

AUGUST 2005

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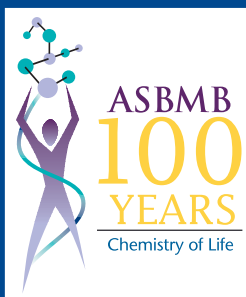
ASBMB *Today*

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AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

Human Chromosome, Bearer of Genetic Information

ALSO
ASBMB CENTENNIAL CELEBRATION
PAGES 10-17



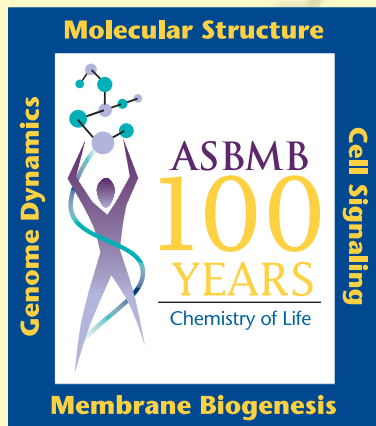
Molecular Structure

Genome Dynamics

**ASBMB
100
YEARS**
Chemistry of Life

Cell Signaling

Membrane Biogenesis



ASBMB 2006 Centennial Celebration

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Thematic Meetings

MOLECULAR STRUCTURE

Macromolecular Structure and Dynamics
Andrej Sali, UCSF

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

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

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

GENOME DYNAMICS

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

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

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

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

CELL SIGNALING

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

Signaling in Growth and Development
Michael B. Yaffe, MIT

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

MEMBRANE BIOGENESIS

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

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

MINORITY AFFAIRS COMMITTEE SPONSORED SYMPOSIA

Juliette Bell, Fayetteville State University

Issues in Breast Cancer Among Minority Populations
Chair: K.V. Venkatachalam, Nova Southeastern University

Minorities and the HIV/AIDS Epidemic
Chair: Juliette Bell, Fayetteville State University

Education and Professional Development: Focus on the Future, Shape the Debate

J. Ellis Bell, University of Richmond

Plenary Lecture: My Life in Science
Edmond H. Fischer, University of Washington School of
Medicine and Edwin G. Krebs, University of Washington
School of Medicine

Shaping the Debate: Molecular Evolution
Chairs: Michael M. Cox, University of Wisconsin – Madison
and J. Ellis Bell, University of Richmond

EPD/MAC Symposium – Undergraduate Student/Faculty Science
Chairs: Joseph Provost, Minnesota State University-Moorhead,
Mark A. Wallert, Minnesota State University-Moorhead and
Phillip A. Ortiz, Empire State College

Plenary Lecture: Evolution
Elizabeth Blackburn, University of California, San Francisco

EPD/MAC Symposium – Outreach and Public Education
Chairs: Neena Grover, Colorado College and Thomas D.
Landefeld, California State University, Dominguez Hills

*Matching Expectations: Employers and Education in the Molecular
Life Sciences*

Chairs: Ronald L. Niece, Research Resources and Technologies,
Tustin CA and Greg P. Bertenshaw, Clearant, Inc.

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Special Events

Centennial Opening Celebration

**An Evening with the
San Francisco Symphony**

A Taste of San Francisco

Award Lectures

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of Biological Chemistry Lectureship**

ASBMB Amgen Award

**ASBMB Award of Exemplary Contributions to
Education**

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Avanti Award in Lipids

FASEB Excellence in Science Award

Herbert A. Sober Lectureship

Howard K. Schachman Public Service Award

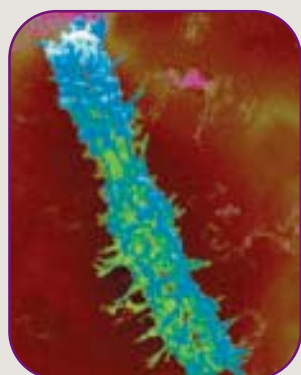
Schering-Plough Research Institute Award

William C. Rose Award

ASBMB Today

AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

AUGUST 2005,
Volume 4, Issue 5



ON THE COVER:

**Human chromosome,
bearer of genetic
information in the
human body**

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So You Think You Know Biochemistry History?

Try the ASBMB Centennial Quiz

Let's see how well you do answering these questions about events during ASBMB's first hundred years.

1. When was the term "genetics" introduced?
2. Who coined the name "vitamin," and when?
3. Who showed that xerophthalmia in rats is due to a lack of Vitamin A, and when?
4. When was the word "biotechnology" first used, and by whom?
5. Who discovered the human growth hormone, and when?
6. Who was the first ASBMB member to win a Nobel Prize, and in what year?
7. Who discovered penicillin, and when?
8. How many ASBMB members won Nobel Prizes in 1962, and who were they?
9. In what year did the FDA declare that genetically engineered foods are "not inherently dangerous" and do not require special regulation?
10. How many ASBMB members received the Nobel Prize in 1989 and who were they?

If you get all 10 of the answers to these questions right, you are entitled to be called an ASBMB Centennial Expert and will be eligible for all the perquisites thereof.

NOTE: Information for this test was supplied by William Lennarz, SUNY at Stony Brook, New York.

ANSWERS:

1. 1906
2. Funk isolated crystals with Vitamin B activity and coined the name vitamin.
3. McCollum showed that xerophthalmia in rats is due to lack of Vitamin A.
4. The word "biotechnology" was first used in 1919 by a Hungarian agricultural engineer.
5. The human growth hormone was discovered by Evans and Long in 1920.
6. Otto Meyer in 1922.
7. Alexander Fleming discovered penicillin in 1928.
8. Five ASBMB members won the Nobel Prize in 1962. They were Francis Crick, John Kendrew, Max Perutz, James Watson, and M. H. F. Wilkins.
9. The FDA declared genetically engineered foods "not inherently dangerous" in 1993.
10. Four ASBMB members received the Nobel in 1989. They were Thomas Cech, Sidney Altman, J. Michael Bishop, and Harold Varmus.

Art and Science



Dr. Judith Bond

When I was a college student in a small liberal arts women's college, Bennington College in Vermont, I was a science major in a school known for the arts. I loved the opportunity to be associated with those talented, creative people who could communicate so masterfully in the realm of music, painting, sculpture or dance, but I knew my talents and interests were elsewhere, and I believed there was a big gulf between the arts and the sciences.

As time has passed, however, I have come to realize that there are some very fundamental similarities between the arts and sciences. For example, artists and scientists deal with abstract phenomena, they aim to describe the world around us, create a new view of the universe or a very small part of the universe, and they learn by doing, experimenting, and creating a product (a painting, a performance, a manuscript). Basically both artists and scientists are experimentalists, and work in a 'laboratory' or 'studio' setting. Both have to deal with peer review, funding issues, presenting and 'marketing' their work, and both strive to provide new insights.

Artists and scientists select methods and strategies to express their ideas uniquely. An artist may choose to paint or sculpt; a scientist may choose to investigate molecules or populations of organisms.

The artists may describe their concepts in abstract renderings or in life like portraits or statuary; the scientists may build molecular models based upon theoretical premises or may provide a rigorous and detailed analysis of the cleavage site of a proteinase. Some artists work alone, in quiet contemplation and in solitary rendition of the imaginary in their mind; others conceive of grand projects that require many apprentices

and associates to complete, or even collaborators with different skills, such as a sculptor calling upon a foundry for a source of the appropriate molten metal.

Scientists too may work alone, like the solitary astronomers of yesteryear, or in small groups with trainees, or in large consortia, calling upon collaborators with different skills. Artists subject their work product to peer review, or a 'juried' process; scientists to journal and grant peer review, and award committees.

Both artists and scientists rely on two levels of review, that by others in the same modality, and by a wider public, the consumers of the work product. The work may be paid for by a commission, sponsor, grant or contract. The artist and the scientist both have the dual roles of satisfying the client, whether it is a patron or foundation, a company, or a governmental agent, and of educating the recipient of the work product about its quality and contribution. Although both the professional artist and the professional scientist must at some point satisfy a sponsor, the true motivation of both is the need to express unique interpretations of phenomena. Once articulated, the artist and the scientist

each have a sense of self-satisfaction in a completed work, and an inner yearning to improve upon it or develop the story in the next rendition.

So, both artists and scientists can understand the importance of "Being there when the picture is being painted" (P Reichard, *Ann Rev Biochem* 1995). And I believe all would agree that science and art are "10% inspiration and 90% perspiration" (Albert Einstein).

My thoughts on arts and sciences were rekindled during a recent meeting of the FEBS/IUBMB (Federation of European Biological Sciences/International Union of Biochemistry and Molecular Biology) in Budapest, Hungary (July 1-8, 2005). The organizers recognized and featured the congruence of art and science and creativity with a daily series focusing on a different aspect of science-based art, especially painting and sculpture. The spirit of the activity was captured by the umbrella descriptor "Science is Fun." Indeed it was fun, and you will hear more about that meeting in the September issue of *ASBMB Today*.

Judith Bond
President, ASBMB

Molecular and Cellular Proteomics Retains Number #1 Rank

Based on the new impact factors calculated for the past year, *Molecular & Cellular Proteomics* remained first in the category of Biochemical Research Methods (51 entries), which also contains many of the other journals primarily devoted to this field. The journal received an impact factor of 9.6, up from its initial evaluation last year of 8.3. (although the journal first appeared

in 2002, impact factors are not calculated until a journal has been publishing for two years). Interestingly, with this score, MCP ranked #100 in all journals (5968) in biology and medicine evaluated, placing it in the top 2%. Kudos to the ASBMB staff and the MCP associate editors and editorial board for their hard work in making MCP clearly successful in such a short time.

House Completes Work on 2006 Appropriations Bills

In an impressive display of party discipline, the GOP-controlled House of Representatives passed all 11 appropriations bills by the end of June—a rare event in recent years.

The Labor-HHS-Education bill, which funds the National Institutes of Health, passed the House on June 24. The House would provide \$28.507 billion for the NIH, but the 0.5 percent increase would be the first time in 24 years that the NIH budget would fail to keep pace with economy-wide inflation.

L/HHS Subcommittee Chairman Ralph Regula (D-OH) acknowledged the difficult choices he had to make, noting that the subcommittee was forced to use \$900 million of its allocation to help fund a Medicare prescription drug law. That left the total they had to distribute to popular education and health programs well under the previous year's levels.

Ranking subcommittee Democrat Dave Obey (D-WI) complained about the small increase proposed for NIH, stating that “over time, the reason we have had the best economy in the world is because of our critical investments in science.” He added that he failed to understand how members could vote for a bill that would fund 505 fewer research grants than in 2004.

During floor debate, Texas Republican Randy Neugebauer tried to eliminate funding for two research grants supported by the National Institute of Men-

tal Health. He said his amendment was intended to “save federal funding for serious mental health research.” One of the targeted grants, held by a researcher at the University of Iowa, dealt with the “perceptual bases of visual concepts,” or the understanding of vision and perception. The second grant, to a researcher at SUNY-Buffalo, focused on “perceived regard and relationship resilience” and looked at factors that contribute to successful marriages.

NIH Director Elias Zerhouni said of the Neugebauer amendment, “Defunding meritorious grants on the floor of Congress is unjustified scientific censorship. It undermines the historical strength of American science which is based on our world renowned, apolitical and transparent peer review process.”

In spite of the biomedical research community's efforts to defeat the Neugebauer amendment, it passed on a voice vote, although not on its merits. Rather, it was included in a group of several amendments passed “en bloc” with no debate, “to save time” according to Obey. Rep. Jim Leach (R-IA), one of whose constituents was being defunded, made a brief statement expressing concern about the amendment, but did not try to get the House to defeat it. He asked Regula and Obey to fix the problem in conference (we strongly suspect this will occur).


The Senate is lagging well behind the House, with no action on the Labor-HHS-Education bill expected before mid-July.

