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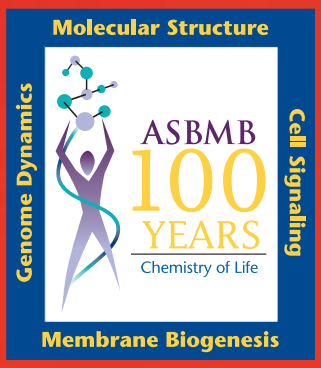

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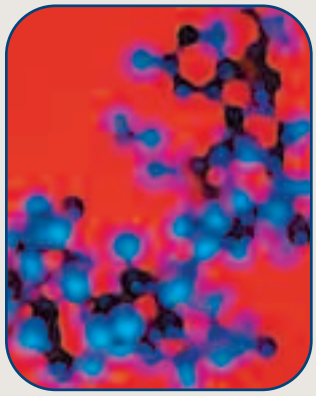
features



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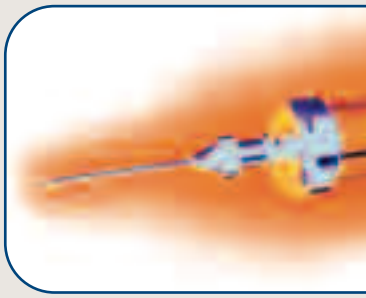

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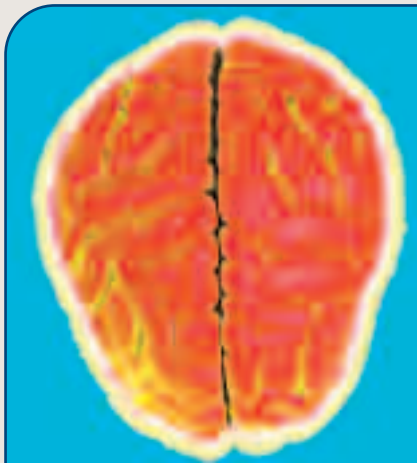

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Intelligent Design Fails Scientifically

To the Editor:

The Intelligent Design movement is based on Michael Behe's claim that complex systems, such as the visual mechanism, blood clotting, immune system, and bacterial *flagellum*, cannot have arisen by a Darwinian sequence of mutation-selection steps, which would have been too slow. He calls these systems 'irreducibly complex', meaning that when a single component (e.g., a protein) is removed, the system loses its function. He poses that such systems result from 'Intelligent Design' (not further defined) rather than from evolution. Behe et al claim that this is a scientific hypothesis, but do not present evidence in support of it. Actually, there are quite some published data that contradict Behe's thesis.

1. Evolution can be much faster than expected for a series of mutation-selection steps. Whereas the 5-mm-size shrimp *Xenoleberis* has not evolved in 425 million years, the cichlid fish in Lake Victoria developed 500 species in only 12,000 yrs. The marine stickleback has 35 body plates and three pelvic spines, which it loses within a few generations upon transfer to fresh water. Breeding the fresh-water form in seawater reverses the changes in two generations. A single gene, *Pitx-l,* is responsible. This gene is active in sea water and inactive in fresh water. Not the mutation of a gene, but its (in)activation is responsible for this large phenotypical change. Gene regulation (epigenetics) appears to playa large role in evolution. None of this is mentioned in the publications of Behe et al.
2. None of Behe's prime examples is quite 'irreducibly' complex, and all show some evidence of evolutionary development. *Rhodopsin,* the light-sensitive visual pigment, consisting of a retinaldehyde bound to the protein opsin is found in all three eye types (insect, cephalopod, vertebrate), but also in bacteria, where it serves as the light-sensitive element of a proton pump. It may thus be some 600 million years old and flexible enough to serve two quite different functions and operate in three widely different eye types. In samples of microbial populations collected from the Sargasso Sea, 782 *rhodopsin* homologs (varying in opsin amino acid composition) were detected. This indicates that *rhodopsin* is not irreducibly complex and suggests a gene-based evolution of the many different types of *rhodopsin*.

