Burge is a rare commodity among computational biologists in that he invariably couples his analyses with experimental tests of their validity. Thus, his important. conclusions have foundations in real biology and can be applied with confidence by consumers of bioinformatics." I first came to admire Chris's approach during his postdoctoral work with Phil Sharp. His thorough analysis of the phylogenetic distribution of U12-type introns served as the basis for formulating a novel, and I think reasonable, hypothesis as to the origins of this unanticipated second class of introns and the spliceosome that excises them. His 1997 *Cell* and 1998 .*Molecular Cell* papers proposed that the two spliceosomes evolved from a common ancestor in separate lineages that later fused; subsequent conversion over time of U12-type introns to the U2-type, with more flexible consensus sequences, nicely explains the rarity and distribution of such introns in the genes of modem metazoans.

Upon assuming a more independent position (Bioinformatics Fellow) in 1999, Chris extended his.analyses of the behavior of introns to the most challenging question in pre-mRNA splicing-how fidelity in splice site choice and pairing is achieved. These phenomena underlie alternative splicing, which we now appreciate has multiplied the functional potential of the 28,000 genes estimated to comprise the human genome. Burge's 2001 *PNAS* paper found that "intron definition" works slightly differently in different organisms and framed a picture of the minimal set of features being recognized - in each case. Equally impressive was his 2002 Science paper that combined computational prediction of exonic enhancer sequences with experimental verification of their functioning. The interested biologist was therefore not left dangling in computational space waiting for someone else to test the conclusions.

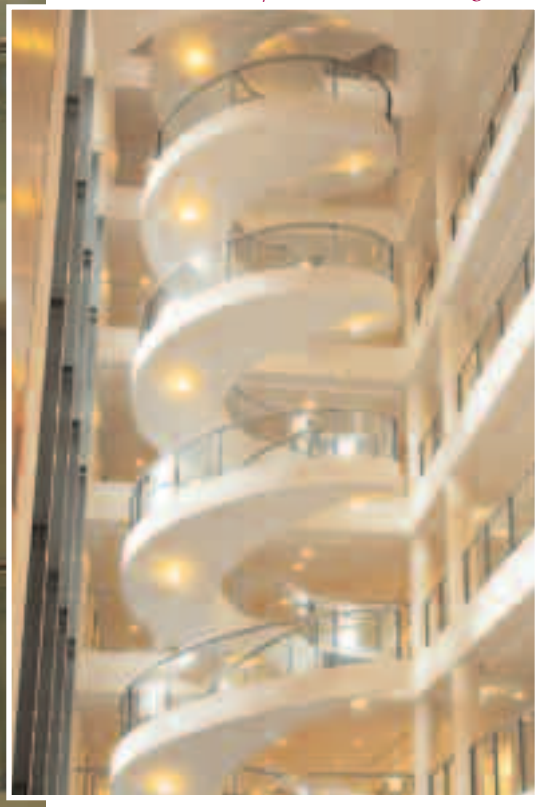

Dr. Christopher Burge

In his subsequent analyses of ahernatively spliced introns, Burge has coupled a clever *in vivo* reporter-based screen with computational approaches to identify decameric exonic splicing silencers, some of which correspond to known recognition sequences for abundant nuclear RNA-binding proteins. Likewise, exons conserved between mouse and man, identified by an exon classification algorithm, were confirmed to exist in alternatively spliced transcripts by RT -PCR sequencing. Interesting differences between the use of alternative splicing in mouse and man have been uncovered and have evolved into useful data bases.

One of Australia's Garvan

The Garvan Institute of Medical Research was founded in 1963. Initially a research department of St.Vincent's Hospital in Sydney, it is now one of Australia's largest medical research institutions with approximately 400 scientists, students and support staff. The Garvan Institute's main research programs are: Cancer, Diabetes and Obesity, Arthritis and Immunology, Osteoporosis, and Neuroscience. It is part of the St. Vincent's Hospital Campus and is affiliated with the University of New South Wales.

The current facilities are only ten years old, and feature an open plan layout of laboratories, around an



The Garvan is positioned to the east of the Sydney central business district, in a trendy café suburb called Darlinghurst.

Largest Medical Research Institutions

atrium that facilitates interaction between scientists from different research disciplines. The stand-out architectural feature is an iconic spiral staircase that represents the DNA helix.

Since its very beginning, the Garvan has placed great importance on combining fundamental research discoveries with clinical outcomes. The Business Development Unit provides the link between Garvan discoveries and the pharmaceutical and biotechnology sector. In 2006, in one of the largest commercial deals in Australian biotech history, the Garvan licensed an anti-inflammatory antibody against the C5a receptor to the Danish company Novo Nordisk.

Research in the 1960s was focussed on diabetes, an area in which Garvan has a strong track record. The institute's scientists were among the first to show that abdominal fat is a high risk factor for type 2 diabetes and that intra-abdominal fat, rather than subcutaneous fat, is the key problem. Microarray analyses of intra-abdominal fat are currently underway to identify proteins with altered levels in insulin-resistant subjects.

The institute's collaborations extend to hospitals and academic research organizations within Australia and around the globe. The Garvan has forged links with the Shanghai Institute of Biological Sciences and has recently provided biochemical and physiological evidence to help confirm that certain traditional Chinese medicinal plants have beneficial effects for people with type 2 diabetes.

Cancer research continues to make fundamental discoveries, such as the recent finding that non-methylated genes that reside in a particular 'suburb' near methylated genes are silenced in cancer; whereas, until now, it was thought that only individual single genes were silenced by methylation. In addition, Garvan's attention to translational cancer research over the last decade has resulted in several key findings. These include: identification of the protein EDD as a new prognostic marker for early ovarian cancer relapse, which may predict the development of chemoresistance; and the finding of a novel prostate cancer marker that helps identify men whose prostate cancer is likely to spread.

Partnerships between the institute's neuroscientists and immunologists has led to the discovery of the mechanism by which neuropeptide Y, a molecule that is proving to have an array of functions in different physiological systems, can suppress the immune system. A similar team effort with scientists in the Bone Program revealed the role of NPY and leptin in bone formation—research that could possibly result in new treatments for osteoporosis.

The Garvan's strengths lie in the calibre of its scientists, unique cross disciplinary collaborations, and the belief that technology is an important component of competitiveness in medical science. The institution was the first in Australia to implement the Affymetrix Microarray Technology. The challenge, as Garvan continues to expand, is to ensure it retains the dynamics of these fruitful interactions and keeps up the excitement and momentum of the research.

Associate Professor Susan Clark

Associate Professor Susan Clark

Professor Clark runs the epigenetics group in Garvan's Cancer program. Her interest in science began with a fascination for growing seeds. At school, Susan's interest in botany grew into other scientific areas, but eventually led her to the study of biochemistry at Australian National University. Her postgraduate years at the University of Adelaide were in the department that first introduced recombinant biology and DNA sequencing to Australia. The next move was into the biotechnology industry where Clark again pioneered an Australian first, this time making the first recombinant vaccine for porcine diarrhea, which is still used today. Clark was also involved in producing the first recombinant interleukins in mammalian cells. A stint at Cambridge followed, after which Clark returned to Australia to join the lab of Marianne Frommer. The research that followed has pushed Susan Clark into the international scientific arena. Her implementation of the bisulphite sequencing method for detecting epigenetic changes is used around the world and has spearheaded a new quest for an international human 'epigenome' project in normal and diseased cells that goes far beyond the DNA sequence of genome. In 2004, Clark received the prestigious German Science Prize, the Biochemisch Analytik Preis.

The Garvan's strengths lie in the calibre of its scientists, unique cross disciplinary collaborations, and the belief that technology is an important component of competitiveness in medical science.