NSF Appropriations Moving

By contrast, funding for NSF is moving in both houses. The House approved the Science-State-Justice-Commerce bill on June 16, and the Senate Appropriations Committee approved its version of the bill on June 23.

The House bill provides NSF with \$5.64 billion, about 3% over the FY 2005 level. Increases to the research and education accounts at NSF account total about \$117 million, although NSF's total budget only increases \$38 million above the FY 2006 request. The \$79 million difference will have to come out of other NSF accounts, probably those funding major research equipment purchases, as well as salaries and expenses.

On June 23, the Senate Appropriations Committee approved the 2006 Commerce-Justice-Science Appropriations bill and provided \$5.53 billion for NSF. The appropriation, while \$58 million above last year's funding level, is still \$74 million below the President's request. NSF research programs are funded at \$4.35 billion, about 3% above last year. Education is funded at \$747 million, a whopping 11% below the current level.

The Senate has passed three of its 12 appropriations bills, and may take up at least a few more before the traditional August recess. It is not clear if NIH and NSF's parent bills will be among the favored few. 

Top 25 Medical Schools Receiving NIH Awards in FY 2004

Listed below in rank by dollar amount, are the top 25 medical schools that received NIH awards in Fiscal Year 2004. For a complete listing of all institutions receiving awards, the number of awards and total amounts, including training grants, fellowships R&D contracts, and other awards, go to the NIH website, <http://www.nih.gov>.

Rank	Organization	All Awards	Research Grants	R&D Contracts
1	Johns Hopkins University	\$449,470,782	\$403,903,065	\$24,979,647
2	University of Pennsylvania	393,623,671	364,361,779	6,112,029
3	University of California San Francisco	379,851,608	326,624,970	36,039,127
4	Washington University	371,719,472	345,546,335	8,739,234
5	University of Washington	307,873,069	265,568,425	18,567,611
6	Duke University	304,740,667	284,476,656	8,167,114
7	Yale University	287,811,325	268,713,821	0
8	David Geffen School of Medicine at UCLA	285,852,720	268,345,066	6,417,006
9	University of Pittsburgh	270,642,802	251,687,854	8,283,769
10	Stanford University	265,499,858	239,795,063	5,951,356
11	Baylor College of Medicine	248,451,313	229,839,778	8,709,219
12	University of Michigan	245,342,433	219,531,538	9,424,275
13	Case Western Reserve University	232,074,070	207,848,975	15,663,790
14	University of California San Diego	231,023,209	214,378,639	8,354,992
15	Vanderbilt University	226,826,142	206,509,582	5,178,874
16	Columbia University	226,575,848	203,699,837	8,579,858
17	University of North Carolina Chapel Hill	212,868,565	190,454,545	9,489,597
18	University of Alabama at Birmingham	207,078,637	164,468,537	31,775,521
19	Emory University	178,147,069	168,196,353	3,210,102
20	University of Colorado Health Science Center	172,322,577	160,046,858	1,646,501
21	University of Texas at Dallas	172,246,995	159,669,984	6,176,476
22	Yeshiva University Albert Einstein College	170,228,596	157,902,008	4,830,480
23	Oregon Health Sciences University	162,756,282	150,457,689	2,022,586
24	Harvard University	161,450,328	148,227,162	0
25	New York University at Mount Sinai	153,194,929	143,986,315	4,081,278

Scientists Discover How

Working independently, two research teams funded by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), have identified how Nipah and Hendra viruses, closely related viruses first identified in the mid-1990s, gain entry into human and animal cells.

Nipah and Hendra are emerging viruses that cause serious respiratory and neurological disease. People can get these deadly viruses from animals. Beginning in 1994, public health officials have recognized disease outbreaks in Malaysia, Singapore, Bangladesh and Australia.

Both viruses use a protein essential to embryonic development to enter cells and begin their often-fatal attack, report researchers at the University of California, Los Angeles (UCLA) and the Uniformed Services University of the Health Sciences (USUHS) in Bethesda, Maryland.

The UCLA team, headed by Dr. Benhur Lee, describes its findings in a *Nature* paper posted online on July 6. The report by the USUHS researchers, led by Christopher Broder, Ph.D., is appearing online the week of July 4 in the *Proceedings of the National Academy of Sciences*.

The first reported outbreak of Nipah virus occurred in 1998-1999 in Malaysia, sickening 265 people and killing 105, according to the World Health Organization. This outbreak, which in this case spread from pigs to

humans, was contained by culling more than a million pigs. Hendra virus, so far less of a threat to human health, was first identified in 1994 in Australia when it spread from horses to humans.

"In addition to our concern about Nipah and Hendra viruses as emerging global health and economic threats, we worry about their potential use as bioterror agents," says Anthony S. Fauci, M.D., director of NIAID. "This work, funded through our biodefense research program, is a major step towards developing countermeasures to prevent and treat Nipah and Hendra infection."

Using different methods, both teams identified a specific cell surface receptor, Ephrin-B2, as the doorway used by Nipah and Hendra viruses to get inside cells. This receptor is found on cells in the central nervous system and those lining blood vessels. It is crucial for the normal development of the nervous system and the growth of blood vessels in human and other animal embryos. Ephrin-B2 is found in humans, horses, pigs, bats and other mammals, which explains the unusually broad range of species susceptible to Nipah and Hendra virus infection.

Dr. Broder and his colleagues collaborated with researchers at the National Cancer Institute, also part of the NIH, and the Australian Animal Health Laboratory. The team narrowed the search for the Nipah/Hendra receptor by first sifting through the genetic sequences of 55,000 possible receptors using microarray technology as a molecular "sieve."

The scientists compared microarray signals from the 55,000 genetic sequences in one set of Nipah virus-resistant human cells with microarray signals from three sets of human cells that the virus can infect. This enabled the research team to narrow the possible number of receptor proteins to 120 by identifying those present in the virus-susceptible cells but absent in the virus-resistant cells. They winnowed the possibilities further — to just 21 — by selecting only those candidate receptors within the molecular weight range they expected. They selected 10 expressed at high levels in the susceptible cell lines and inserted them, one by one, into the cells that resisted Nipah virus to identify the receptor. When they inserted the gene for Ephrin-B2, the previously Nipah-resistant cells admitted the virus.

The UCLA team, with collaborators at the University of Pennsylvania, took a different approach, using tools of advanced molecular biology as well as old-fashioned detective work to identify the Ephrin-B2 receptor. They knew the receptor would be abundant among the type of cells Nipah virus attacks, that is, nerve cells and cells lining blood vessels.

To identify the human cell receptor, they created a bait: the Nipah protein that docks to that unknown receptor was attached to part of a human antibody, like a worm on a fishing hook. When they placed this bait onto cells susceptible to Nipah virus infection, it


Nipah Virus Enters Cells

attached to a protein on the cell surface. When placed on Nipah-resistant cells, however, the antibody did not attach to the cells. The scientists used an instrument that sorts molecules by weight to identify that Ephrin-B2 was the cell receptor protein that bound to the antibody/Nipah protein “fishing pole” they had made.

They wanted to confirm their findings, but since they did not have

access to a high-level biosafety laboratory as Dr. Broder’s team did, the UCLA researchers engineered a harmless virus with Nipah virus proteins embedded in its coat. The UCLA team found that this artificial construct could infect cells vulnerable to Nipah virus but was unable to infect Nipah virus-resistant cells. They also showed that this engineered virus could infect nerve cells

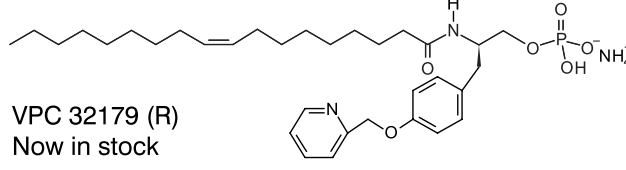
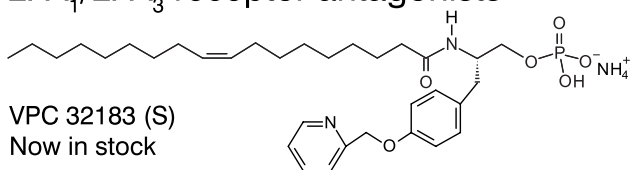
and cells lining blood vessels using Ephrin-B2 as the receptor, in the same way as actual Nipah virus would infect these cells.

Knowing the identity of the Nipah and Hendra receptor will not only help in developing vaccines and treatments, but also promises to lead to better understanding of how the viruses cause disease in people and a variety of animals, the researchers say. 

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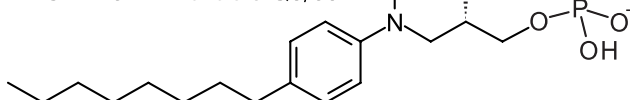
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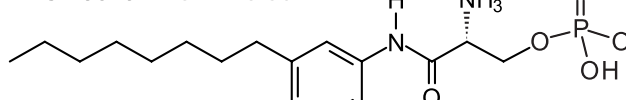


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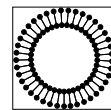
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Some Brain Cells 'Change Channels' to Fine-Tune the Message

Johns Hopkins researchers have identified the proteins that allow specific brain cells to "change channels," a rare ability that tweaks what can come into the cell. The findings, described in the March 24 issue of *Neuron*, may let researchers harness the process, perhaps one day using it to protect cells that die in Lou Gehrig's disease.

Much as turning the television dial changes what comes into the living room, these brain cells are able to change what they allow in by swap-

ping one kind of channel, or membrane opening, for another. Doing so lets the cells fine-tune their messages and adjust connections within the cerebellum, the brain region that controls fine motor skills.

"We don't know yet whether this happens in muscle-controlling nerve cells, but we're looking into it,"

— Dr. Richard Huganir

ping one kind of channel, or membrane opening, for another. Doing so lets the cells fine-tune their messages and adjust connections within the cerebellum, the brain region that controls fine motor skills.

Although the cells' channel-changing ability has been recognized for a few years, the key players controlling it hadn't been identified. Now, by studying mice, the Hopkins team has identified two proteins, called PICK1 and NSF for short, that help replace channels that let calcium ions in with

another kind of channel that keeps calcium out. If muscle-controlling nerve cells can do the same thing, forcing the swap might help protect them from a calcium overdose that can kill them.

"We don't know yet whether this happens in muscle-controlling nerve cells, but we're looking into it," says Richard Huganir,* Professor of Neuroscience and a Howard Hughes Medical Institute investigator in Johns Hopkins' Institute for Basic Biomedical Sciences.

So far, no one has really looked for channel changing in other cells in the brain, he says, in part because the swapped channels are most common in these particular cells in the cerebellum (so-called stellate cells). But Huganir thinks the channel changing is going to be relatively common in the brain.

Whether through channel changing or other, better understood ways of fine-tuning its responsiveness, a brain cell's activity level depends on its neighbors, the nerves and other cells that connect to it. Although they don't physically touch, the cell and its neighbor are so close to one another at these connection points, called synapses, that molecules released from one cell travel immediately to the next.

These molecules dock at specific places, or receptors, on the cell and trigger "channels" in the cell's membrane to open. Depending on the receptor and the channel, in will flow sodium, calcium, chloride or other




Dr. Richard Huganir

charged atoms that then keep the communication process going.

Of the cells in the cerebellum, a channel made of proteins called AMPA receptors, built from subunits called GluR3 and GluR4, is usually found at the synapse. If the cells are shocked with an electric current, within minutes the channels are replaced by ones made of GluR2 and GluR3. After the swap, sodium can still get in, but calcium is kept out.

To learn more about how this takes place, the Hopkins researchers studied brain cells from genetically engineered mice. Through their experiments, the researchers determined that the PICK1 and NSF proteins are both required for the calcium-forbidding channel to move into place at the synapse. Exactly how they help the channels move is still unknown, as is why the cells change their channels.

Part of the answer is likely to be self-preservation: Too much calcium inside nerve cells can kill them. But Huganir points out that calcium does a lot of things inside cells, suggesting that the channel swap might be accomplishing more than just keeping the cell alive. "Calcium turns some processes on, and it turns others off," he says. "My personal belief is that the cells might be doing more than just protecting themselves by keeping calcium out."