The human blood clotting system consists of 12 factors that work together in a cascade to produce blood clotting. The dolphin misses Factor XII, yet it has normal blood clotting, while humans missing this factor are haemophiliacs. A primitive clotting system was already present in hagfish and lamprey that diverged over 450 million years ago. It consists of three factors, tissue factor, prothrombin and fibrinogen, all part of the present mammalian system. Thus, the blood clotting system appears to have evolved over a period of at least 450 million years, and is not 'irreducibly complex'.

The immune system has as a crucial component the protein immunoglob-

Continued on next page

Dr. Judith Bond

Prepared Minds, and the Joy of Science

During the orientation for new graduate students at Penn State College of Medicine, Dr Elliot Vessel, now emeritus Chair of Pharmacology, used to highlight his presentation with a quote from Louis Pasteur: *"Dans les champs de l'observation le hasard ne favorise que les spirits."* (Lecture, University of Lille (December 7, 1854). The translation of this quote is:

"In the fields of observation chance favors only the prepared mind"

This is an important message for newer members of the research community, where we build on foundations of the past and 'prepare' the mind. The prepared mind comes through hard work, long hours of observation and data collection, assimilation of the base of information gained from lectures, readings and laboratory experiences. These experiences prepare the mind to 'get lucky,' take advantage of and 'see' an opportunity, make connections, and ultimately an advance in science. At the same time, aspiring scientists must be challenged to keep an 'open mind,' a critical mind, and a creative mind. This is asking a lot of our students, but there is great satisfaction for the student and teacher when the student accepts the challenge, gets engaged in science, takes responsibility and makes an important contribution.

Pasteur also said, "Let me tell you the secret that has led me to my goal. My strength lies solely in my tenacity." The longer one experiences a career in science, the more important Pasteur's messages seem to be. Scientists work hard, and what drives them are curiosity, the 'ah-ha' experiences, the completion of a considerable body of work, the generation of a new insight, and communication of a novel thought, insight or new connection, creative insight or synthesis of a large body of knowledge.

Now in the era of 'big science,' one wonders how many people will experience the excitement of science as members of a huge team or consortium. Big science is focused on generating large data sets, which are subjected to analysis by a panel of algorithms, to identify heretofore unrecognized relationships. The mapping of genomes or proteomes, translational science, drug testing, high throughput technology, developments of devices through nanotechnology all are useful and powerful goals, but will the same satisfactions exist for the individuals producing or assembling the data? Targeted research shares many of the attributes of 'big science,' raising some of the same reservations. Is there room for serendipity, curiosity, and individual achievement? Must we all be part of a grand scheme to develop a cure by following a protocol step by step? There will be jobs in science, there will be advances, but what about the joy of science in the new era. Does the next generation have to fit into a box rather than create their own box?

Funding strategies must provide opportunities for exploring new ideas, taking advantage of an unexpected finding or serendipitous discovery. There is no single path to discovery, problem-solving and knowledge creation. But it is critical for the nation's scientific enterprise, innovation and economic future to maintain a balanced portfolio of investigator-initiated research, led by a spectrum of early, mid-career and senior scientists, working independently and in teams. And to give them the freedom to follow leads, experience serendipity, and make the jumps.

Judith Bond, ASBMB President

Continued from previous page

ulin G (IgG), which is responsible for the production of antibodies. Human IgG is made up of four protein chains, two heavy and two light ones, permitting the production of millions of different antibodies. Camel IgG has no light chains, so it can produce only a few thousand antibodies. Yet, the camel lives happily with his restricted system. *Drosophila* has a gene *Dscam* that can encode up to 38,000 slightly different proteins functioning as primitive antibodies. It appears to be an early step in immuno globulin evolution. Again not 'irreducibly complex'.

The bacterial *flagellum* is composed of a membrane-embedded base formed by 10 proteins, to which is attached a tail made up of 20 proteins. The same 10 base proteins form the type III secretion system of gram-negative bacteria by which they insert their toxins into the host cell. So the flagellum does not fit Behe's definition of an irreducibly complex system and shows evidence of evolution.