Professor David James

The director of Garvan's Diabetes Program, David James, has spent his entire scientific career studying the link between insulin receptor signalling and glucose uptake into muscle and fat cells. Since his early days as a Garvan Institute Ph.D. student he has continued to make valuable contributions to the field of metabolism. But David's knowledge of biology was not always so extensive. After having failed to be admitted to medical school and struggling to pass first year biology, he ended up taking biochemistry. He has never looked back. While a postdoctoral researcher at Boston University in the lab of Paul Pilch, and later with Mike Mueckler in St Louis, James discovered and cloned the GLUT4 transporter that is found on muscle and fat cells and is regulated by insulin. Since then, he has focussed his attention on connecting the dots between insulin binding to its receptor at the membrane and increased glucose uptake. In 1999, James won the Glaxo Wellcome Medal recognizing his contribution to this field. This year, he received the highest award given by the Australian Diabetes Society, the Kellion Award. James balances his workload at the Garvan with kayaking in Sydney Harbor and surfing on the local beaches.

Professor David James

Associate Professor Trevor Biden

Trevor Biden heads the Garvan's Diabetes Signalling Unit. He undertook his Ph.D. on insulin secretion in London, following relocation of his mentor's laboratory from Sydney University. Subsequently as post-doc with Claes Wollheim in Geneva, he was introduced to signal transduction, and contributed to early studies characterizing IP3 as a second messenger. Shifting both fields and location, Biden returned to Australia and set up a small lab at the Garvan where he successfully cloned PKCiota, the last of the PKC family to be discovered. In ensuing years, Biden's work has continued to focus on the nexus between signalling, cellular function and the pathophysiology of diabetes, be it investigating the molecular mechanisms of insulin resistance, or pancreatic beta cell dysfunction. He believes that his current pet projects, endoplasmic reticulum stress in beta cells, and the surprising re-emergence of PKC as a therapeutic target for diabetes, are some of the most exciting of his career. He feels fortunate to have been a part of the tremendous development of the Garvan over the last 15 years. Biden may have returned to Sydney for life-style reasons, and commuting via a harbour ferry continues to hold an attraction, but it is the science that now keeps him here.

Associate Professor Trevor Biden

Dr. Robert Brink

Robert Brink recently joined the Garvan Institute as a group leader in the rapidly-expanding Immunology and Inflammation Program. The focus of his laboratory is B cell development and antibody production. A Sydney lad, Brink first became interested in the immune system when he attended an undergraduate lecture describing the way in which B cells rearrange and mutate their immunoglobulin genes in order to generate antibody diversity. For his Ph.D. research, he studied the first series of antigen-specific immunoglobulin transgenic mice and on completion was awarded a CJ Martin Overseas Biomedical Fellowship. But by this time, Brink had become severely allergic to mice, so much so that he ended up in a hospital emergency ward. His overseas postdoctoral years were spent at the Whitehead Institute in Boston, where he furthered his molecular skills and worked on TNF receptors and immune system signaling molecules. The late 1990s saw Brink returning to Sydney, to the Centenary Institute, where he concentrated on generating various gene-targeted mice for understanding B cell biology without handling them himself. These mouse

models are now providing new insights into how B cells respond to antigens and survive in the body.

Professor Roger Daly

Professor Roger Daly

As a child in England, Roger Daly had lots of science projects on the go, from growing crystals to collecting fossils. But an article in *Scientific American* stirred his interest in the molecular and cellular biology of cancer, the area in which he now works. Daly carried out his Ph.D. studies on cloning oestrogen responsive genes from breast cancer cells at the University of Liverpool, UK, and continued this theme for his first postdoc at what was then the Imperial Cancer Research Fund in London. This led to an interest in growth factor action, and combined with exciting developments in the signalling field in the late 1980's, drew Daly into the analysis of tyrosine kinase signalling mechanisms. His second postdoc, with Joseph Schlessinger at New York University, led to the cloning and characterization of Grb2, which established a paradigm for adapter protein signalling. This research resulted in a joint first author *Cell* paper that has been cited more than 1,000 times. Daly's next move was to the Garvan Institute in 1993. His Signal Transduction Group recently cloned Grb14 and determined that it is a physiological regulator of insulin action. They have also found a new role for the cytoskeletal protein cortactin in preventing degradation of a cell surface receptor involved in cancer development.

Professor John Shine, FAA AO

John Shine is the Executive Director of the Garvan institute of Medical Research, a post he has held since 1990. His name is known to most undergraduate biology students for his role in defining the Shine-Dalgarno gene sequence, which is responsible for the initiation and termination of protein-synthesis. However he has a number of other significant scientific 'firsts' under his belt. Shine was a central figure in the cloning of the insulin and growth hormone genes; was the first to clone a human hormone gene; was responsible for cloning of an endorphin gene, and was the first to demonstrate that hormone genes cloned in bacteria could be expressed in a biologically active form. He also determined the first sequence responsible for replication of a cancer-causing virus. Shine started out doing veterinary science at the University of Sydney, for no particular reason, at the age of 16. He dropped out when he ran out of money and went to work in the public service in Canberra while doing a part-time science degree at the Australian National University. Lecturer Lynn Dalgarno inspired John in the field of molecular chemistry, despite Shine's previous dislike for biochemistry. He went on to do his Ph.D. with Dalgarno – years that were incredibly productive.

Shine had the usual share of rejection letters when applying for postdoctoral positions, but ended up with three options in three different countries, and chose San Francisco. This move, in 1975, proved to be one of the best choices in Shine's scientific career and was where he went on to clone numerous genes as well as develop techniques to do this, for example he is the sole inventor on a patent for using phosphatase to direct the joining of DNA molecules.

After heading back to Canberra for six years, Shine returned to the States and took up a joint position as an Adjunct Professor of Medicine at UCSF and Director of Research for a newly formed biotech, California Biotechnology Inc.

Professor John Shine

He was appointed President of the company in 1986 and guided it from a staff of some 15 scientists in 1984 to over 200 in 1987. During this period, Cal Bio developed several important new therapeutics including treatments for congestive heart failure, infant respiratory distress syndrome, burns, and general wound healing agents. At the same time, Shine developed an interest in the generation of functional diversity in the nervous system, a research area he established on joining the Garvan.

Science is also an integral part of Shine's outside interests. He enjoys racing his thoroughbred horses and is fascinated by the art of the sport; in particular, how genetics and the environment come together to determine the horses' chances of success in a specific race on a certain racecourse. His scientific successes, however, haven't been replicated on the track—yet.

Helen Davies Honored for Excellence in Medical Education

Helen C. Davies, Ph.D., M.S., Professor of Microbiology and Ombudsman for Students at the University of Pennsylvania School of Medicine, is the recipient of an Alpha Omega Alpha (AOA) Robert J. Glaser Distinguished Teacher Award. Davies is being recognized by the Association of American Medical Colleges (AAMC) for her efforts to provide the nation's next generation of doctors with an exceptional educational experience.


Dr. Helen Davies

Davies' educational efforts have been focused on recruiting, mentoring, and retaining minority groups and women in biomedical careers. For 35 years, she has incorporated unique methods into her own lessons to help her students learn and retain information on the symptoms and mechanisms of various infectious diseases. Davies writes original song lyrics and performs them to the tunes of popular songs, and her songs are hits among her medical students. One of her more famous songs, "Leprosy," is set to the tune of the Beatle's "Yesterday."

During her 40-year teaching career, Davies has achieved many "firsts." She was the first female faculty member named to Penn's Department of Microbiology (1965), the first woman faculty member to be designated "master of a college house" at Penn (1995-2002), and the first woman to ever receive the American Medical Student Association's National Excellence in Teaching Award (2001).