The researchers were funded by the Robert Packard Center for ALS Research at Johns Hopkins, the National Institute of Neurological Disease and Stroke, and the Howard Hughes Medical Institute. 

*ASBMB member

New Fat Needed to Clear Old Fat From System

Where fat comes from determines whether the body can metabolize it effectively. Researchers at Washington University School of Medicine in St. Louis have found that the “old” fat stored in the body’s peripheral tissues—that is, around the belly, thighs or bottom—can’t be burned efficiently unless “new” fat is eaten in the diet or made in the liver.

The research team developed genetically engineered mice missing an important fat synthesizing enzyme in the liver. As a result, the mice, called FASKOL mice (Fatty Acid Synthase KnockOut in Liver) could not produce new fatty acids in the liver. Because liver fatty acids are vital for maintaining normal sugar, fat and cholesterol metabolism, these mice must take in dietary fat to remain healthy.

Reporting in the May issue of the journal *Cell Metabolism*, the researchers say these mice developed fatty liver disease when placed on a zero fat diet.

“When we took dietary fat away from the FASKOL mice, their livers quickly filled with fat,” says senior investigator Clay F. Semenkovich, Professor of Medicine and of Cell Biology and Physiology. “Their ‘old’ fat stores mobilized to the liver, but their livers could not initiate fat burning, and the fat just accumulated. We concluded that to regulate fat burning, the liver needs ‘new’ fat.”

New fat is the fat that is consumed in food or is newly made in the liver as glucose is converted to fat by fatty acid synthase, the enzyme missing in the FASKOL mice. When the system takes in

high amounts of glucose, fatty acid synthase in the liver makes it into new fat.

In addition to fatty livers, the transgenic mice developed low blood sugar levels on the zero fat diet. Both symptoms were reversed with dietary fat, and in fact on a normal diet, the transgenic mice were no different than normal mice in terms of body weight, body fat, metabolic rate and food intake.

The effect of added dietary fat was duplicated when the mice were treated with a drug that activates a protein called PPAR-alpha. Liver fat declined to normal in the FASKOL mice within 10 days of receiving the PPAR-alpha activating drug.

PPAR-alpha is a protein found in all mammals and is central to metabolic processes that extract energy from dietary components like carbohydrates and fats. Because the PPAR-alpha activating drug did the same work that dietary fat does, the investigators concluded that new fat may be crucial to initiating the PPAR-alpha pathway.

“Scientists have argued that PPAR-alpha is activated by fats,” says Semenkovich, who also directs the Division of Endocrinology, Metabolism and Lipid Research and is a staff physician at Barnes-Jewish Hospital. “But we’ve never known which fats or where they come from. This study suggests that new fat is a ‘key’ that unlocks the ‘door’ for PPAR-alpha in the liver.”

The liver is very important for processing nutrients consumed in the diet and sending them on to the rest of the body. Abnormal processing of glucose


or lipids in the liver contributes to problems of type 2 diabetes and atherosclerosis, and fatty liver disease often is seen in people who are obese or suffer from insulin resistance.

“There’s also good evidence that the liver plays a key role in mediating cardiovascular risk through the secretion of multiple proteins associated with inflammation,”

Semenkovich says. “In these mice we found that when too much fat got into the liver, there was excessive inflammation.”

With Dr. Manu Chakravarthy, an endocrinology fellow and first author of the paper, Semenkovich found that new fat seems to solve those problems.

The research team is now trying to identify fats that could be given in small amounts to activate the PPAR-alpha pathway. They also are studying liver cells and fat cells to see how the liver can tell the difference between old fat and new fat.

Eventually, Semenkovich believes these findings could lead to more effective strategies for the treatment of obesity, type 2 diabetes and other metabolic problems. For now, he says that dieters who want to lose fat stored in peripheral tissues may find it useful to take in small amounts of dietary fats, such as fish oils, that might more effectively activate PPAR-alpha and fat burning pathways through the liver. 



Dr. Clay Semenkovich

At Centennial Meeting: ASBMB to Sponsor

By Peter Farnham, CAE, ASBMB Public Affairs Officer

The ASBMB Public Affairs Advisory Committee (PAAC) will sponsor a public affairs symposium on *Teaching the Science of Evolution Under Threat from Alternative Views* at the ASBMB Annual Meeting, April 1-5, 2006, in San Francisco. The symposium is scheduled for April 4.

The decision to sponsor this symposium is a response to continuing and ongoing efforts in many states and localities around the country to mandate the teaching of philosophical alternatives to the theory of evolution in K-12 science classes. The principle alternatives usually discussed are “creation science” or its close relative, “intelligent design.”

The Problem. Charles Darwin first proposed the theory of evolution in 1859. After almost 150 years of attacks on its validity, as well as patient testing of the theory’s central hypothesis, Darwin’s theory is now overwhelmingly accepted within the scientific community as one of the crowning achievements of scientific thought. Indeed, evolution has been called the “central organizing principle of modern biology.”

However, polling data going back more than 20 years show that while scientists accept the theory of evolution, only about one third of the public at large does. A 1980 Gallup poll found that about 38% of the American people believe that “the Bible is the actual word of God and is to be taken literally, word for word.” Given the broad public belief in the infallibility of the Bible, it should not be surprising that Gallup found in a 2004 poll that 45% of Americans believe that God created human beings, close

to their present day form, approximately 10,000 years ago. Only about a third of Americans believe that Darwin’s theory is a well-supported scientific theory. The 2004 poll also reaffirmed the earlier finding that a third of Americans consider themselves to be biblical literalists.

Lest it be thought that this poll is an anomaly, an NBC News poll conducted in March 2005 on religion in public life found that 33% of the public ascribe to the theory of evolution, while 44% believe the account of creation as described in the Book of Genesis.

Further, new data generated by a Research!America poll indicate that 51% of the public believes God created humans in their present form, and 29% believe humans evolved from lower life forms over millions of years but God directed the process. 15% believe humans evolved from lower life forms over millions of years without divine direction.

In addition, Research!America found that 35% of respondents do not consider Darwin’s theory of evolution to be well supported by scientific evidence; 34% do; and 31% do not know enough to say.

Of course, this is not a new controversy; evolution, and the implications it sparks for deeply held spiritual beliefs, has provoked outrage ever since Darwin proposed the theory. Anti-evolution sentiment even made it into popular culture in the 1920s in the wake of the Scopes trial.

Consider the lyrics below, excerpted from “*The Bible’s True*” by country music icon Uncle Dave Macon (recorded on April 14, 1926, less than a year after John Scopes was convicted of

teaching evolution in the Dayton, Tennessee schools):

*God made the world and everything’s
in it.*

*He made man perfect and the monkey
wasn’t in it.*

*What you say, what you say,
Bound to be that way,*

*Lord, yes!**

As these data—and the Dave Macon song—show, public opinion has changed very little in the last 80 years, and the American people continue to be skeptical about the theory of evolution. Some Americans go so far as to blame most of society’s ills on the theory of evolution.

Political and Legal Battles over Teaching Evolution

This skepticism about evolution is reflected in continuing efforts to denigrate its validity in the public schools. While efforts to criminalize the teaching of evolution are no longer being attempted, there were attempts in the 1970s and 1980s to force “creation science” to be taught in science class along with evolution. In 1987, in the case *Edwards v. Aguillard*, the Supreme Court ruled that such attempts were unconstitutional, on the grounds that they injected religion into the public schools.

Federal Level Efforts

However, Justice Antonin Scalia, in a dissenting opinion, left the door open to teaching alternative theories of how

* (Song lyrics from *Goodbye Babylon*, Dust to Digital Records, Atlanta, Georgia, October 2003.)

Symposium on Teaching Evolution

life began on earth. This subsequently led a number of groups to begin promoting the concept of “intelligent design” (ID), which holds that life is so complex that it could not have appeared naturally, but had to have been designed by some intelligent power. In addition, Senator Rick Santorum (R-PA) managed to get report language included in the No Child Left Behind Act in 2001 to promote the teaching of alternatives to evolution. This language has been used by a number of state legislatures in drafting anti-evolution statutes.

State Legislative Activities

As of this year, more than a dozen states are considering legislation related to teaching evolution in the public schools. While bills in Arkansas, Mississippi, and Montana have either died in committee or not been formally introduced, bills are under consideration in Alabama, Georgia, Kansas, Missouri, Pennsylvania, and South Carolina. These bills include such provisions as requiring teachers to challenge the validity of the theory of evolution; requiring changes in textbooks to promote alternative theories of origin; allowing school boards to add intelligent design to curricula; and revising how textbooks are selected—a clear effort to intimidate textbook publishers into giving intelligent design equal footing with evolution in biology and science texts.

Local and State School Boards

There are other efforts ongoing in local school districts to continue attacks on evolution. The Kansas state

school board, recently taken over by an anti-evolution majority for the second time in five years, held hearings in May on science standards, and is expected in the near future to require so sort of equal treatment of intelligent design in science curricula in the Kansas public schools. Meanwhile, Charles County, Maryland is considering the elimination of textbooks “biased” toward Darwinian evolution.

There are also several court cases pending on the issue. The Cobb County, Georgia public schools are in litigation regarding stickers pasted into textbooks that denigrate evolution as “only a theory.” The stickers were ruled unconstitutional at the local level, but the schools are appealing. And in Dover, Pennsylvania, where the public schools had required teachers to read to their high school biology students a statement supporting intelligent design, some teachers refused, and with the American Civil Liberties Union and some parents went to court over the issue. In the meantime, administrators—not teachers—are reading the statement.

Against this backdrop of divided public opinion and resulting turmoil in K-12 science education, the ASBMB Public Affairs Advisory Committee has decided that science teachers, many of whom feel beleaguered over this issue, need some assistance. Therefore, the committee decided to hold its symposium.

The Symposium Program

The symposium will provide a discussion of arguments (both scientific and philosophical) that support evolutionary theory and counter arguments advanced by “young earth creation-

ists” and supporters of intelligent design. These arguments will include a review of the biological record, a review of the fossil record, positive theological perspectives on evolution, and a review of public views on evolution. The session will be followed by a discussion period in which questions will be taken from the audience. The session will be chaired by PAAC Chair Bill Brinkley, Baylor College of Medicine. An outstanding panel of speakers will address the symposium. They include:

Dr. Ken Miller, Brown University, a prominent cell biologist and advocate for the theory of evolution who has authored a book on the subject, *Finding Darwin's God*.

Dr. Don Johanson, founder of the Institute of Human Origins at Arizona State University, Tempe, is a world-famous paleoanthropologist who is the discoverer of the “Lucy” fossil, the 3.2 million-year-old partial skeleton of a female member of the species *Australopithecus afarensis*.

The Reverend Ted Peters, Center for Theology and the Natural Sciences, Berkeley, California, speaks frequently on the compatibility of science and religion, and is a co-editor of the journal, *Theology and Science*.

Dr. Eugenie Scott, a major spokesperson for the theory of evolution and executive director of the National Center for Science Education, in Oakland, California.

The Public Affairs Advisory Committee hopes that all who plan to attend the ASBMB Centennial Meeting will make it a point to keep the noon hour on April 4, 2006 reserved for this important symposium on a vital public policy and science education issue. ☞



ASBMB Centennial Celebration: Chemistry of Life Structure, Function and Assembly of Membranes

Organizer: William Dowhan, University of Texas Medical School, Houston, TX

Remarkable progress has been made in recent years in defining the molecular details of biogenesis and assembly of the two major components of membranes. The umbrella theme of Membrane Biogenesis will be divided into two complementing parts dealing with the sub-themes of *Biochemistry and Molecular Biology of Lipids* and the *Structure, Function and Assembly of Membranes*. The former, which will be summarized in an upcoming issue of *ASBMB Today*, will focus primarily on the lipid component of membranes. The latter will focus on the protein component of membranes but will also integrate information on how membrane proteins interact with lipids. Presentations within these two themes will also be integrated to allow attendance at all oral presentations with the poster sessions held together to foster interaction. Combined social events are also planned to further stimulate interaction.