Again, none of these findings is mentioned by Behe et al. This brief survey suggests the invalidity of Behe's hypothesis. For an extensive, fully referenced paper see: S.L. Bonting, Evolution and Intelligent Design, Metanexus, vol. 5 (12), Dec. 2005 <www.metanexus.net/digest/>.

Sjoerd L Bonting
Professor Emeritus, Chairman, Biochemistry

by Peter Farnham, CAE, ASBMB Public Affairs Officer

Anti-Evolution Measures Continue to Appear

A variety of measures, generally aimed at undermining the theory of evolution in favor of so-called "alternative explanations" for the diversity of life on earth, have been introduced this year in a number of states throughout the country. Among the newest ones that present varying levels of concern are bills in Maryland, South Carolina, New York, and Utah.

What is especially remarkable about these states is their diversity, varying widely in population, region of the country, and dominant political leanings. Maryland and New York are both strongly "blue" states, and at the national level have been mainstays of democratic politics for twenty years or more. By contrast, South Carolina and Utah are quintessentially "red" states, and thus almost always counted as reliably republican. And yet, in keeping with national polls that indicate that approximately half the American public rejects the theory of evolution, it is not surprising that anti-evolution measures would appear in both red and blue states.

What is also surprising is that at least so far, anti-evolution forces in the various states have not had a lot of success. They have consistently lost in the courts, and none of the measures below are expected to take effect any time soon, if ever.

Maryland House Bill 1531, the Public Schools and Institutions of Higher Education Academic Freedom Acts, was introduced on February 16 by Rep. Emmett C. Burns, Jr., (D-Baltimore). The bill would, if enacted, "expressly protect the right of teachers identified by the United States Supreme Court in Edwards v. Aguillard . . . to present scientific critiques of prevailing scientific theories; and [to] expressly protect the right of students to hold a position on any views."

Edwards v. Aguillard is the 1987 Supreme Court decision striking down Louisiana's law requiring that creationism be taught in the public schools. However, language in the opinion indicated that teaching different scientific theories about how life on earth developed would be all right (thus, giving birth to the concept of "creation science"—creationism under another name).

HB 1531 would provide that teachers in Maryland's public schools and faculty members in Maryland's public institutions of higher education "shall have the affirmative right and freedom to present scientific information to [sic] the full range of scientific views in any curricula or course of learning." A subsequent provision repeats the phrase "the full range of scientific views," while adding, "including intelligent design."

The phrase "the full range of scientific views" is evidently taken from language offered by Senator Rick Santorum (R-PA) promoting the study of alternatives to evolution during debate on the federal No Child Left Behind Act, President Bush's main legislative accomplishment in the area of education, signed into law in 2001. Although the Santorum language was removed from the NCLB Act before final passage, the language survived in the Conference Report.

A number of provisions in the Maryland bill attempt to immunize it from the charge that it would allow the teaching of religious doctrines and discredited science. For example, the bill forbids instructors to "stress any particular denomination, sectarian, or religious doctrine or belief" while providing "supporting evidence on the theory of intelligent design," and insists that it is not to be construed as protecting the teaching of "a view that lacks published or empirical or observational support."

Representative Burns has introduced a second bill dealing with evolution. HB 1228, the "State Board of Education – Intelligent Design – Regulation" Act, requires the Maryland State Board of Education to prohibit the teaching or discussion of the theory of intelligent design in science classes, but permit it in humanities or philosophy classes; and prohibits the State Board from requiring the teaching or discussion of the theory of intelligent design in any class.

What is remarkable about these bills is that they are not consistent with each other. HB 1531 gives teachers and university professors the freedom to teach "the full range of scientific views in any curricula or course of learning," while HB 1228 requires that ID not be taught in science class, thus contradicting the language about it being allowed to be taught in "any curricula or course of learning."

Hearings on both bills are scheduled for March; perhaps these inconsistencies will be cleared up then.