Dill Named for Distinguished Service by Biophysical Society

Ken A. Dill, University of California San Francisco School of Pharmacy faculty member, Associate Dean for Research, and an expert in protein folding, has been named winner of the 2007 Distinguished Service Award by the Biophysical Society. Dill served as President of the Society from 1998 to 1999 and currently co-chairs the Public Affairs Committee.

The award recognizes Dill's contributions to the field of biophysics as well as to the society, and in particular his contributions to the Bridging the Sciences Coalition. In 2003 he co-founded the coalition, which brings together science societies across the United States to speak as one voice for deeper innovation and for federally funded research that bridges the physical/computational and the biological sciences. The ultimate effect of deeper innovation at this interface, according to the coalition, will be the more effective and quantitative approaches to discovering drugs and curing diseases that transcend today's more cumbersome lab bench, disease-by-disease and molecule-by-molecule approaches.


Dr. Ken A. Dill

Wang Elected to Royal Society of Canada

Yu-Tian Wang of the University of British Columbia's Brain Research Centre has been elected to the Royal Society of Canada. Awarded by the Academies of Arts, Humanities, and Sciences of Canada, Wang joins a total of 82 new Fellows, 2 Foreign Fellows, and 1 Specially Elected Fellow. Founded in 1882, the Royal Society of Canada is Canada's oldest scholarly organization, and election represents one of the highest honors for Canadian scholars, artists, and scientists.


Dr. Yu-Tian Wang

In keeping with the motto of the Society, "*Different paths, one vision,*" the newly elected Fellows, while coming from diverse backgrounds and disciplines, are dedicated to achieving excellence in their endeavors, thus enhancing Canada's competitiveness on a global basis.

Wang's research has transformed the understanding of fundamental mechanisms of synaptic transmission and neural plasticity serving essential roles in cognition and emotion. His most revolutionary discovery demonstrated that dopamine and gamma-aminobutyric acid (GABA) receptors influence each other via protein-protein interactions. Wang's discoveries have been used to guide the development of novel drugs for modulation of aberrant synaptic plasticity related to mental illness.

Randy Schekman Named New Editor of PNAS

Following a review of more than 60 nominees, the National Academy of Sciences has appointed Randy Schekman, Ph.D., as the new editor-in-chief of the *Proceedings of the National Academy of Sciences* (PNAS).

Schekman is Professor of Cell and Developmental Biology in the Department of Molecular and Cell Biology at the University of California, Berkeley, and an investigator of the Howard Hughes Medical Institute. Elected to the National Academy of Sciences in 1992, Schekman served on the editorial board of PNAS in 2001-2005 and is currently the chair of the Academy's Biological Sciences division.

Dr. Randy Schekman

Schekman succeeds former Editor-in-Chief Nicholas R. Cozzarelli, who died of Burkitt's lymphoma in March. Solomon H. Snyder, M.D., took on additional leadership duties for PNAS during Cozzarelli's illness and has served as Senior Editor since January 2005.

Schekman, whose term runs through 2010, said he already has a list of goals and ideas for PNAS. These include seeing a broader range of science and more integrative science represented in the journal and allowing research to be explored in greater depth in the articles.

Sydney Brenner Receives Singapore National Science and Technology Medal

Nobel Laureate Sydney Brenner, Distinguished Professor at the Salk Institute for Biological Studies, was awarded the Singapore Agency for Science, Technology, and Research (A*STAR) National Science and Technology Medal. The medal, which is the highest honor given by A*STAR, recognized Brenner's distinguished and strategic contributions to the development of Singapore's scientific capability and culture, particularly in the biomedical sciences sector.

Over the past 20 years, Brenner, who is also Chairman of the A*STAR Biomedical Research Council, has devoted his time and energy to helping Singapore develop into an emerging global hub for biomedical research. He played an instrumental role in convincing the government to establish the Institute of Molecular and Cell Biology (IMCB) in 1987. This proved to be a strategic milestone and critical starting point for Singapore's efforts to develop biomedical sciences. Brenner served as Chairman on IMCB's Scientific Advisory Board from 1987 to 1997 and continues to serve as a member on that board to this day.

Dr. Sydney Brenner

Seven ASBMB Members Elected to IOM

In October, the Institute of Medicine announced the names of 65 new members, 7 of whom are members of ASBMB. These include:

Stephen P. Goff, Ph.D., investigator, Howard Hughes Medical Institute, Higgins Professor of Biochemistry and Molecular Biophysics, and professor of microbiology, Columbia University Medical Center, New York City;

Susan L. Lindquist, Ph.D., investigator, Howard Hughes Medical Institute; member, Whitehead Institute for Biomedical Research; and professor of biology, Massachusetts Institute of Technology, Cambridge;

Joseph Loscalzo, M.D., Ph.D., Hersey Professor of the Theory and Practice of Physics, Harvard Medical School, and chair, Department of Medicine, Brigham and Women's Hospital, Boston;

Martha L. Ludwig, Ph.D., research biophysicist and J. Lawrence Oncley Distinguished Professor, Department of Biological Chemistry, University of Michigan, Ann Arbor;

Joan Massagué, Ph.D, investigator, Howard Hughes Medical Institute, and Alfred P. Sloan Chair, cancer biology and genetics program, Memorial Sloan-Kettering Cancer Center, New York City;

Baldomero M. Olivera, Ph.D., Distinguished Professor of Biology, Department of Biology, University of Utah, Salt Lake City;

Ajit P. Varki, M.D., Distinguished Professor of Medicine and Cellular and Molecular Medicine, Department of Medicine, University of California, San Diego.

The new members raise the total active membership of the IOM to 1,501. Current active IOM members elect new members from among candidates nominated for their professional achievement and commitment to service. An unusual diversity of talent is assured by the institute's charter, which stipulates that at least one-quarter of the membership be selected from outside the health professions, from such fields as the natural, social, and behavioral sciences, as well as law, administration, engineering, and the humanities.

Nancy Goldman Nossal, NIH Scientist

Nancy G. Nossal, 69, a scientist at the National Institutes of Health and former ASBMB member, died September 28 of cancer at her home in Bethesda. Dr. Nossal was born in Fall River, Mass., and grew up in Newton, Mass., and Syracuse, N.Y. She received a bachelor's degree from Cornell University in 1958 and a doctorate in biochemistry from the University of Michigan in 1964.

She joined the scientific staff at NIH in 1964, and advanced to chief of the laboratory of molecular and cellular biology at the National Institute of Diabetes and Digestive and Kidney Diseases, a position she held at the time of her death. In the 1960s, Dr. Nossal became one of the first women working in the then-new field of molecular biology, directing her research toward fundamental questions about how viruses affect DNA replication and how proteins function at a molecular level.

She published more than 60 papers and was on the editorial boards of the *Journal of Biological Chemistry* and the *Journal of Virology*. She served on a number of advisory and review committees, and in 2005 was elected to membership in the American Academy of Arts and Sciences.

Survivors include her husband of 47 years, Ralph Nossal of Bethesda; three children, Susan Nossal of Madison, Wis., Steven Nossal of Reston, Virginia, and Michael Nossal of Washington, DC; her mother, Dorothy Goldman of Chicago; a sister; and a brother.

Dr. Jack Griffith, of the University of North Carolina Lineberger Cancer Center, whose lab worked closely with Dr. Nossal's lab, recalled that over the past 10 years a significant portion of her experimental efforts have been directed at examining the model for the architecture of the moving replication fork first proposed by Bruce Alberts of the University of California, San Francisco, nearly 30 years ago, and modified by herself and others in the field. This model was based on the T4 phage replication system termed the "Trombone model." There were two central aspects of this model which suggested a solution for the problem that the leading and lagging strands at the fork are synthesized in the same enzymatic direction but opposite physical direction. If the replisome at the fork is a single large protein machine that replicates the DNA, Alberts suggested that there are two polymerase molecules, one synthesizing the leading strand and one the lagging strand. Further, he proposed that the lagging strand loops back at the fork to generate a loop which grows and then contracts through each cycle of Okazaki fragment synthesis, hence the analogy with a trombone slide.