Our view of membranes as islands of proteins floating in a sea of lipids is rapidly changing as details are being revealed about membrane protein structure at the molecular level, the specific interaction of lipids with proteins, and the organization of defined lipid-protein complexes in the membrane. The "Structure, Function and Assembly of Membranes" theme will feature the application of genetic manipulation of proteins and membrane lipid composition and the determination of high-resolution structure of membrane proteins. *In vivo* and *in vitro* approaches will be integrated aimed at understanding the structural organization of membrane components, the mechanism of G-protein signaling, the details of the assembly of membrane components, and the structure of solute transport proteins. A common theme will be a focus on structure function relationships and

the role protein lipid interactions play in determining function. Each symposium will be organized around the presentation of three invited lecturers supplemented with three short talks selected from the poster abstracts submitted to each symposium theme. To stimulate participation and to recognize outstanding contributions by graduate students and postdoctoral fellows to the short talks and poster presentations, cash awards have been underwritten with primary and secondary support thus far from the Schering-Plough Research Institute, Kenilworth, NJ and New England Biolabs, Beverly, MA, respectively.

Protein-Lipid Interactions As Determinants Of Function

Dr. Dowhan will chair this session and will illustrate the use of molecular genetic manipulation of membrane lipid composition to define new roles for lipids in cell function. Genetic alteration of membrane lipid composition has revealed that protein sequence and the protein insertion machinery are not the sole determinants of orientation with respect to the lipid bilayer of transmembrane domains of polytopic membrane proteins. Topological organization of some proteins is determined by interaction of topogenic signals within the protein sequence with specific membrane lipids. Dr. Paula Booth (University of Bristol, United Kingdom) will continue the theme of lipid-protein interactions. She will discuss how the physical properties of lipids influence the insertion, folding, and stability of membrane proteins. Once proteins are stably integrated into the membrane bilayer, their lipid environment is not static but is dynamic as proteins move from one organelle to

another and within one membrane into and out of organized domains of proteins and lipids. Dr. Richard Epan (McMaster University, Canada) will



Dr. William Dowhan

detail the biochemistry and biophysics of the interactions that determine lipid and protein sequestration into and exclusion from lipid rafts.

Membrane Protein Synthesis, Insertion And Assembly

The targeting of proteins to the membrane and their insertion into the membrane bilayer rely on an increasingly complex assembly of proteins that either direct the insertion of protein domains into the membrane bilayer or translocate protein domains to the opposite side of the membrane. Dr. Ross Dalbey (Ohio State University) will chair this session. He will discuss recent insights into the role YidC protein plays in the membrane insertion and folding of hydrophobic domains of membrane proteins. The translocase complex is necessary for both protein domain insertion into and translocation across membranes. Dr. Tom Rapoport (Harvard Medical School) will share new insights, based on recent structural analyses, into how membrane proteins are processed by the translocase complex. Once hydrophobic domains are released into the membrane bilayer by the insertion machinery, they must fold into their final tertiary structure. Dr. Donald Engleman (Yale University) will focus on the highly specific interactions between helical domains that determine the final organization of a membrane protein into a native structure.

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Chromatin Structure, Expression, Regulation

Organizer: Sharon Dent, University of Texas M.D. Anderson Cancer Center

DNA is highly compacted within the nucleus of the eukaryotic cell by association with highly basic histone proteins. The histone octamer acts as a spool for the wrapping of DNA along its surface, forming a nucleosome. Nucleosomes serve as a basic repeat unit for the overall organization of DNA into chromatin.

Modulations in chromatin structure are a central theme in the regulation of gene expression and other DNA-driven processes. Chromatin remodeling can be achieved through at least three different mechanisms. Alterations in post-translational modifications of the histones affect nucleosome-nucleosome interactions as well as the interactions of other proteins with chromatin. In addition, large multi-subunit complexes use the energy of ATP to alter histone-DNA interactions, ultimately affecting nucleosome locations. Lastly, the incorporation of variant histone proteins allows subtle changes to nucleosomal structure and may provide a mechanism for resetting modification states. Combinations of these remodeling mechanisms are also possible, allowing a large dynamic range of chromatin structures. However, how chromatin remodeling is regulated, and the molecular details of these various remodeling mechanisms are not yet clear. These questions are especially important given the many connections between epigenetic changes related to chromatin alterations and disease development that have come to light over the last few years. The programs of these symposia will highlight recent advancements in our understanding of the structure and regulation of chromatin.

Chromatin Remodeling

This symposium is focused on the molecular mechanisms of chromatin remodeling. Dr. Brad Cairns (HHMI,

Huntsman Cancer Institute, Univ of Utah School of Med) will chair this session and will present his work on the regulation and function of the essential RSC complex in yeast which uses ATP to actively translocate DNA, repositioning histone-DNA contacts, ultimately resulting in nucleosome movement. Dr. Mitch Smith (Univ. of Virginia) will discuss the importance of histone variants to the structures of very specialized, stable regions of chromatin, such as centromeres, and to the flexibility of dynamic chromatin structures, such as occur in the coding regions of actively transcribed genes. Dr. Ronen Marmorstein (Wistar Institute) will describe molecular details of histone modification reactions as revealed by X-ray crystallography.

Chromatin and Transcription

Specific histone acetylation, methylation, ubiquitylation, and phosphorylation events affect several steps in the process of transcription. Dr. Brian Strahl (Univ of North Carolina School of Med) will chair this symposium and will describe physical and functional interactions between RNA polymerase II and histone modifying enzymes. Dr. Shelley Berger (Wistar Institute) will describe her findings that demonstrate a single histone modifying complex can house multiple enzymatic activities. Dr. Ali Shilatifard (St. Louis University Health Science Center) will describe the components and functions of a methyltransferase complex in yeast called COMPASS, which is highly similar to a human assembly




Dr. Sharon Dent

that contains the MLL protein. Translocations in the MLL gene are often associated with childhood and treatment-induced leukemias.

Chromatin and DNA Repair

Several recent studies highlight the importance of chromatin remodeling to efficient DNA repair. Dr. Craig Peterson (U Mass Worcester) will chair this symposium and will discuss mechanistic links between chromatin remodeling associated with both DNA repair and transcription. Dr. Xuetong Shen (Univ. Texas M.D. Anderson Cancer Center) will describe exciting new connections between histone variants, the Ino80 ATP-dependent chromatin remodeling complex, and DNA repair in yeast. Dr. Jacques Cote (Laval Univ Cancer Research Center) will present his studies addressing how different chromatin modification events are coordinated during repair of double-stranded DNA breaks.

Chromatin in Development and Disease

Inappropriate changes in chromatin structure can lead to disease states such as cancer. Proper chromatin folding is also essential for normal developmental processes. Dr. Sharon Dent (Univ Texas M.D. Anderson Cancer Center) will chair this session, and she will discuss the role of the GCN5 acetyltransferase in mouse development. Dr. Danny Reinberg (HHMI, UMDNJ) will describe the functions and regulation of several important chromatin modifying and transcription proteins. Dr. Ed Seto (Moffitt Cancer Center) will discuss the biology of histone deacetylases. Small molecule inhibitors of these enzymes are currently in clinical trials for the treatment of various cancers. 



Metabolic Regulation

Metabolism has enjoyed a renewed interest that has moved it to the forefront of current biomedical research. This is due, in part, to the advances in molecular genetics that permit the genetic manipulation of genes of metabolic interest in mice and to the increased incidence of metabolic diseases such as obesity and Type 2 diabetes. There are also a number of new and sensitive techniques available that permit the determination of alterations in metabolic flux *in vivo*. These techniques have greatly extended the possibilities for the analysis of phenotypic changes caused by gene manipulation in mice and genetic diseases in humans. It is thus timely to include a theme at the ASBMB's Centennial meeting in April 2006, on Metabolic Regulation. This theme will emphasize the genetic and biochemical basis of the Metabolic Syndrome and related metabolic problems. The presentations have been organized in four general thematic areas and are designed to present an overview of some of the current excitement in the area of control of metabolic processes.

Genetic and Metabolic Approaches to the Study of Metabolic Syndrome

The Metabolic Syndrome, which is a collection of related metabolic disorders, including insulin resistance, type 2 diabetes mellitus (T2DM), obesity, dyslipidemias, atherosclerosis, and hypertension, is unfortunately, on the increase worldwide. The underlying metabolic basis for this syndrome is a topic of considerable medical interest, since Metabolic Syndrome is associated



Dr. Daryl K. Granner

with Type 2 diabetes. The first symposium will focus on the systemic factors that are involved in this syndrome. The speakers will assess the genetic and genomic approaches to understanding the molecular basis of insulin resistance, a process that is fundamental to Type 2 diabetes. C. Ronald Kahn (Joslin Diabetes Center) will open the session with a review of the basic mechanisms of insulin action using examples based on studies of gene function in genetically modified mice and in studies of human populations that are prone to Type 2 diabetes. The role of alterations in mitochondrial metabolism has become an important paradigm for understanding the effects of obesity and the important role of fatty acid oxidation in the induction of insulin resistance in humans. Vamsi Mootha (MIT) will review the insights that have been derived from the use of genomics to probe the change in mitochondria metabolism in humans. The control of level of fatty acids in the blood is a critical factor in the development of insulin resistance in humans. The final speaker in this session will be Luciano Rossetti (Albert Einstein College of Medicine), who will review recent research on the role of the hypothala-

mus in sensing nutrients and the impact of this process on energy metabolism in tissues.

The Role of Nuclear Receptors in Metabolic Syndrome

Nuclear receptors play a critical role in coordinating the transcription of a number of genes involved in energy metabolism. Many of these receptors have been implicated in the control of carbohydrate and lipid metabolism in the liver and adipose tissue and are candidate targets for drugs aimed at regulating these processes. This section of the Symposium will review our current understanding of the molecular mechanisms by which this class of transcription factors control gene expression. Daryl K. Granner (Vanderbilt University) will open the session by discussing the role of nuclear receptors in the control of transcription of the gene for PEPCK-C in the liver. The factors that are responsible for the regulation of the transcription of this gene have been extensively studied since PEPCK-C is a pace setting enzyme in both hepatic gluconeogenesis and glyceroneogenesis. A model will be presented to show the complexity of the control of transcription of this gene. Peter Tontonoz (UCLA) will follow with a discussion of his recent research on the role of nuclear receptors in the control of lipid metabolism and inflammation, which underlie atherosclerosis, and may play a role in obesity and T2DM. The complexity of the control of gene transcription by nuclear receptors is illustrated by their interaction with a number of transcriptional co-activators. One of the most important of these transcriptional reg-

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Organizers: Richard W. Hanson, Professor of Biochemistry, Case Western Reserve Medical School and Daryl K. Granner, Director, Vanderbilt Diabetes Center, Vanderbilt University School of Medicine

ulatory proteins is PPAR γ Coactivator-1 α (PGC-1 α) discovered by Bruce Spiegelman and his colleagues. This session will be capped off with a presentation by Dr. Spiegelman (Harvard University) on the role this protein plays in the control of the transcription of genes of importance in glucose homeostasis, as well as in the development of specific phenotypes in muscle brown adipose tissue and other metabolically active tissues.