Moving down the Atlantic seacoast, in South Carolina, the state's Educa-

in States; But Adoption Not Guaranteed

tion Oversight Committee, after months of wrangling, recommended on February 14 (by a vote of 10-2) that state high school biology education standards incorporate "critical analysis" of evolution. The recommended wording for Standard B-5 follows (italics indicate the added wording):

The student will demonstrate an understanding of biological evolution and the diversity of life *by using data from a variety of scientific sources to investigate and critically analyze aspects of evolutionary theory.*

However, as was noted by State School Superintendent Inez Tenenbaum during the February 14 hearing, most scientists and science educators consider the phrase, "critically analyze" as merely another way to get the teaching of intelligent design into biology classrooms. She recommended that the Committee reject the recommendation. As quoted in the local press, Tenenbaum said, "There's ample room as (the standards are) written to allow students to understand what scientists have to go through" when studying the history of life. "Science is not up for debate."

The State Board of Education opposes inclusion of the new language in the standard, and both the EOC and the Board must approve such changes before they take effect. Tenenbaum has said if the two bodies do not agree on new standards, science teachers will continue to use old standards in place since 2000.

South Carolina Governor Mark Sanford has said he supports changing the evolution curriculum to introduce alternatives to evolution.

In New York, a bill has been introduced requiring schools to provide "instruction on all aspects of the controversy surrounding evolution and the origins of man in their curriculums…including, but not limited to, intelligent design and information effectively challenging the theory of evolution."

It seems unlikely that this bill will go anywhere, however. First, it was introduced by two republicans in an overwhelmingly democratic state, Reps. Daniel Hooker, and David McDonough. Republicans are outnumbered in the New York State Assembly almost 3 to 1. Furthermore, Hooker is currently deployed on military duty, and is thus unable to actively promote the legislation as he is out of the country. Thus, the bill has been languishing in committee for over a year and will likely remain there; an observer tells *ASBMB Today,* "There's no way Hooker's bill will come out of whatever committee it finds itself in for a vote on the floor. At the end of this session it will die in committee."

Finally, in Utah, the House on February 27 voted down a bill challenging the theory of evolution in high school science classes. The bill died after being amended by Republican majority whip Stephen H. Urquhart, who, according to the *New York Times,* "said he thought God did not have an argument with science."

The bill had been seen as an important test case by observers on both sides of the issue because Utah is such a conservative state. But the bill died on a 46-to-28 vote in the Republican-controlled House. The Urquhart amendment stripped out most of the bill's language, leaving only the phrase that the state board of education "shall establish curriculum requirements relating to scientific instruction." Legislative officials said the bill was not likely to be revived before the scheduled adjournment of the Legislature on Wednesday.

As introduced, the bill created another "disclaimer" type requirement, as is currently being litigated in Georgia, that would have forced teachers to tell their students that not all scientists agree about evolution and the origin of species. It did not mention intelligent design or any other alternative to evolution, but was clearly aimed at undermining the central organizing theory of all modern biology.

Joe Conn, a spokesman for Americans United for Separation of Church and State, noted after the bill was defeated that "If the creationists can't win in a state as conservative as Utah, they've got an uphill battle."

All of these bills indicate that although anti-evolutionists are not in a majority in the various states, they still are present in significant enough numbers to require constant vigilance in your state legislatures. If you become aware of such a bill being introduced in your state legislature, please inform ASBMB Public Affairs Officer Peter Farnham at pfarnham@asbmb.org. ASBMB depends on you, our members, to help us in the fight to keep pseudoscience masquerading as real science out of the classroom.

In Fiscally Tight Year; Some Hope Remains

By Jon Retzlaff and Suzanne Price

Since the President's State of the Union address, there is no question that fiscal responsibility is the House Republicans' mantra for FY2007. House Speaker Dennis Hastert (R-IL) commented that the President's budget has helped lay the groundwork for reining in federal spending and reducing the deficit, which is forecasted to reach $423 billion in 2006.