Dr. Nancy G. Nossal

The presence of a loop at the lagging strand loop had been visualized in the late 1990's by Jack Griffith and Charles Richardson and their colleagues in the simpler T7 system. Working with the Griffith laboratory, Nancy Nossal and her group used electron microscopy to examine the architecture of the moving fork using the more complex T4 replication system. In one paper published in *Molecular Cell*, they were able to examine Okazaki fragment synthesis on single replicating DNAs and show that even at a single molecule level, the size distribution of Okazaki fragment length is great and does not fit current models. In a paper published in the *Journal of Biological Chemistry,* Nossal and colleagues presented the long sought-after evidence in the full T4 system directly demonstrating the presence of trombone loop at a moving fork. Further they showed that the single stranded segments at the fork are not extended but present in compact particles bound by the T4 single strand binding protein.

In a paper which will shortly appear in the *JBC*, the Nossal and Griffith laboratories applied a new EM method originally developed by Steve Bell at MIT and Griffith, in which nano-scale "biopointers" are designed and synthesized to detect the presence and location of specific proteins in a complex DNA-protein complex. Using this technology Nossal spent much of her own time in the laboratory over the past three years combining this method with classic biochemical approaches. Her goal was to test a basic assumption that there are indeed two polymerase molecules at a moving fork. The results presented in this paper provide the first direct proof which has been in waiting for nearly 30 years that there are indeed two polymerase molecules at a moving fork, and that in the more rare cases where two Okazaki fragments are being synthesized on the same molecule at the same time three polymerases could be detected.

Griffith noted that Nancy Nossal represents the finest example of a senior scientist who by remaining close to the lab bench herself, became not only a leading expert in the complex field of DNA replication, but also an invaluable resource of technical and scientific insight for all of her colleagues.

Inside the Education and Professional Development Committee

Last weekend the Education and Professional Development (EPD) Committee held its annual fall retreat where members gather to discuss a variety of topics related to education and professional development. This year the EPD met with the Undergraduate Affiliates Network (UAN) Committee, and the focus of the meetings were the new Education and Professional Development Web Site (coming soon to a computer near you) and the infrastructure of the UAN program, as well as several potential initiatives for the future including discussion of how to enhance ties with industry, interactions with the community college system and outreach to K-12, particularly focusing on interactions with science teachers. The committee itself has members from all aspects of academia as well as industry and in the past several years has included representation from both graduate students and postdoctoral fellows. The UAN Committee, two members of which also serve on the EPD Committee, consists of the regional directors of the UAN program. This year there are two new members of the UAN committee, Takita Sumter from Winthrop University, who will help run the Southeast region, and David Peterson from Texas A & M, who will take over in the South Central region. Marilee Benore Parsons from the University of Michigan, Dearborn, who is the North Central UAN coordinator, will also assume editorial duties for the UAN Newsletter, Enzymatic. Enzymatic will come out four times a year with Marilee's first issue being March 1, 2007. Subsequent issues will come out June 1, September 1, and December 1 with each issue featuring news from each of the UAN regions as well as highlights of student, faculty, and program activities and various resources and lead articles. Each year the UAN will present an "outstanding chapter" plaque for a school from each region as well as a national award for the top chapter in the country.

During October and early November, the North Central, North West, and South East UAN regions held regional undergraduate symposiua for local schools where travel awards to the DC national meeting were awarded to the best undergraduate presenters at the meeting. The North Central meeting was held in conjunction with the Argonne National Laboratory Annual Symposium for Undergraduates in Science, Engineering and Mathematics, and three travel awards were given to best presenters. The North West meeting attracted over 80 attendees from several states and featured 33 undergraduate posters from 10 different schools. Four ASBMB travel awards were presented. The South East event was held on Friday October 20, and Saturday, October 21, 2006, and was hosted by the Department of Biochemistry at Virginia Commonwealth University (VCU). This event involved presentations of research projects performed by students enrolled in colleges and universities throughout the Southeast. Participants had the opportunity to present research posters to a diverse audience, consisting of graduate students, postdoctoral researchers, and faculty from VCU and other participating universities. Three travel awards were presented.

Next year it is hoped that each region of the UAN will host one or more regional Undergraduate Meeting in the fall where travel awards to the next spring's national meeting will be awarded for best presentations by undergraduates. If you are interested in hosting such a regional meeting please contact the ASBMB UAN Program. Next year, in addition to the UAN and regional meeting travel awards there will still be a number of competitive undergraduate travel awards that any student can apply for.

The Saturday at the Washington DC National Meeting will again have a major focus on undergraduate participation and faculty from undergraduate institutions. In addition to the Undergraduate Poster session, jointly sponsored by EPD and the Minority Affairs Committee there will be two morning workshops geared towards teaching faculty, one on incorporation of outreach and service learning activities into the curriculum and the other on using physical models to teach protein structure function relationships. There will be limited space available in each workshop so be sure to register for them when you register for the meting if you are interested.

Again this year, various Graduate Programs will be sponsoring "recruiting tables" at the Undergraduate Poster Symposium on Saturday Afternoon where both the many undergraduates attending the session, and their faculty mentors will have the opportunity to visit with faculty, post docs and graduate students from the participating graduate programs. If your graduate program is interested in sponsoring a table and participating in this event please contact ASBMB.

By Nicole Kresge, Science Editor

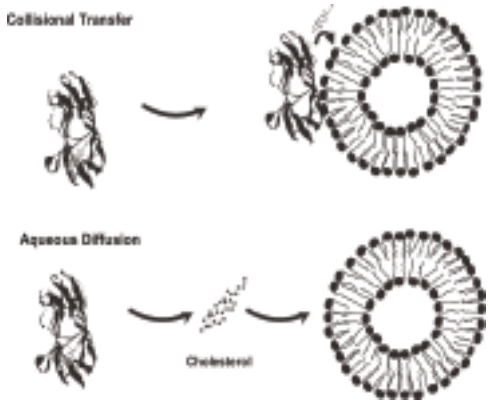
ASBMB Bio Bits

Mechanism of Cholesterol Transfer from the Niemann-Pick Type C2 Protein to Model Membranes Supports a Role in Lysosomal Cholesterol Transport

Sunita R. Cheruku, Zhi Xu, Roxanne Dutia, Peter Lobel, and Judith Storch

J. Biol. Chem. 2006 281: 31594-31604

Niemann-Pick type C disease is a lipid storage disorder characterized by the accumulation of unesterified cholesterol and glycolipids in the endosomal/lysosomal system. The disease is caused by defects in either of two genes that code for the proteins NPC1 and NPC2. NPC2 is a small intralysosomal protein that has been characterized biochemically as a cholesterol-binding protein. Using a fluorescence dequenching assay, the authors of this paper monitored the kinetics of cholesterol transfer from NPC2 to model phospholipid membranes. They showed that transfer of cholesterol from NPC2 likely involves a collisional mechanism and is optimal in an acidic environment such as the endosomal/lysosomal compartment. They further demonstrated that NPC2 dramatically increases the rate of transfer of lyso-bisphosphatidic acid-containing vesicles. These studies support a role for the NPC2 protein in the transport of low density lipoprotein-derived cholesterol out of the endosomal/lysosomal compartment.



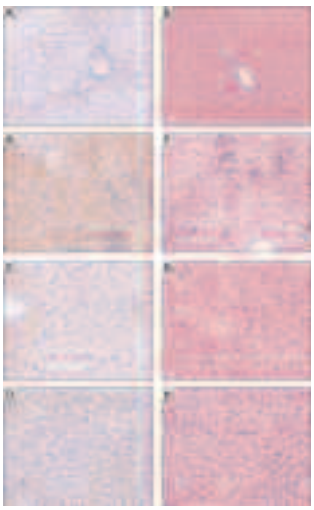
Potential mechanisms of cholesterol transfer from NPC2 to membranes.