New Approaches to Metabolic Regulatory Mechanisms

The renewed interest in metabolic research has been fueled by the advances in molecular genetics, which allow the genetic modification of mice as well as by a number of new techniques, which permit the sensitive and non-invasive analysis of the metabolic phenotype in the animals and in humans. These include techniques to assess metabolic flux *in vivo* and the use of NMR as a tool in metabolic analysis. New and potentially revolutionizing approaches are also on the horizon for use in metabolic studies. One of these approaches involves the use of newly developed nanoparticles for the analysis of metabolites in both cells and animals. The potential for this approach will be the topic of a presentation by Homme Hellenga (Duke University). New tools for comprehensive metabolic analysis are emerging that provide promise for gaining insights into fundamental metabolic regulatory and disease mechanisms. A presentation by Christopher Newgard (Duke University) will focus on the analysis




Dr. Richard Hanson

of metabolic flux using stable isotope NMR, and mass spectrometry-based metabolic profiling, as tools for understanding of mechanisms of diabetes and obesity. Several examples of the applications of these techniques will be provided, including insights into metabolic signals that control fuel-stimulated insulin secretion, pyruvate exchange with TCA cycle intermediates ("pyruvate cycling") and the role that cytosolic NADPH plays in the control of insulin release. He will also discuss the factors responsible for the development of insulin resistance in response to high fat diets in animal models and the alterations in mitochondrial handling of lipids and consequent accumulation of lipid-derived metabolites. Finally the potential for these new techniques in the comprehensive metabolic profiling of obese humans will be presented. Kitt Falk Petersen (Yale University) will review her research on the use of NMR-based imaging and metabolic flux analysis in humans to determine the rates of critical processes that are involved in the control of energy metabolism during insulin resistance, Type 2 diabetes and obesity.

Genetic and Metabolic Approaches to Obesity

The discovery of a number of compounds that are synthesized by metabolically important tissues, such as adipose tissue and the small intestine, have added greatly to our understanding of metabolic control. Several of these factors will be discussed in the

final session in this symposium. Barbara B. Kahn (Harvard University) will present her work on a novel adipocyte-secreted molecule that contributes to insulin action in diabetes and obesity, while Philipp E. Scherer (Albert Einstein College of Medicine) will discuss the systemic impact of adipocyte-derived factors as they relate to glucose and lipid homeostasis in the context of diabetes and inflammation. Finally Type 2 diabetes arises from a combination of impaired insulin action and defective pancreatic β -cell function. Genetic studies of the insulin-signaling pathway have led to a critical reappraisal of the integrated physiology of insulin action. These studies indicate that insulin signaling affects β -cell function and regulation of β -cell mass, thus raising the possibility that insulin resistance may be the overarching feature of diabetes in all target tissues. Domenico Accili (Columbia University) and his colleagues have shown that the forkhead protein, Foxo1, is an insulin-regulated transcription factor and that insulin-dependent phosphorylation inhibits the ability of Foxo1 to stimulate transcription of prototypic insulin-responsive genes in liver. Foxo1 is a key effector of insulin action in several tissues: liver, where it controls insulin inhibition of glucose production; pancreatic β -cells, where it controls proliferation and differentiation; pre-adipocytes, where it controls insulin-dependent adipose differentiation; myoblasts, where it controls myotube formation; and brain, where it controls expression of hypothalamic neuropeptides. Inhibition of Foxo1 holds promise as a therapeutic approach to insulin resistance and diabetes. 

Membranes... continued

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Structure And Function Of G Proteins And Their Receptors

An important function of membranes is the organization of integral membrane components for the purpose of signal transduction across membranes. A large class of such organized structures is made up of the heterotrimeric G proteins and their membrane receptors. The mode of interaction of the seven transmembrane domain G protein coupled receptors (GPCRs) with their cognitive GDP/GTP binding G proteins determines the signal transmitted across the membrane. Dr. Heidi Hamm (Vanderbilt University Medical Center) will chair this session and describe the use of recent atomic resolution structures of G proteins and the known interaction sites between

G proteins and GPCRs to probe the mechanism of G protein activation. Dr. David Siderovski (University of North Carolina-Chapel Hill School of Medicine), who has used naturally occurring and artificial peptides that interact with and affect G protein function, will extend this theme. These peptides have been effectively used to examine the specificity of GPCR-effector coupling. Dr. John Tesmer (University of Texas, Austin) will provide new insights into the molecular interactions between GPCRs and heteromeric G proteins based on atomic resolution of complexes between the components of the GTP dependent signaling cascade.

Structure And Function Of Transport Proteins And Channels

Solute transport proteins and channels have been among the most resist-

ant membrane proteins to analyze by X-ray crystallography. Remarkably, in the past few years several high-resolution structures of such proteins have been determined. In this symposium the structure of three different types of solute transport proteins will be related to their function. Dr. Ron Kaback (University of California, Los Angeles) will use the recently derived structure of the lactose permease symporter to provide new insight into the mechanism of solute transport across membranes. Dr. Douglas Rees (California Institute of Technology) will describe the detailed structure of the more complex ABC transporters and how this structural information provides new mechanistic insight into transporter function. Detailed structural information on a Na⁺/H⁺ antiporter will be used by Dr. Etana Padan (Hebrew University, Israel) to provide insights into the mechanism of pH regulation across membranes. 

Protein Structure Initiative Enters Production Phase

With the announcement of 10 new research centers, the Protein Structure Initiative (PSI) launches the second phase of its national effort to find the three-dimensional shapes of a wide range of proteins. This structural information will help reveal the roles that proteins play in health and disease and will help point the way to designing new medicines.

Selection of the centers, slated to receive about \$300 million over the next five years, marks the second half of the decade-long initiative funded largely by the National Institute of General Medical Sciences (NIGMS), part of the National Institutes of Health.

When the PSI established its pilot centers beginning in 2000, its goal was twofold: to develop innovative approaches and tools, such as robotic instruments, that streamline and speed many steps of generating protein structures, and to incorporate those new methods into pipelines that turn DNA sequence information into protein structures.

Now, the focus shifts to a production phase during which the new centers will use methods developed during the pilot period to rapidly determine thousands of protein structures found in organisms ranging from bacteria to humans. These efforts will facilitate

structure determination on a much larger number of proteins through computer modeling.

"The PSI has transformed protein structure determination into a highly automated process, making it possible to go from a selected target to a completed structure much more rapidly than before," said Jeremy M. Berg, Ph.D., director of NIGMS. "Building on these achievements, the new centers will take the PSI to the next level, yielding large numbers of structures and tackling significant new challenges. Importantly, the technology developed as part of the PSI will con-

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Proteomics and Bioinformatics

Organizers: Michael Snyder, Department of Molecular, Cellular and Developmental Biology, Yale University, and David Eisenberg, Department of Chemistry and Biochemistry, UCLA.

The DNA sequences of over 250 genomes have been determined, and a major challenge ahead is to determine the function and regulation of the entire set of gene products encoded by each organism. New technologies have recently been invented for globally analyzing the expression, modification and biochemical activities of large set of proteins. This information allows an understanding of not only individual proteins in different cell states, but also how entire systems and regulatory pathways operate. This symposium will highlight recent advances in proteomics and bioinformatics research in humans and model organisms, with regard to elucidating protein function and regulation and its applications to biomedical research. In addition to the speakers listed below, three short talks for each session will be selected from abstracts.

Protein Profiling in Normal and Disease States

Recent advances in mass spectroscopy allow the analysis of thousands of proteins in different tissues and disease states. Has protein profiling advanced to the point that it is possible to detect disease markers in bodily fluids and biopsy tissue samples? How well correlated are such markers with diagnosis and prognosis? This session will cover the latest approaches in mass spectroscopy and other proteomic approaches and their application to protein profiling in different tissue types and disease states. Speakers include Katheryn Resing who



Dr. David Eisenberg

Dr. Michael Snyder

will discuss "High throughput Proteomics Analysis," Gil Omenn "Plasma Proteome Profiles Associated with Cancers," and Richard Caprioli "Tissue Imaging and Profiling of Proteins by Mass Spectroscopy for Discovery in Clinical and Biological Research."


Posttranslational Modifications

Although much regulation occurs at the level of protein modifications, until recently little attention has been devoted to the global analysis of protein modifications. This problem is significant, given that a large fraction of all genes encode proteins that covalently modify proteins and nucleic acids. This session will cover the large-scale analysis of a wide range of protein modifications, including phosphorylation, methylation, acetylation and SUMOylation. John Yates will present "Advances in Post-translational Modifications," Donald Hunt will present "Comparative Analysis of Post-translationally Modified Proteins and Peptides by Mass Spectrometry: New Technology and Application in the Study of Cell Migration, the Histone Code and Cancer Vaccine Development," and Tony Pawson will present "Proteomic analysis of Regulated Protein Interactions."

Global Analysis of Protein Function and Biochemical Activities

The vast information derived from sequenced genomes provides little direct information on protein function. Functions must be inferred by further analysis of sequences, a rapidly expanding subfield of biochemistry and molecular biology. A myriad of new technologies have emerged to analyze the function and properties of proteins, including both experimental and computational approaches. David Eisenberg will present "Which proteins are prone to forming amyloid-like fibrils," Susan Dutcher "Global Analysis of Ciliary Proteins and Insights Into Human Disease," and Edward Marcotte will present "A Probabilistic View of Protein Function."

Regulatory Networks

The lives of cells are controlled by networks of interacting macromolecules. The recent ability to collect and analyze large data sets allows the elucidation of these intricate networks controlling key cellular and developmental processes such as cell growth and division. This session will highlight recent advances in regulatory networks using experimental and computational approaches. Michael Snyder will present "Eukaryotic Transcriptional and Posttranslational Regulatory Networks," Brenda Andrews will present "Protein Kinase Networks in Yeast," and Marc Vidal will present "Interactome Networks." 

Researchers at UT Southwestern Discover New Function for Old Enzyme

In a step toward understanding the early evolution of the cell, researchers at the University of Texas Southwestern Medical Center, Dallas have discovered that an enzyme important in the production of energy also protects the mitochondria, the energy factory itself.

The enzyme, called aconitase, is a well-known component of the pathway in cells that produces energy. But in a study using baker's yeast, Dr. Ronald Butow,* professor of molecular biology, has shown a new function for the enzyme - keeping the mitochondrial genome intact. The study appeared in the February 4, 2005 edition of the journal *Science*.

Mitochondria are the powerhouses of cells and create energy for all cellular processes. It is thought that mitochondria are descended from bacteria that originally took up residence in early cells. Through elements of a little-understood symbiotic relationship between the bacteria and the cell, the bacteria lost their independence and evolved into an organelle that provides energy for the cell. The relationship between mitochondria and the cell make each vital to the other's survival, and may explain a key biological event - the development of an efficient energy producer to allow the evolution of more complex aerobic life forms.

Because of their supposed microbial origins, mitochondria have their own DNA, which is separate from the DNA in the cell nucleus. Cells that have lost their mitochondrial DNA do not pass on working mitochondria when they divide. Without working mitochondria, cells cannot produce energy efficiently. Events that lead to mitochondrial DNA defects are associated with neuromus-

cular diseases and premature aging disorders in humans.


"Mitochondrial DNA was discovered in the 1960s, and we still do not know much about how it is organized, packaged or inherited," said Dr. Butow. "What is really amazing is that we very recently discovered proteins associated with mitochondrial DNA that were thought to only have metabolic functions, and that aconitase, one of these proteins, is essential for mitochondrial DNA maintenance and inheritance, a new function independent of its normal enzyme activity."

To determine the region of aconitase that keeps mitochondrial DNA intact, Dr. Butow's group made mutations in parts of the enzyme that are important for its catalytic activity. In spite of these mutations, aconitase still functions in the maintenance of mitochondrial DNA. The researchers concluded that aconitase's role in protecting the mitochondrial genome is independent of its role in making energy, giving a new face to the long-known enzyme.

Genes in the cell's nucleus code for aconitase, and once made, the protein is shuttled to the mitochondria to serve its functions. According to Dr. Butow, aconitase may participate in an internal cell communication system known as retrograde signaling. Retrograde signaling serves as a status-check in cells, where the mitochondria signal to the nucleus if something is wrong and when things are better again. By protecting the mitochondrial DNA, aconitase may be part of the "A-OK" signal after the cell experiences stress.