In addition, the conservative Republican Study Group and moderate members belonging to the Republican Main Street Partnership have indicated that they will object to any bill that would overrun budget caps. "We are concerned about the growth of the budget deficit and would like more emphasis in 2006 on fiscal responsibility," said Sarah Chamberlain Resnik, Executive Director of Main Street. "Prioritizing spending so the federal government is both fair and equitable while at the same time efficient and restrained is our overall goal."

On the Senate side, Budget Committee Chairman Judd Gregg (R-NH) has stated that he wants to reduce the deficit, control non-defense discretionary spending, and slow the growth of entitlement spending. "If we fail to address the skyrocketing growth of mandatory programs, the retirement of the Baby Boomers will overwhelm the current system and place an unsustainable financial burden on future generations. I am hopeful that Congress will continue to address the growth of entitlements so that we do not pass a tax burden to our children that robs them of the promise of economic security," said Gregg.

Fortunately, Senate/Labor/HHS Appropriations Chairman Arlen Specter (R-PA) is on record saying that he will not vote for a budget resolution that includes the dollar amounts proposed by the President. In fact, Specter has pointed out that the President's allocation to his committee is $4 billion below last year's level, which rises to $7 billion below last year's level if inflationary increases are accounted for in the agencies FY2007 budgets.

House Appropriations Committee Chair Jerry Lewis (R-CA) recently stated the group's goals this year, and they are clearly focused on reducing spending: "We in the House Appropriations Committee are committed to supporting the President's call for fiscal responsibility. In the past year, we reduced non-security discretionary spending below the prior year's levels for the first time since the Reagan Administration. We reduced spending on member projects by $3 billion, and limited extraneous provisions on three large emergency supplemental spending bills as requested by the President. We stand ready to continue this progress in 2006, and commend the President for his dedication to eliminating the federal deficit and bringing restraint to the federal budget."

Senate/Labor/HHS Appropriations Chairman Arlen Specter has declared that he will not vote for a budget resolution that includes the dollar amounts proposed by Bush.

However, there is a glimmer of hope in an election year. The Republicans are caught between making real headway in limiting the size and role of the federal government and realizing the political fact that votes to cut programs which help the lives of millions of people could make them especially vulnerable to Democratic attacks in the fall. Flat funding for NIH is a chief example of underfunding an agency that improves the health of millions of people.

Jon Retzlaff, FASEB's Director of Legislative Relations, declared, "It is an election year and the public expects their Congressional Representatives to make the right decisions when choosing priorities. FASEB's Federal Funding Report arms the legislators with information about how NIH and its support of biomedical research improves lives and reduces the burden of disease. We plan to aggressively request that Congress make NIH a priority once again."

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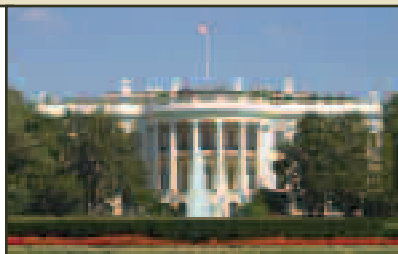

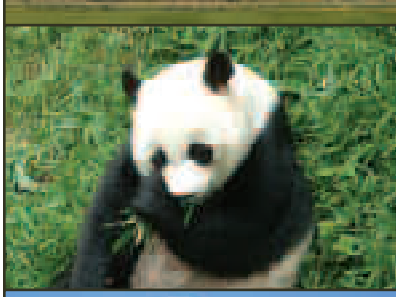

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Polyphosphate Speeds Blood Clotting; Helps Clots Last Longer

A serendipitous comparison prompted by an old scientific image and involving an ancient but understudied molecule may lead to a new treatment strategy for injuries or illnesses in which blood clotting is paramount to survival.

In a paper published in the January 24, 2006, issue of the *Proceedings of the National Academy of Sciences*, researchers from the University of Illinois at Urbana-Champaign and the University of Georgia report that a linear polymer known as polyphosphate speeds blood clotting and helps clots last longer. The paper appeared online January 9, 2006, on the PNAS Web site.