The Medicinal Plant Goldenseal is a Natural LDL-Lowering Agent with Multiple Bioactive Components and New Action Mechanisms

Parveen Abidi, Wei Chen, Fredric B. Kraemer, Hai Li, and Jingwen Liu

J. Lipid Res. 2006 47: 2134-2147.

Increased plasma low density lipoprotein cholesterol (LDL-c) level is thought to be the primary risk factor for the development of coronary heart disease and atherosclerosis. In humans, more than 70% of LDL-c is removed from plasma by low density lipoprotein receptor (LDLR)-mediated uptake in the liver. In previous studies, the authors of this paper showed that the compound berberine (BBR), an alkaloid isolated from the Chinese herb huanglian, acts a unique cholesterol-lowering drug that up-regulates hepatic LDLR expression by mRNA stabilization. Now, the authors show that the root extract of goldenseal, a BBR-containing medicinal plant, is highly effective in up-regulation of liver LDLR expression in HepG2 cells and in reducing plasma cholesterol and LDL-c in hyperlipidemic hamsters, with greater activities than the pure compound BBR. This higher potency is achieved through concerted actions of multiple bioactive compounds in addition to BBR.

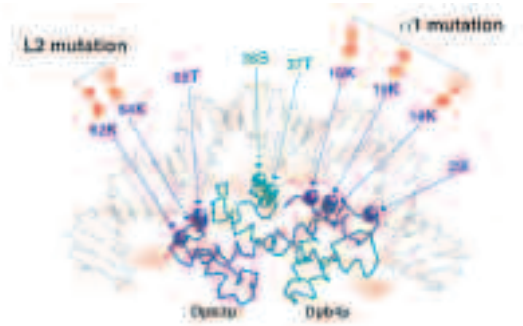


Goldenseal administration reduces hepatic fat storage in hyperlipidemic hamsters.

Double-stranded DNA Binding, an Unusual Property of DNA Polymerase ε, Promotes Epigenetic Silencing in Saccharomyces cerevisiae

Toshiaki Tsubota, Rie Tajima, Kunitomo Ode, Hajime Kubota, Naoshi Fukuhara, Takeshi Kawabata, Satoko Maki, and Hisaji Maki

J. Biol. Chem. 2006 281: 32898-32908



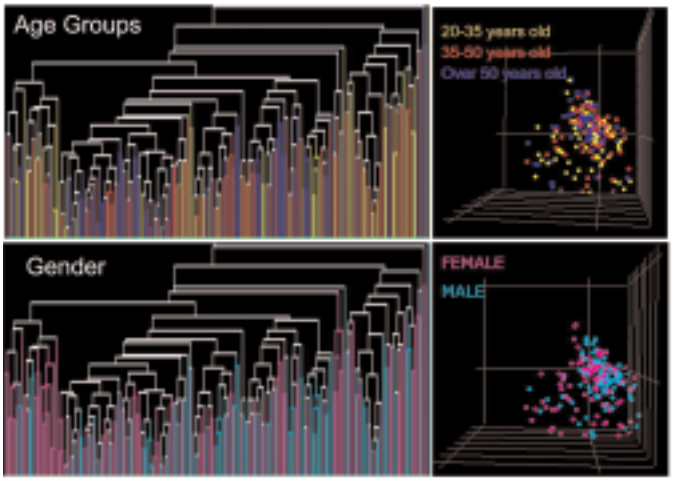
DNA polymerase ε binds to double-stranded DNA.

Epigenetic gene silencing can result from modifications in gene expression caused by changes in DNA methylation or chromatin structure. In Saccharomyces cerevisiae, DNA polymerase ε (Pol ε) has been shown to bind to double-stranded DNA (dsDNA) and to participate in the stable inheritance of the silenced state of chromatin. Pol ε is a four-subunit complex that contains a catalytic subunit, Pol2p, and three auxiliary subunits, Dpb2p, Dpb3p, and Dpb4p. Dpb3p and Dpb4p contain a histone-fold motif, and cells lacking DPB3 and/or DPB4 are defective in silencing, suggesting the subunits' involvement in dsDNA binding. In this paper, the authors show that neither Pol2p-Dpb2p nor Dpb3p-Dpb4p binds stably to dsDNA but that binding is efficiently reconstituted when the two subassemblies are combined, indicating that both complexes are required for stable association with dsDNA. Further characterization of mutant forms of Pol ε suggested that the Dpb3p-Dpb4p subassembly in Pol ε binds dsDNA around its dimeric histone-fold structure in a manner resembling the histone-DNA interaction. The Pol ε mutants also displayed reduced telomeric silencing, suggesting that the dsDNA binding property of Pol ε is required for epigenetic silencing at telomeres.

Serum Peptidome Patterns That Distinguish Metastatic Thyroid Carcinoma from Cancer-free Controls Are Unbiased by Gender and Age

Josep Villanueva, Andrew J. Martorella, Kevin Lawlor, John Philip, Martin Fleisher, Richard J. Robbins, and Paul Tempst

Mol. Cell. Proteomics 2006 5: 1840-1852



Clustering and analysis of peptide profiling data from healthy men and women.

The small numbers of blood proteins in human serum serve as a substrate pool for cancer-derived proteases, which then generate cancer-specific serum peptides. Following development of a unique, semiautomated serum peptide profiling platform and after completing investigations to eliminate common experimental bias, the authors of this paper have now studied possible effects of gender and age on serum peptidomes of 200 healthy men and women, ages 20–80, and of 60 patients (30 men and 30 women) with metastatic thyroid carcinomas. Extensive MALDI-TOF MS and data analysis suggests negligible contributions of both age and gender to the serum peptidome patterns except that healthy men and women under 35 years, but not older individuals, could be distinguished with ~70% accuracy. Considering the more advanced age of most patients, this finding is unlikely to interfere with peptidomics analysis of most cancers.

by John D. Thompson, Editor

Merck Buys Maker of Gene-Silencing Drugs

Merck & Company will pay $1.1 billion to acquire Sirna Therapeutics, one of the leading companies pursuing the technology that was the basis for the 2006 Nobel Prize in medicine shared by Andrew Fire of Stanford Unversiy and the University of Massachusetts Craig Mello.

The deal is the largest sign yet of interest among pharmaceutical companies in the technology, RNA interference. Merck's all-cash offer for Sirna was worth $13 a share, more than double Sirna's $6.45 closing price.

RNAi is already used widely in laboratories to study the functions of genes, but Merck and Sirna hope the technique may also be used one day to treat diseases—killing viruses or tumors, for instance, by turning off their genes. "There's a potential for RNAi to change the way drugs are discovered and developed," said Peter S. Kim, President of Merck Research Laboratories.

The Nobel Prize in Physiology or Medicine this year went to Andrew Z. Fire of Stanford University and Craig C. Mello of the University of Massachusetts for their discovery of RNAi, a natural process that apparently evolved as a way for cells to fight viruses. The awarding of the prize only eight years after the discovery was a sign of how important RNAi has become.

Merck, trying to recover from the withdrawal of its Vioxx painkiller from the market and setbacks on some experimental drugs, is trying to diversify beyond pills to other forms of medicine. In May it agreed to pay $480 million to acquire two small companies to help it move into protein drugs, the province of biotechnology companies like Amgen and Genentech.

In RNAi, Merck already had a collaboration with Sirna's chief rival Alnylam Pharmaceuticals. However Merck expects that the Alnylam collaboration would continue.