The role of aconitase in stabilizing the mitochondrial genome may be an evolutionary adaptation where the mitochondria co-opt a nuclear-

ly encoded protein to ensure survival of its genome, said Dr. Butow. "The cell takes care of the nucleus, because that is where its genome is," he said, "but the mitochondrial genome is not looked after. It has to take care of itself."

Other UT Southwestern researchers who participated in the study are lead author Dr. Xin Jie Chen, assistant professor of molecular biology, and Xiaowen Wang, research assistant in molecular biology. Dr. Brett A. Kaufman, a former graduate student at UT Southwestern now with the Montreal Neurological Institute, also contributed. 

* ASBMB member.

Protein... continued

Continued from page 16

tinue to impact structural studies beyond the PSI."

The PSI production phase includes two types of centers. Four large-scale centers, established during the pilot phase, expect to generate between 3,000 and 4,000 structures. Six specialized centers will develop novel methods for quickly determining the structures of proteins that traditionally have been difficult to study. These include small protein complexes; proteins that attach to a cell's outer envelope, or membrane; and many proteins from higher organisms, including humans.

While both sets of centers are charged with developing new methods for handling these more difficult proteins, the specialized centers will focus particularly on this task.

The PSI centers will submit their structures and related findings to the Protein Data Bank (www.rcsb.org/pdb/), an NSF- and NIH-supported public repository of three-dimensional biological structure data.

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PUBLICATIONS

Impacting Life Science.

Roger D. Kornberg Receives Alfred P. Sloan Jr. Prize

By Nicole Kresge, Staff Science Writer

Roger D. Kornberg,* Winzer Professor of Structural Biology at Stanford University, has been awarded the 2005 Alfred P. Sloan Jr. Prize. The prize is part of the General Motors Cancer Research Awards which were established to recognize basic and clinical scientists throughout the world who have made seminal contributions to cancer research. Dr. Kornberg accepted the award and delivered a lecture on June 15 as part of the two-day General Motors Cancer Research Annual Scientific Conference at the National Institutes of Health in Bethesda, Maryland.

The Sloan Prize, one of three cancer prizes General Motors presents each year, honors a basic science contribution that helps to explain cancer. The award consists of a gold metal and \$250,000 and is named in honor of Alfred P. Sloan, Jr., former President and Chairman of General Motors. To date, 108 scientists have received cancer research awards from General Motors and 13 of them have gone on to win the Nobel Prize.

Dr. Kornberg received the Sloan Prize for his discoveries, made over the past three decades, which revealed the basis of eukaryotic gene regulation at the level of transcriptional control. He is most known for solving the structure of RNA polymerase, the molecule translates DNA to RNA, in multiple states of activity. This is the largest protein structure that has been solved so far. Some of his other important findings include the discovery of the nucleosome and the demonstration of the key role it plays in the regulation

of transcription; the isolation, purification, and elucidation of the subunit structures of yeast RNA polymerase II and several transcriptional factors and co-activators; and the reproduction of transcriptional gene regulation *in vitro*. According to General Motors, the work of Dr. Kornberg and his associates represents a watershed in the molecular understanding of eukaryotic gene expression, which laid the basis for future studies of transcription initiation and regulatory mechanisms.

Currently, Dr. Kornberg's research is focused on discovering the molecular machines involved in transcription, reconstitution of transcription process with purified components, structure determination of the transcription machinery, and structure-function relationships in chromatin. He is especially interested in solving the structure of the entire


transcription apparatus at atomic resolution and understanding the mechanism of transcription control in living cells.



Dr. Roger D. Kornberg

Dr. Kornberg has recently discovered a human homolog of the 20-protein yeast Mediator complex. Mediator is the central processing unit of gene regulation. It receives both positive and negative inputs and transduces the information to the transcription machinery. He has also determined the structure of the entire transcription initiation complex by two-dimensional protein crystallography and discovered a stably altered nucleosome produced by a purified chromatin-remodeling complex.

Dr. Kornberg is the son of Arthur Kornberg, who shared the Nobel Prize in Medicine in 1959 for his laboratory synthesis of DNA.

The recipient of many honors, Dr. Kornberg was been awarded the Eli Lilly Award (1981), the Passano Award (1982), the Ciba-Drew Award (1990), the Harvey Prize (1997), the Gairdner International Award (2000), the Welch Award in Chemistry (2001), and the ASBMB-Merck Award (2002) for outstanding contributions to research in biochemistry and molecular biology. He is an elected member of the National Academy of Sciences and the American Academy of Arts and Sciences and an honorary member of the Japanese Biochemical Society. 

*ASBMB Member

According to General Motors, the work of Dr. Kornberg and his associates represents a watershed in the molecular understanding of eukaryotic gene expression, which laid the basis for future studies of transcription initiation and regulatory mechanisms.

'Scientific Ambassador' Bettie Sue Masters



Bettie Sue Masters, the Robert A. Welch Foundation Distinguished Professor in Chemistry in the Health Science Center's Department of Biochemistry, was awarded an Honorary Doctorate in Medical Sciences from Charles University in Prague, the oldest and most prestigious Czech university founded in 1348, and one of the 12 oldest universities in the world.

As the recipient of the Doctorate Honoris Causae, Dr. Masters joins an elite group of Nobel Laureates and former Secretary of State Madeleine Albright.

"I am immensely honored by this recognition," Dr. Masters said. "I've attended several of these ceremonies in past years and I know what a beautiful and honorific occasion it will be."

Dr. Masters' research focuses on determining the structure and function of the nitric oxide synthases, which produce nitric oxide in various organs for mediation of neural signaling, dilation of blood vessels, or killing of foreign cells such as tumors and bacterial or fungal agents. She will be honored for her scientific contributions to the nitric oxide synthases field during a ceremony on May 30 that will be attended by all of the presidents and

provosts of universities throughout the Czech Republic.

Dr. Ferid Murad who received the Nobel Prize in physiology or medicine in 1998 with Dr. Robert Furchgott and Dr. Louis Ignarro, was also be awarded the honorary degree for his original research on nitric oxide as a signaling molecule in the cardiovascular system.

"I was involved in discovering how proteins and enzymes produced nitric oxide," Dr. Masters said. "So, while Dr. Murad worked on the biological aspects of nitric oxide, I focused on the chemical mechanisms. I felt very privileged to be sharing the stage with this Nobel Laureate."


Dr. Masters has been involved in activities in Prague, such as educating and training scientists as well as scientific interchange, for the past 10 years, and co-organized an international meeting in Prague in 2002. Through her colleague, Dr. Pavel Martásek, Adjunct Professor of

Dr. Masters, fourth from right under the watchful eye of former King Charles IV, was awarded an Honorary Doctorate in Medical Sciences from Charles University in Prague.

Biochemistry at the Health Science Center and Professor of Pediatrics and Medicine at Charles University, she has assisted the Czech Republic in learning the American systems of peer review and recognition of scientific achievement. The Czech Republic has established its own systems based on the U.S. model.



Dr. Masters displaying her Charles University medallion

Dr. Masters has served as president of the American Society for Biochemistry and Molecular Biology, as chair of the U.S. National Committee of the National Academy of Sciences to the International Union of Biochemistry and Molecular Biology, and as a member of the Advisory Committee to the director of the NIH. She was inducted into the prestigious Institute of Medicine of the U.S. National Academies in 1996. 

by John D. Thompson, Editor

Nation's Universities In Battle For Biotech Dollars

The nation's universities are gearing up in an east vs. west competition to attract top biotech scientists and the research dollars that they hope will follow them. Key players in the battle are, on the East Coast, Harvard and the Massachusetts Institute of Technology, and on the West Coast, Stanford and the University of California, San Francisco.

Billions of dollars in government-research dollars and millions more in potential royalties from biotech start-ups licensing campus lab discoveries. Those start-ups—often launched in a university's backyard—could create thousands of high-paying jobs for those working to create cancer drugs, pest-free crops, and other biotech products.

Some examples of the key players weaponry on the East Coast:

- ❖ MIT's newly installed President Susan Hockfield, the first neuroscientist to lead a school primarily run by engineers, declared in her inaugural address, "MIT can and must lead in this essential new field-of-all-fields."
- ❖ Harvard President Larry Summers, launched a multimillion-dollar stem-cell research program last year, and picked a scientist, Steven Hyman, as Harvard's top academic officer.

On the West Coast:

- ❖ University of California officials decided to base California's new \$3 billion embryonic stem-cell research program near UCSF's developing life-sciences campus.
- ❖ Stanford announced last month that two scientists, one from Harvard and the other from the University of Michigan, are joining its Institute for Cancer/Stem Cell Biology and Medicine this fall. The school said they

came partly because of California's abundant stem-cell-research dollars.

Stem-cell research, while controversial, is emerging as a promising area of biotech discovery, and recent advances in human stem-cell and genetics research spur hopes that biotech is closer to cures for spinal-cord injuries and other maladies. That could transform biotech into a profit machine just as states are leaning more on universities for help in boosting their economies.

Cambridge, Massachusetts, and the San Francisco Bay area are home to a combined 1,000 biotech firms and 100,000 biotech workers, and many industry leaders such as Genentech in south San Francisco and Biogen Idec and Genzyme in Cambridge, trace their births to the area's universities.

The University of California's 43-acre Mission Bay campus is next door to an area that in the next 15 years is expected to be home to buildings

housing biotech companies with up to 5,000 workers. This \$1.5 billion project, UCSF officials say, is the nation's biggest university biomedical expansion. A centerpiece is QB3, a joint venture between UCSF and sister UC campuses in Berkeley and Santa Cruz. QB3, with a \$100 million building budget, will combine 1,500 scientists from biology to computer science to physics aiming to solve medical mysteries.

QB3 Executive Director Regis Kelly who took office in June sees the Broad Institute, a joint venture of Harvard and MIT similar to QB3, as his major competitor. Broad, which was launched last year with a \$100 million gift from Los Angeles entrepreneur Eli Broad, has 400 researchers and other employees from Harvard, MIT, and affiliated hospitals, all of them working on cancer cures. They are hunting for what Broad calls cancer's "Achilles' heel"—genes that cancers need to survive.

Ireland on the Offensive in Search for Biotech Business

Ireland's initial pitch to U.S. high-tech companies was based on its flexible, educated work force, and low corporate taxes. But now, Ireland's Minister of Education Mary Hanafin recently explained to *New York Times* Columnist Thomas Freidman, the country has started a campaign to double the number of Ph.D.'s it graduates in science and engineering by 2010, has set up funds to get global companies to come to Ireland to do research, and is even actively recruiting Chinese scientists.

"It is good for our own quality students to be mixing with quality students from abroad," said Hanafin. "Industry will go where the major research goes."

The goal, said Minister for Enterprise and Trade Micheal Martin, is to generate more homegrown Irish companies and not just work for others. His ministry recently set up an Enterprise Ireland fund to identify "high-potential Irish startup companies and give them mentoring and support."

Biopolis Expansion Fuels Singapore's Growth as a Biomedical Hub

The demand for research laboratories at Singapore's Biopolis biomedical R&D hub has reportedly been so strong that development of Phase II is already underway less than two years after Biopolis opened. Phase I with two million square feet of space is over 90% occupied, and Phase II will add two new buildings providing an additional 400,000 square feet to house the R&D operations of pharmaceutical and biotechnology companies.

"The overwhelming demand for space at Biopolis leading to the accelerated Phase II development, signals the exponential growth of the biomedical sciences R&D community in Singapore. It bears testimony to Singapore's success in building a world-class R&D environment," according to Yeoh Keat Chuan, Deputy Director, Biomedical Sciences Group of the Singapore Economic Development Board.

Chong Lit Cheong, CEO of JTC Corporation, the Biopolis developer, added, "The demand from pharmaceutical and biotechnology companies for Phase II is expected to be equally high, as companies are attracted by the ability to conduct world-class science in Singapore. We expect more blue chip companies to follow the lead set by heavyweights like GSK, Novartis and the 15 other companies that have established R&D facilities at Biopolis."

More than 2,000 scientists are currently working at Biopolis currently, and Singapore authorities expect this number to grow to 4,000 when Phase II is finished. Among those already working at the Biopolis are:

Edison Liu, Executive Director of the Genome Institute of Singapore and former Director of Clinical Sciences at the U.S. National Cancer Institute.

Sir David Lane, Executive Director of the Institute for Molecular and Cell

Biology and founder of Scotland's biotech company, Cyclacel.

Alan Colman, CEO of ES Cell International, who was formerly with UK-based PPL Therapeutics.

Alex Matter, Director of the Novartis Institute for Tropical Diseases, who led the development of Novartis's cancer therapeutic, Gleevec.

Tuas Biomedical Park

Biopolis developer JTC also built the 183-hectare Tuas Biomedical Park located at the western tip of Singapore. Designed to cater to pharmaceuticals and biologics manufacturers, the park has attracted a roster of companies that includes Pfizer, Wyeth, Merck Sharp & Dohme, Novartis, and Ciba Vision. Now, JTC is working on the development of an additional 188 hectares at Tuas in the expectation of further growth in Singapore's biomedical manufacturing sector.

Wyeth Biopharma Announces Research Collaboration With Dublin City University

Wyeth BioPharma, the biopharmaceutical business unit of Wyeth Pharmaceuticals, announced in June that it had entered into a four-year research agreement with Ireland's Dublin City University (DCU) to generate scientific knowledge that will facilitate the creation and industrialization of biopharmaceutical production.

The agreement reflects Wyeth's concerns that while the biopharmaceutical market is projected to grow exponentially over the next few years, current technology is not expected to be sufficient to meet the production capacity requirements of the biopharmaceuticals currently in the company's development network.

Scientists at Wyeth BioPharma's campuses at Grange Castle in Dublin, Ireland and Andover, Massachusetts, and at Ireland's National Institute for Cellular Biology at DCU will use Wyeth's proprietary Chinese Hamster Ovary (CHO) cell technology and gene expression profiling to examine cell performance under industrial production conditions. DCU, with support of 4 million Euros (\$480 million) from the Science Foundation of Ireland (SFI), will provide research personnel and expertise, proteomics and full-length gene cloning technology. Wyeth will make a comparable commitment in the form of research personnel and expertise, proprietary CHO cell lines, cell culture process and CHO chip

technologies, and gene sequencing. Both groups will contribute to the mRNA expression profiling, bioinformatics, and functional evaluation aspects of the joint research program.

"The greatest challenge facing the biopharmaceutical industry is the ability to produce these therapeutic proteins in sufficient quantities. It is estimated that the industry must increase cell culture capacity by five or six times to meet future demands" said Maurice Treacy, Director of Biotechnology at SFI. "This precedent setting collaboration between DCU and Wyeth should generate new solutions to complex biological and technical problems that could benefit the entire industry."

Scientists Find 'Missing Enzyme' Used By Bacteria to Scavenge Iron

Scientists have discovered that a protein that was originally believed to be involved in tuberculosis antibiotic resistance is actually a "missing enzyme" from the biosynthetic pathway for an agent used by the bacteria to scavenge iron.

The research appeared as the "Paper of the Week" in the April 8 issue of the *Journal of Biological Chemistry*, an American Society for Biochemistry and Molecular Biology journal (2005, 280: 13978 – 13986).

Mycobacterium tuberculosis, the causative agent of tuberculosis, is responsible for more morbidity in humans than any other bacteria. The

Mycobacterium tuberculosis, is responsible for more morbidity in humans than any other bacteria.

emergence of multi-drug resistant strains of *M. tuberculosis* has prompted the search for new drug targets and a better understanding of the mechanism of resistance in this bacterium.

Several spans of DNA in the *M. tuberculosis* genome have been annotated as antibiotic resistance genes due to their sequence similarity to existing antibiotic resistance genes. Dr. Edward N. Baker of the University of Auckland in New Zealand explains, "Generally the sequence of the open reading frame is compared with the sequences of genes for other proteins (most of which are from different species) in

sequence databases. If a close match is found, it is assumed that the function is the same or similar."

Rv1347c is one of these annotated antibiotic resistance genes in *M. tuberculosis*. It encodes a putative aminoglycoside N-acetyltransferase that is thought to be involved in resistance to aminoglycoside antibiotics such as streptomycin.

"The aminoglycoside antibiotics have sugar rings with amino groups attached," explains Dr. Baker. "The N-acetyltransferase chemically modifies the sugar amino group by transferring an acetyl group to it. This inactivates the antibiotic because it can no longer fit into its target."

However, in vitro biochemical assays have failed to demonstrate aminoglycoside N-acetyltransferase activity in Rv1347c. By solving the three-dimensional structure of Rv1347c, Dr. Baker and his colleagues have discovered that the enzyme most likely plays an entirely different role in *M. tuberculosis*.

"What the structure showed, when combined with careful analysis of the sequence, its neighbors in the genome, and the fact that its gene was also regulated by iron, was that Rv1347c was almost certainly a "missing enzyme" from the pathway for biosynthesis of the iron scavenging agent mycobactin," recalls Baker.

"Mycobactin is a small molecule which binds iron very tightly. Bacteria synthesize it so that they can acquire the iron they need to grow – it is secreted out into the external environment where it scavenges iron and then

(with iron bound to it) it is taken up by the bacterium again."

Although Rv1347c is not involved in antibiotic resistance, it still remains a target for the design of new anti-TB drugs. "Enzymes that synthesize mycobactin are drug targets, because if mycobactin biosynthesis is stopped, the bacterium cannot acquire the iron that it needs for survival," explains Dr. Baker. "Importantly this seems to be true even of the bacteria that are taken up by macrophages in the lung and enter a dormant state – these are the hardest to attack with drugs." ❧

ASBMB Welcomes New Ph.D.s

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

Michael E. Barnett
Kansas State University

Magnus M. Che
Howard University

Doug Roberts
University of Utah

Aubrey A. Smith
Howard University

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

Retiree Health Benefit Costs:

What Will the Future Bring to Academia?

Could retiree health benefit costs choke academia? That was the question posed in *View*, a quarterly publication of TIAA-CREF which manages retirement funds for employees in the academic, health, and research fields. While a disproportionate number of faculty are baby-boomers or older, *View* stated that most institutions have failed to “put aside the funds to pay for this group’s retiree health benefits.”

“It appears that most institutions of higher learning in both the private and public sectors have not funded retiree health benefits obligations as they have accrued historically,” wrote Sylvester Schreiber in a TIAA-CREF research report, “The Outlook for Retiree Health Benefits.”


Schreiber, Vice President of Watson Wyatt Worldwide, a consulting firm that specializes in, among other things, employee benefits, stated, “This raises the prospect that in the future management of institutions that continue to sponsor these benefits will become hamstrung with obligations that are not properly anticipated and that have the potential to become so large that they pose a threat to the long-term viability of the institutions.”

Public entities, including colleges and universities, follow financial standards set by the Governmental Accounting Standards Board (GASB), which expects to impose new standards for reporting retiree health benefits in 2006. Public employers will be required to recognize the cost of accruing benefits during the

employee’s work years, to calculate and report actuarial accrued liabilities for promised benefits and to indicate future cash flows required to meet those obligations.

Institutions will have to start setting aside money for active employees’ future retiree medical benefits while simultaneously paying for benefits of existing retirees and the potentially large numbers about to join their ranks. To offset higher costs, colleges and universities might decide to

increase the minimum number of years an employee must work to receive retiree health benefits, or to require those eligible for benefits to pay a portion, or higher portion, of the insurance premiums.

But, Schieber notes, colleges and universities might continue to grow more rapidly than the rest of the economy, potentially enabling this sector to continue to sidestep the retiree health benefit cost problems that have plagued other parts of the economy. 

MOLECULAR AND CELLULAR NEUROSCIENTIST

The M.I.N.D. Institute and an Academic Department (to be identified at a later date)
UNIVERSITY OF CALIFORNIA, DAVIS, SCHOOL OF MEDICINE

The M.I.N.D. (Medical Investigation of Neurodevelopmental Disorders) Institute at the University of California, Davis, School of Medicine (www.mindinstitute.org) and an academic department to be identified at a later date, are recruiting for one (1) full-time faculty position (Assistant/Associate/Full Professor In Residence) whose research interests are in the molecular and cellular mechanisms of early neurodevelopment. Candidate must possess a Ph.D. and/or M.D. degree and at least four years of productive postgraduate experience. Individual selected for the position will be expected to build a successful, independent research program and to achieve excellence in the teaching of basic sciences to medical and graduate students. In addition, this scientist should be committed to directing a substantial portion of their program to research in animal models of autism and related neurodevelopmental disorders. Investigators whose research incorporates stem cell technology in understanding neurodevelopmental disorders are encouraged to apply. The most important criteria in the consideration of applicants are: (1) a record of excellence, creativity, and initiative in research, which establishes a strong potential to build a vigorous and competitive research program; and (2) a demonstrated ability to communicate as a teacher. Candidates will have trained in modern methods of molecular and cellular neurosciences with substantial expertise using animal stem cell models of neuronal development. The Candidate will carry out basic research that will compliment existing collaborative programs at the M.I.N.D. Institute. Appointment in the appropriate UC Davis department will be made at the Assistant/Associate/Full Professor rank (In Residence series) based on experience. The position includes a highly competitive salary and laboratory start-up package.

Applicants pursuing other areas of biomedical research directly relevant to understanding autism and related disorders are also encouraged to apply. Candidates should send (1) curriculum vitae; (2) brief statement of research interests and plans; (3) names and contact information for at least five references to: David G. Amaral, Ph.D., Director of Research, c/o M.I.N.D. Institute, 2825 50th Street, Sacramento, CA 95817. This position will be “Open Until Filled”. For full consideration, applications should be received by August 1, 2005. The University of California is an Equal Opportunity/Affirmative Action Employer.

The Protein Society

Seeks a New *Protein Science* Editor-in-Chief

The Protein Society is seeking to fill the position of Editor-in-Chief (EIC) of *Protein Science* by January 1, 2007. Candidates should have a Ph.D., M.D., or an equivalent academic degree, broad experience in biochemistry, protein science, proteomics, bioinformatics, structural biology and/or computational biology as they pertain to proteins at the molecular and cellular level, and prior experience in editorial activities related to these scientific fields. Applicants are expected to have an accomplished scientific career with a significant publication record and appropriate editorial experience. Candidates should also possess strong leadership qualities, intellectual vision, and outstanding interpersonal skills.



The EIC has primary responsibility for the submission, review, and publication process and for the management of the Editorial Office. The EIC will keep abreast of current trends in publishing to initiate innovations, modifications, or new activities that will promote and enhance the scientific content and delivery of that information. The EIC also serves as the operating liaison between the journal and the publisher, Cold Spring Harbor Laboratory Press, and plays a key role in negotiating contracts with the publisher.

The EIC reports to the Executive Council of The Protein Society through the Society's Publication Committee, and the successful candidate would have flexibility in selecting the Associate Editors and the Editorial Advisory Board. The appointment is for an initial term of 5 years with a possible second term, at the discretion of the Executive Council.

Interested individuals are invited to submit an application package that includes a curriculum vitae, the names of three references, a succinct letter of interest and qualifications, and a vision statement for *Protein Science*, including innovations that may be considered. Nominations of potential candidates are also welcome.