Brazil to Expand Sugarcane Output 55% in Six Years

Brazil, the world's largest ethanol exporter, will expand sugarcane acreage and output by about half over the next six years as demand for biofuel grows, supported by made higher oil prices. Eduardo Pereira de Carvalho, head of an association representing about 85% of sugar and ethanol production in Brazil, said cane output may rise 55% over the next six years to about 730 million metric tons, while planting may grow 45% to about 9 million hectares (22.2 million acres).

A doubling of oil prices over the past three years, which raised the cost of gasoline, has boosted demand for ethanol in Brazil and the U.S., while Japan and other countries plan to start using the biofuel as additive. Carvalho said he expects the price for a barrel of oil to remain near or above $60 in coming years, encouraging investments in ethanol production in Brazil.

"With oil prices around $60, the trend is for continuous progress in demand here and abroad," Carvalho, chairman of the Center-South Sugar and Ethanol Industry Association. "We will have the incentive to continue to boost ethanol production."

Brazilian ethanol exports jumped 91 percent last month from a year earlier to 545 million liters (144 million gallons) on surging demand from the U.S., the Trade Ministry said on its Web site today.

Carvalho said he expects annual ethanol exports to rise to 7 billion liters over the next six years, from 3.1 billion liters in the crop year ending next April.

Cloning Bill Squeezes Through Australian Senate

The Australian Senate passed the human embryo cloning legislation last month, but deleted a controversial provision that would have allowed the use of animal eggs in the procedure. Senators voted 34 to 32 in favor of the legislation, a tighter result than the initial vote earlier that day.

The vote came after the legislation's major advocates agreed to a proposal to disallow the use of animal eggs - a move critics have described as opening the way to animal-human hybrids.The Australian Democrats Andrew Bartlett said he proposed the amendment because scientists had indicated research was possible without the use of animal eggs. He told the *Herald* newspaper earlier that he was still wrestling with the view conveyed by the legislation that embryos created by cloning "have lesser intrinsic value than an embryo created through a sperm and an egg".

The Senate also agreed to amendments including a proposal for a comprehensive review and tougher penalties, which mean anyone offering to pay for a human egg, sperm or embryo faces 15 years' jail. Democrat Senator Natasha Stott Despoja said she trusted scientists to do the right thing and the bill would give them the tools to embark on "some potentially dazzling research".

Schering CEO Tells MarketWatch M&A Prices are 'Breath-Taking'

"The prices that are being paid by our competitors are breath-taking," said Schering-Plough Corp. Chief Executive Officer Fred HassanHassan, in a recent interview with MarketWatch. "They would've been unthinkable five years ago."

Indeed, the price tags attached to the most recent deals appear to underscore Hassan's observations. Note Merck's recent announced that it was paying a 102% premium, $2.1 billion in cash, for research group Sirna Therapeutics which co-markets its erectile dysfunction drug Cialis, for $2.1 billion in cash. Big Biotech also got into the game. And in mid-October, Genzyme Corp. agreeing to pay $580 million in cash for the development-stage company. The attraction, said Genzyme, was AnorMed's Phase III drug candidate Mozobil, which is being tested for use in stem cell transplantation in cancer patients.

According to Hassan, the takeover craze has been fueled by recent rash of patent expirations on some of the industry's biggest-grossing products, such as Merck's Zocor, Bristol-Myers' Pravachol, and Pfizer's Zoloft. "The industry's R&D engines are struggling to keep up with the expirations," said Hassan, noting that the trend towards acquisitions has been in place for some time.

Hassan added that the windfalls seen by companies under the American Jobs Creation Act of 2004, which allowed U.S. companies to repatriate foreign profits at a special tax rate, has also powered the trend. Under that measure, companies can use the cash for such purposes as mergers and acquisitions.

As for Schering-Plough, Hassan said the company doesn't feel as strong a need to make a major merger or acquisition deal, "as our existing products [patents] go into the next decade." If Schering-Plough were to pursue an acquisition, he added, it would be to complement its existing therapeutic product areas: cancer, inflammatory illnesses, hepatitis C, cholesterol-maintenance, and respiratory conditions.

German Firm to Build Neuroscience Center at Singapore Hospital

German-based BrainLAB AG has signed a contract with Singapore Health Services (SingHealth) for the establishment of the world's first fully digital neuroscience centre at Singapore General Hospital (SGH). The S$26 million project covers the installation of a five-suite operating facility to be set up in the next 12 months. For the first time, a comprehensive range of the latest technologies in healthcare will be available in one location, digitally integrated to provide clinicians with effective access to and intelligent management of digital medical information. From diagnostics through treatment, this new infrastructure will provide clinicians with timely information and more treatment options, resulting in better-informed medical decisions, and the ability to seamlessly combine multiple treatments.

University Sues Pfizer Over COX-2 research

Brigham Young University and Daniel Simmons, a researcher in its Department of Chemistry and Biology, have filed a lawsuit alleging that Monsanto, a precursor company to Pfizer, misappropriated Simmons' research on COX-2 to develop its blockbuster painkiller Celebrex.

The suit, filed against Pfizer in the U.S. District Court in Salt Lake City, Utah, came after more than five years of discussions between the parties, and failed efforts at mediation earlier this year. "We know what we are dealing with, and we are prepared to persevere," BYU spokesperson Michael Smart told *The Scientist*.

According to the plaintiffs, Monsanto entered a contract with BYU and Simmons in 1991 to partner on the development of painkillers that targeted COX-2, but left COX-1 unaffected. Simmons and BYU claim that Monsanto subsequently used their research methodologies and data to develop Celebrex outside of the partnership in order to avoid having to share the profits. They are requesting actual and punitive damages, and asking that 75 patents be amended to include Simmons among the inventors.

The suit claims that Simmons first identified COX-2 mRNA at the end of 1988, while at Harvard University. After he relocated to BYU the following year, he characterized the gene and sequenced it, noting the applicability of his discovery immediately. However, during contract negotiations, the suit charges that Monsanto "wrongly advised Dr. Simmons that he should not patent these items because any such patent would not be enforceable or defensible."

For Your Lab/For Your Lab/For Your Lab

The information in For Your Lab has been provided by manufacturers and suppliers of laboratory equipment. For further information about any of these products listed contacts are listed at the bottom of each panel. When contacting any of these companies, please mention that you saw their product in *ASBMB Today*. Please note that a listing in *ASBMB Today* does not imply an endorsement by the American Society for Biochemistry and Molecular Biology or by any of its members or staff.

Manufacturers and suppliers, to include your products in For Your Lab contact Molly at adnet@faseb.org or 301-634-7157 (direct) or 1-800-433-2732 ext. 7157.

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POSTDOCTORAL RESEARCH ASSOCIATE

The Biology Department of Brookhaven National Laboratory (BNL) currently has a research associate position available in the laboratory of John Shanklin. Research will involve structure-function relationships of plant desaturase enzymes. The Shanklin lab (http://www.biology.bnl.gov/plant-bio/shanklin.html) focuses on understanding the basic biochemical mechanisms of oxygen-dependent diiron lipid modification enzymes. Current work focuses on the dimeric organization of the desaturases and understanding the structural basis for regiospecificity. A PhD in biochemistry, chemistry, or plant biology with experience in enzymology is required. Knowledge of molecular biology is preferred.

BNL, a scientific research facility operated by Brookhaven Science Associates under contract with the US Department of Energy, is located on Long Island 50 miles from New York City. It has strong programs in Physics, Chemistry and Biomedicine in addition to Biology. It is also affiliated with the State University of New York at Stony Brook (located 15 miles away).

Interested candidates should send the following to shanklin@bnl.gov: Ph.D. thesis title and date granted, a list of up to three most recent publications, and the names and contact information of three referees. Brookhaven National Laboratory is an equal opportunity employer committed to workforce diversity.