Applications and nominations will be received through September 15, 2005. Please address them to:

Editor-in-Chief Search Committee Chair

c/o The Protein Society

9650 Rockville Pike

Bethesda, MD 20814

Email: cyablonski@proteinsociety.org

EOE

The Protein Society is the leading international society devoted to furthering research and development in protein science. The purpose of the Society is to provide national and international forums to facilitate communication, cooperation, and collaboration with respect to all aspects of the study of proteins. The Protein Society members represent academia, industry, government, and non-profit institutions from around the world.

www.proteinsociety.org

Career Opportunities

POST-DOCTORAL POSITION IN BIOCHEMISTRY AND MOLECULAR MICROBIOLOGY

A Post-Doctoral position is available immediately to study membrane biogenesis and protein translocation systems in *Streptococcus* with particular emphasis on the signal recognition particle (SRP) pathway. Applicants should have a strong background in biochemistry and molecular microbiology. Experience with cellular fractionations and membrane extractions; protein chemistry techniques such as density gradient centrifugation, electrophoresis, chromatography and protein purification; and techniques to evaluate protein-protein interactions such as two-hybrid systems, fluorescence methods, calorimetry, chemical cross-linking, immunoprecipitation and familiarity with mass spectrometry, nuclear magnetic resonance, circular dichroism and surface plasmon resonance will be given preference. English language proficiency is required. Salary is commensurate with experience and range follows NIH guidelines. **Send CV and three letters of reference to L. Jeannine Brady, Ph.D. at The University of Florida, Department of Oral Biology, P.O. Box 100424, Gainesville, FL 32610 or jbrady@dental.ufl.edu.**

STAFF SCIENTIST/FACILITY HEAD

Department of Health and Human Services National Institutes of Health

The National Institute on Aging, a major research component of the National Institutes of Health (NIH) and Department of Health and Human Services, is recruiting for a Staff Scientist/Facility Head who will serve as the Staff Scientist/Facility Head of the Behavioral Neuroscience Section, Laboratory of Experimental Gerontology (LEG) of the Intramural Research Program (IRP). The incumbent will be responsible for managing a longitudinal study of aging and nutrition in rhesus and squirrel monkeys housed at the NIH Animal Facility in Poolesville, Maryland, under an interagency agreement with the Veterinary Research Program as well

as those maintained at the Oregon National Primate Research Center, in Beaverton, Oregon, under a contract. Applicants must have a D.V.M. or Ph.D. or equivalent degree in Physiology, Biochemistry, Anthropology, or related sciences. Experience working with non-human primates is required. The incumbent will be responsible for the administrative and scientific direction of studies at both sites. The Staff Scientist/Facility Head will serve as the on-site point of contact for all project decisions. The Staff Scientist/Facility Head oversees day-to-day operation of the program, including budget, training, safety, animal care and use issues, and weekly lab meetings. The Staff Scientist/Facility Head oversees an interagency agreement involving several contracts used to conduct the study and coordinate the individual projects. The Staff Scientist/Facility Head will be the direct contact with the Principal Investigator and ensure that daily operations meet a high scientific standard and will work directly with NIH veterinarians to discuss and plan animal clinical care. Scientific duties would include design and planning of new studies, conducting physiological procedures, protocol preparation, managing a database, analyzing data, writing scientific papers, and making presentations at scientific meetings. The Staff Scientist/Facility Head will

organize and serve as chairperson for annual collaborator, scientific advisory committee, and grantee meetings. As well, this position will coordinate and plan additional interest group meetings providing participants with relevant background information and post-meeting summaries. Applicants must have a record of scientific accomplishments, including excellence in laboratory research and qualifications to manage and coordinate studies of aging in non-human primates.

Salary is commensurate with experience and accomplishments. The salary range for Staff Scientist/Facility Head is \$74,782 - \$151,182. A full Civil Service package of benefits (including retirement, health, life and long-term care insurance, Thrift Savings Plan, etc.) is available. Applicants should send curriculum vitae, bibliography, and three letters of recommendation to: Chair, LEG Staff Scientist/Facility Head Search Committee; Vacancy # NIA-IRP-05-05; c/o Peggy Grothe, Intramural Program Specialist; Office of the Scientific Director, National Institute on Aging, 5600 Nathan Shock Drive, Baltimore, MD 21224. Applications will be accepted until October 1, 2005. If additional information is needed, please call 410-558-8012.

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Calendar of Scientific Meetings

AUGUST 2005

Joint Cold Spring Harbor Laboratory/Wellcome Trust Conference Interactome Networks

August 31 - September 4 • Hinxton, UK

For information contact:

Email: wtmeetings@wtconference.org.uk

Website: <http://meetings.cshl.edu/meetings/interuk05.shtml>

SEPTEMBER 2005

European Life Scientist Organization Meeting

September 3-6 • Dresden

For information contact: Ph. +49 6224 925613

Website: www.elseo.org/index.php?id=elso2005

Second World Congress on Synthetic Receptors

September 7-9 • Salzburg Congress Centre, Salzburg, Austria

Abstract Deadlines: 25 March 2005 (oral and poster papers)

For information: Conference Secretariat, Elsevier, The

Boulevard, Langford Lane, Kidlington, Oxford OX5 1GB, UK

Tel: +44 (0) 1865 843691; Fax: +44 (0) 1865 843958

Email: jm.seabrook@elsevier.com

Website: www.syntheticreceptors.elsevier.com

Strategies for Engineered Negligible Senescence [SENS], 2nd Conference

September 7-11 • Queens' College, Cambridge, England

Conference organizer: Aubrey de Grey

Email: ag24@gen.cam.ac.uk

Website: www.gen.cam.ac.uk/sens2/CSBMCB

International Conference on Enzyme Technology RELATENZ 2005

September 20-23 • Varadero, Matanzas, Cuba

Contact: Autopista a Varadero km 3 ?

Matanzas, C.P.44740, Cuba

Email relatenz.umcc@umcc.cu

Website: www.umcc.cu/EnzymeTechnology/relatenz.htm

2nd Symposium on Enabling Technologies for Proteomics

September 22-23 • The Fairmont Palliser, Alberta, Canada

For information contact www.conciergeconnection.com/etp/

Email: etp@genomeprairie.ca

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

September 22 - 25 • Iowa State University, Ames Iowa

Ph: 515-294-7978; Email: gfst@iastate.edu

Website: www.bb.iastate.edu/~gfst/homepg.html

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

September 23-27 • Gaylord Opryland Resort and Convention Center, Nashville, Tennessee

Abstract Submission Deadline: April 27, 2005

For more information call (202) 367-1161

Email: asbmr@smithbucklin.com; Website: www.asbmr.org

ComBio 2005

September 25-29 • Adelaide Convention Center, Australia

For information contact: Email: asbmb@bigpond.net.au

Tel.: 618 8362 0009; Website: www.asbmb.org.au/combio2005

OCTOBER 2005

Supramolecular Chemistry

October 14-19 • Obernai (near Strasbourg), France

A European Science Foundation conference. For information:

Ph: +33 (0)3 88 76 71 35; Fx: +33 (0)3 88 36 69 87

Email: conferences@esf.org

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

October 21-22 • North Carolina Biotechnology Center, Research Triangle Park, NC. 2005

Deadline for registration and abstract submission: July 1

Email: stu_maxwell@ncsu.edu.

Website: <http://www.med.unc.edu/pmbb/nc-rna-soc.html>

NOVEMBER 2005

International Workshop on Biosensors for Food Safety and Environmental Monitoring

November 10-12 • Agadir, Morocco

Contact: Université Hassan II-Mohammedia, Faculté des

Sciences et Techniques, B.P. 146, Mohammedia, Morocco

Email a.amine@univh2m.ac.ma

Website: www.univh2m.ac.ma/biosensors

Third Annual World Congress on the Insulin Resistance Syndrome Clinical manifestations of the Insulin Resistance Syndrome - Metabolic Syndrome X

November 17-19 • Palace Hotel, San Francisco

The congress is organized by the International Committee for Insulin Resistance (ICIR) and is jointly sponsored by PESI Healthcare and the Metabolic Endocrine Education Foundation in association with the International Society of Diabetes and Vascular Disease.

For information on registration, abstracts submission, accommodations and exhibits: Ph: 818-342-1889; Fax: 818-342-1538

Email: insulinresistance@pacbell.net

Website : www.insulinresistance.us

DECEMBER 2005

Xth PABMB Congress: Panamerican Association for Biochemistry and Molecular Biology

December 3-6 • Hotel del Bosque, Pinamar, Province of Buenos Aires, Argentina

Organized by the Argentinian Society for Research on Biochemistry and Molecular Biology (SAIB). The Congress will consist of five Plenary Lectures, eighteen Symposia, nine sessions of oral communications, and three poster sessions.

For more information contact:

SAIB President. Ernesto Podestá: ernestopodesta@yahoo.com.ar
SAIB Secretary Carlos Argarña: carga@dqf.fcq.unc.edu.ar, or
PABMB Chairman Juan José Cazzulo: jcazzulo@iib.unsam.edu.ar
website: <http://www.saib.org.ar>

2005 Congress Expanding Proteomics: New Directions in Biology, Chemistry, Pharmaceutical Sciences and Medicine

December 5-7 • Zurich, Switzerland

For information contact:

Email: sps.congress@nlight.ch; Ph: +41 21 802 1163

Website: <http://sps05.swissproteomicsociety.org/qsPortal/Home.asp>

3rd Cachexia Conference

December 8-10 • Rome

For information contact:

Website: www.nataonline.com/LMS-Group/events/2/index.ph

Non-Vesicular Intracellular Traffic

December 15-16 • Goodenough College, London, UK

Contact: Meetings Office, Biochemical Society, 3rd Floor, Eagle House, 16 Procter Street, London, WC1V 6NX

Email: meetings@biochemistry.org

Website: www.biochemistry.org/meetings/focused.htm

Pacificchem 2005

December 15-20 • Honolulu

For information contact:

Website: www.pacificchem.org/e-mail: pacificchem2005@acs.org

JANUARY 2006

Pacific Symposium on Biocomputing

January 3-7 • Wailea, Maui

For information contact: <http://psb.stanford.edu/>

Email: psb@helix.stanford.edu; Phone: (650)725-0659

Building Bridges, Forging Bonds for 21st Century Organic Chemistry and Chemical Biology

January 7-9 • Pune, India

Tel.: 202-872-4523; Email: t_nameroff@acs.org

Website: <http://www.ncl-india.org/occb2006/index.htm>

FEBRUARY 2006

The 11th Annual Proteomics Symposium

February 3-5 • Erskine on the Beach, Lorne, Australia

Email: mp@asnevents.net.au

www.australasianproteomics.org.au/lorne.htm

The 31st Lorne Conference on Protein Structure and Function

February 5-9 • Erskine on the Beach, Lorne, Australia

email: mp@asnevents.net.au; www.lorneproteins.org/

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

February 9-11 • The University of Texas M. D. Anderson Cancer Center, Houston, Texas

This meeting will celebrate the Nobel Prize awarded to Avram Hershko, Aaron Ciechanover, and Irwin Rose for their discovery of the ubiquitin pathway and the 10th anniversary of the discovery of SUMO/Sentrin and NEDD8

Application and Abstract Submission Deadline: Friday, November 11, 2005; For information contact: Amy Heaton

Program Manager, Department Of Cardiology

University of Texas M. D. Anderson Cancer Center

Tel: 713-745-6826; Fax: 713-745-1942

Website: www.sentrin.org

G Protein- Coupled Receptors: Evolving Concepts and New Techniques

February 12-16 • Keystone, Colorado

For information contact:

Ph.: 800-253-0685 / 970-262-1230

Email: info@keystonesymposia.org

<http://www.keystonesymposia.org/Meetings/ViewMeetings.cfm?MeetingID=807>

MARCH 2006

Gordon Research Conference (GRC) on New Antibacterial Discovery & Development

March 5-10 • Ventura Beach Marriott, Ventura, California

For Information: Email: trevor.trust@astrazeneca.com

Website: www.grc.org/programs/2006/antibact.htm

RNAi2006: Advances in RNA Interference Research

March 22-23 • St. Anne's College, Oxford, UK

Conference Organizer: Muhammad Sohail

Biochemistry Department, University of Oxford

Tel: +44 1865 275225; Fax: +44 1865 275259

Email: muhammad.sohail@bioch.ox.ac.uk

Website: <http://libpubmedia.co.uk/Conferences/>

RNAi2006HomeMay2005.htm

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