East Central University

Molecular Biology: The Department of Biology at East Central University (ECU) seeks qualified applicants for the position of a tenure-track, if eligible, Assistant Professor in Biology, beginning August 2007. ECU is a student-centered regional state university located in Ada, Oklahoma.

ECU offers thirty-three undergraduate baccalaureate degree programs in arts and letters, business, education, mathematics and sciences, nursing and the social sciences. Eight master's degrees are offered in education, human resources, and psychology. ECU's 4,500 students come form 24 countries and 34 states. About 70% of the 165 faculty members hold doctorates. Qualified candidates will hold an earned doctorate in an appropriate biological discipline related to molecular biology.

Responsibilities include teaching courses in General Biology, Molecular Biology, and a course in area of expertise; advising biology majors; directing undergraduate research; writing external funding proposals; serving on departmental and university committees and other scholarly activities. Familiarity with a Real Time PCR and an ABI 310 Genetic Analyzer is desired. Each applicant should submit a letter of application, curriculum vitae, official transcripts (undergraduate and graduate), a statement of teaching philosophy and research interests, and three letters of recommendation to Dale Hayden, Director of Human Resources, East Central University, 1100 East 14th Street, Ada, OK 74820. Review of applications will begin immediately and continue until the position is filled. For information about ECU visit http://www.ecok.edu AA/EOE

Baylor College of Dentistry

FACULTY POSITION

The Department of Biomedical Sciences at Baylor College of Dentistry, Texas A&M University System Health Science Center, Dallas, is seeking outstanding candidates for a full-time position at the Assistant to Associate Professor level for either the tenure or non-tenure educator track. A PhD in Biochemistry or a related science area is required. Non-tenure educator track applicants must demonstrate considerable teaching experience (preferably in a dental school setting) with a record of excellent student evaluations. Tenure-track applicants must demonstrate the ability to establish an independent research program and procure extramural funding. The successful tenure-track candidate will participate primarily in a team-taught Biochemistry course to first year dental students and graduate students; for a non-tenure educator track candidate, the teaching load will include participation in additional courses. Current departmental research strengths include genetics and developmental biology of the craniofacial region and inflammation/pain. Applications will be reviewed as they are received and will continue to be accepted until the position is filled.

Applications should include a curriculum vitae, summary of current research activities, statement of career goals and teaching philosophy along with the names and contact information of at least three individuals for letters of recommendation to be submitted in electronic format to: Dr. Bob Hutchins, Search Committee Chair, Department of Biomedical Sciences, TAMUSHSC, 3302 Gaston Avenue, Dallas, TX 75246; Email: bhutchins@bcd.tamhsc.edu

Oak Ridge Associated University

POSTDOCTORAL PROJECT IN PROTEOMICS

Air Force Research Laboratory. Requires expertise in analysis of biological and proteomic samples. Activities for this collaborative effort between the AFRL Applied Biotechnology Branch and the Dept of Molecular and Cellular Biochemistry, Ohio State Univ will be located at the Mass Spectrometry & Proteomics Facility, OSU Columbus, Ohio. For more information, email Jeffrey.Johnson@orau.org.

POSTDOCTORAL PROJECT IN NANOTECHNOLOGY-BASED TARGETED ANTI-VIRAL THERAPEUTICS

Air Force Research Laboratory Bioscience and Protection Division with Wright State University. Fellow will research how metallic nanomaterials interact with & inhibit viral proteins and particles, using cell-based in vitro model systems to evaluate anti-viral effects and host cell toxicity. The stipend ranges $35,000-50,000 depending on experience and expertise. For more information, email Jeffrey.Johnson@orau.org.

POSTDOCTORAL FELLOWSHIPS IN MOLECULAR BIOLOGY AND BIOCHEMISTRY

The Naval Health Research Center Detachment, Environmental Health Effects Laboratory, Dayton, Ohio, has a vacancy for an outstanding viral, cellular, or molecular biologist in the nanotechnology area. The Fellow will conduct research on how nanomaterials interact with and inhibit viral proteins and particles, using cell-based in vitro model systems. For more information, email Jeffrey.Johnson@orau.org.

Calendar of Scientific Meetings

DECEMBER 2006

Second ISN Special Neurochemistry Conference: Neural Glycoproteins and Glycolipids

December 1-5 • Antigua, West Indies
For information contact:www.isnantigua2006.org/

19th World Diabetes Congress

December 3–7 • Cape Town, South Africa
www.idf2006.org/

American Society for Cell Biology 46th Annual Meeting

December 9-13 • San Diego
Ph: 301-347-9300; Email: ascbinfo@ascb.org
Website: www.ascb.org

JANUARY 2007

BioSysBio 2007: Bioinformatics, System Biology, Synthetic Biology

Incorporating the Young Bioinformaticians Forum

January 11-13 • Manchester, UK
For information:www.biosysbio./com
Email: JohnCumbers@biosys.com; Ph: 44-0-207-617-7824

Sanibel Conference

January 19-22 • Sundial Beach Resort, Sanibel Island, Florida
Imaging Mass Spectrometry
Program Chairs: Richard Caprioli, Ron Heeren, and Markus Stoeckli, For information contact: ASMS
505-989-4517; asms@asms.org; www.asms.org

FEBRUARY 2007

Keystone Symposium on Ubiquitin and Signaling

February 4-9 • Big Sky Resort, Big Sky, Monotana
For information: www.keystonesymposia.org/Meetings/ViewMeetings.cfm•MeetingID=860
info@keystonesymposia.org; Ph: 800-253-0685 or 970-262-1230

Proteomics and Pathology—Joint Congress of the Spanish Proteomics Society and the European Proteomics Association

February 10-14 • Valencia, Spain
For Information: www.proteomics-valencia2007.ibv.csic.es/
Email: catedrasg@cac.es; Ph: 34-96-197-46-70

Keystone Symposium on PI 3-Kinase Signaling Pathways in Disease

February 15-20 • Hilton Santa Fe/Historic Plaza, New Mexico
For information: www.keystonesymposia .org/Meeting/ViewMeetings.cfm•MeetingID=864
info@keystonesymposia.org; Ph: 800-253-0685 or 970-262-1230

Keystone Symposia: Bioactive Lipids in the Lipidomics Era

February 20-25 • Taos, New Mexico
For information: www.keystonesymposia.org

German Society for Fat Science (DGF): Oleochemicals Under Changing Global Conditions

February 25-27 • Hamburg
For information: www.dgfett.de/meetings/hamburg/index.html

MARCH 2007

U.S. HUPO 2007

March 4-8 •Seattle
For information contact:www.ushupo.org
Email: USHUPO@USHUPO.org; Ph: 505-9899-4876

Keystone Symposia Metabolic Syndrome and Cardiovascular Risk

March 27-April 1 • Steamboat Springs, Colorado
For information: www.keystonesymposia.org

4th International Symposium on Diabetes and Pregnancy

March 29-31 • Istanbul, Turkey
For information: www.kenes.com/dip07/ref=old
Email: dip07@kenes.com

RNAi2007: The Expanding Roles of Small RNAs

March 29-30 • St. Anne's College
Woodstock Road, Oxford, UK
Organizer: Dr. Muhammad Sohail
Ph: +44(0)1865 275231
Fx: +44(0)1865 275259 (Switchboard)
Email: Muhammad.sohail@bioch.ox.ac.uk
www.libpubmedia.co.uk/Conferences/RNAi2007/Home.htm

Association for Biomolecular Resource Facilities

Mar 31-April 3 •Tampa Convention Center, Florida
For information contact:www.faseb.org/meetings/default.htm
Email: ncopen@faseb.org; Ph: 301-634-7010

APRIL 2007

3rd European Symposium on Plant Lipids

April 1-4 • York, UK
Website: www.eurofedlipid.org/meetings/index.htm

Second Workshop on Biophysics of Membrane-active Peptides

April 1–4 • Lisbon Science Museum, Portugal
The Lisbon Science Museum includes a 19th century lab and lecture room. Conference call for papers: special theme issue of J Pep Sci. Symposia: Membrane-translocating peptides / Cell penetrating peptides, Membrane-permeabilizing peptides / Antimicrobial peptides, Fusogenic peptides, and Structure and Dynamics in peptide-membrane interaction, Plenary lectures: Jöel Schneide: Bioactive properties of peptide surfaces. Robert Hancock: Antimicrobial peptides. Stuart McLaughlin: Electrostatic interaction of basic peptides with acidic lipids in membranes.
Abstract submission, January 15, 2007, Early registration, January 15, 2007, Faculty of Sciences, University of Lisbon, Miguel Castanho, Ph.D.
www.biophysicsmap.com; E-mail: castanho@fc.ul.pt

American Society for Biochemistry and Molecular Biology Annual Meeting in Conjunction with EB2007

April 28–May 2 • Washington, DC
Contact: ASBMB 2007, 9650 Rockville Pike, Bethesda, MD 20814-3008
Ph: 301-634-7145
Email: meetings@asbmb.org
Website: www.asbmb.org/meetings

2nd International Congress on Prediabetes and the Metabolic Syndrome

April 25–28, 2007 • Barcelona, Spain
www.kenes.com/prediabetes2007;
Email: prediabetes2007@kenes.com

MAY 2007

7th International Symposium of the Protein Society

May 12–16, 2007 • Stockholm-Uppsala, CA Sweden
www.proteinsociety.org/pages/page02b.htm
E-mail: cyablonski@proteinsociety.org
Tel.: 301-634-7277

JUNE 2007

55th ASMS Conference on Mass Spectrometry

June 3-7 •Indianapolis
For information contact: ASMS, 505-989-4517
asms@asms.org; www.asms.org

Mitosis Spindle Assembly and Function A FASEB Summer Research Conference in Honor of Dr. B. R. Brinkley

June 9 -14 •Hyatt Grand Champions Resort and Spa, Indian Wells, California
Applications from students and post-docs are especially welcome! For additional information contact the organizers:
Dr. Conly L. Rieder, rieder@wadsworth.org or
Dr. Robert E. Palazzo, palazr@rpi.edu.

76th Annual EAS Congress European Atherosclerosis Society

June 10-13 • Helsinki, Finland
The Congress aims to create a stimulating atmosphere for exchange of the latest scientific and clinical knowledge in the field of atherosclerosis and cardiovascular diseases.
Deadline for submission of abstracts: November 30, 2006
For more information contact:Kenes International, EAS 2007
17, rue du Cendrier; P.O. Box 1726
CH-1211 Geneva 1, Switzerland
Ph: +41 22 908 0488; Fax: +41 22 732 2850
Email: eas2007@kenes.com
Website: www.kenes.com/eas2007

20th American Peptide Symposium—20th Jubilee Peptides for Youth

June 22-27 • Montreal, Canada
For information: www.americanpeptidesociety.com/index.asp?
Email: 20thAPS@UMontreal.ca
Ph: 819-564-5346

JULY 2007

XXIst Congress of the International Society on Thrombosis and Haemostasis

July 6–12, 2007 • Geneva, Switzerland
www.isth2007.com

32nd FEBS Conference: Molecular Machines and their Dynamics in Fundamental Cellular Functions

July 7-12 • Vienna, Austria
Abstracts to be considered for lectures must be received by January 31, 2007. All presenting authors of abstracts chosen for a main talk will receive a registration fee waiver.
For registration information: http://FEBS2007.org/
For Sponsor and Exhibitor information: Email:
Infgo@febs2007.org

2007 ASBMB Annual Meeting

April 28 – May 2, 2007 • Washington, DC

Held in conjunction with EB 2007

Organized by: Benjamin F. Cravatt, The Scripps Research Institute, Michael K. Rosen, University of Texas Southwestern Medical Center and the 2007 ASBMB Program Planning Committee

Early Registration Deadline: March 2, 2007

Preliminary Program

Genome Dynamics

From Genome to Epigenome – Modification and Repair

- *Methylating and De-methylating DNA*
- *Recombining and Modifying DNA*
- *Making and Re-making DNA*
- *Telomeres and Telomerase*

The Chromosome Cycle

- *Centromeres and Kinetochores*
- *Chromatin Structure and Remodeling*
- *Chromosome Duplication and Cohesion*
- *Chromosome Segregation and Aneuploidy*

RNA

- *Molecular Recognition and Enzymology of RNA*
- *RNA-Based Gene Regulation*
- *Small RNAs*
- *RNA Modification: Mechanism and Function*

Protein Synthesis, Folding and Turnover

- *Molecular Mechanisms of Protein Biosynthesis*
- *Co- and Post-Translational Folding*
- *Protein Modification and Turnover*
- *Ribosome and Translation*

Structure and Design

Macromolecular Structure and Dynamics

- *Conformational Transitions and Protein Aggregation*
- *Experimental and Computational Dynamics*
- *Protein-Lipid Interface*
- *Structural and Mechanistic Evolution*

Enzymes – Mechanism and Design

- *Structural Enzymology*
- *The Role of Dynamics in Enzyme Catalysis*
- *Computational Studies of Mechanistic and Dynamical Aspects of Enzyme Reactions*
- *Enzyme Design*

Extracellular Matrix at Multiple Biological Scales

- *Extracellular Matrix at the Cellular Scale*
- *Extracellular Matrix at the Molecular Scale*
- *Extracellular Matrix at the Organism Scale*
- *Extracellular Matrix at the Tissue Scale*

Chemical Biology

- *Chemical Biology of Cell Death*
- *Fragment Based Drug Discovery*
- *Chemistry and Cell Biology of Natural Products*
- *Antibiotics for the 21st Century*

Cell Systems

Metabolism

- *Metabolic Sensing and Signaling*
- *Molecular and Cellular Aspects of Metabolic Disease*
- *Mitochondria in Health and Disease*
- *Aging and Metabolism*

Organelle Dynamics

- *Golgi Structure and Biogenesis*
- *Membrane Biogenesis*
- *Mitochondrial Dynamics*
- *Nuclear Dynamics*

Systems Biology

- *Modeling of Cell Systems*
- *Molecular Profiling of Cell Systems*
- *Proteomics of Cell Systems*
- *Mathematical Biology*

Minority Affairs Committee Sponsored Symposia

- *Best Practices in Program Assessment*
- *Infectious Diseases in Minority Populations – Hepatitis C*
- *Genetic Diseases in Minority Populations – Sickle Cell Anemia*
- *Infectious Diseases in Minority Populations – Tuberculosis*

Signaling

Biochemistry and Signaling of Lipids

- *Biogenesis, Transport and Compartmentalization of Lipids*
- *Chemical Probes of Lipid Systems*
- *Lipids as Transcriptional Regulators*
- *Specific Protein-Lipid Interactions*

Signaling Pathways Controlling Cell Structure and Fate

- *Cytokine and Growth Factor Signaling*
- *DNA Damage Signaling*
- *Cell Cycle*
- *Signaling to the Cytoskeleton*

Public Affairs Advisory Committee Sponsored Symposium

Sponsored by EB participating societies

- *NIH at the Crossroads: How Diminished Funds Will Impact Biomedical Research and what Scientists Can Do About it*

Education and Professional Development Committee Sponsored Symposia

- *Classroom of the Future II*
- *Science at Undergraduate Institutions*
- *Graduate Student/Postdoctoral Starting Faculty Transitions*
- *Preparing for a Successful Career in Industry*

ASBMB
Chemistry of Life

www.asbmb.org/meetings