Polyphosphate was shown to have three important roles, said Dr. James H. Morrissey,* a biochemist in the University of Illinois College of Medicine at Urbana-Champaign. The inorganic compound accelerates two parts of the coagulation cascade–the contact-activation pathway and factor V, a protein that forms thrombin–leading to fibrin and clots. Finally, he said, polyphosphate delays the breakdown of clots, which causes renewed bleeding.

"The net effect is accelerating the rate at which blood clots form and then prolonging how long they last," Morrissey said.

The successful research already has landed the U. of I. a three-year, $300,000 grant from the Roy J. Carver Charitable Trust to establish the Center for Hemostasis Research. The grant, which began last November 1, involves three U. of I. labs with Morrissey the leader.

The PNAS report comes a little over a year after former Illinois scientist Roberto Docampo,* now Professor of Cellular Biology at Georgia's Center for Tropical and Emerging Global Diseases, documented in the *Journal of Biological Chemistry* (October 22, 2004) that dense granules in human platelets contain polyphosphate.

Three of the authors on the PNAS paper aare, from left to right: Jim Morrissey, Stephanie Smith, and Nicola Mutch. Stephanie and Nikki are both postdoctoral fellows in the Morrissey lab..

In the early 1990s, Docampo determined that a tiny granule, a subcellular pouch, in yeast, fungi and bacteria–long thought to be for storage–was a fully operational organelle. It contained pyrophosphatase, a pump-like enzyme that allows proton transport. He named it the acidocalcisome for its acidic and calcium components.

Docampo has since found virtually identical pyrophosphate-containing pouches in numerous prokaryotic organisms, challenging the theory on the origin of eukaryotic organelles and suggesting a targeted approach to killing many disease-causing organisms.

"Because I saw electron microscopy pictures of the blood platelets' dense granules taken many years ago that were almost identical to the pictures we took of the acidocalcisomes of different protozoa," Docampo said, "I thought it would be a good idea to test if they were similar in other aspects. When we found that polyphosphate was released from platelets upon stimulation, I immediately thought about a potential role in coagulation."

In collaboration with Morrissey, an expert on blood clotting, Docampo and a team of U. of I. graduate students and postdoctoral fellows tested the effect of adding polyphosphate to platelet-poor plasma in a series of in-vitro experiments to see if it enhanced blood clotting. The results were dramatic, Morrissey said, adding that the presence of polyphosphate may help explain how platelets accelerate the process of blood clotting.

Polyphosphate is in every living organism, but scientists thought it to

be a molecular fossil conserved from prebiotic time. "This is something that has mainly been studied in bacteria," Docampo said. "There is almost no data on polyphosphates in vertebrates, including humans. No role was seen for them, so there was little interest in studying them."

The Center for Hemostasis Research at Illinois will carry the new discovery further. Morrissey and Illinois colleagues Stephen Sligar,* Professor of Biochemistry, and Lawrence B. Schook, Professor of Animal Sciences, will lead a variety of experiments. Among them, they will test the use of polyphosphate as an additive to topical agents as well as new nanotechnologies in an animal model to develop effective treatments for situations involving uncontrollable bleeding.

Such scenarios, Morrissey said, could include treatment for wounds sustained on battlefields or in accidents, or for hemophilia and other diseases with coagulation deficits.

"The big picture is that we've found a new function for an ancient molecule," he said. "Polyphosphate has been around for billions of years. Roberto's discovery that the granules in platelets are like the granules in trypanosomatids was a key breakthrough."

Docampo's recognition of the acidocalcisome in various organisms has enabled scientists to detect muscle-like motors that operate a variety of movements within cells, said Arthur Kornberg,* who won the 1959 Nobel Prize in Medicine or Physiology for discovering mechanisms in the synthesis of ribonucleic acid and deoxyribonucleic acid.

"Roberto has discovered a novel structure of major metabolic importance that regulates the levels of calcium and phosphate within all cells," said Kornberg, an Emeritus Professor of Biochemistry in Stanford University's School of Medicine. "This acidocalcisome has been identified in cells as diverse as bacteria, the protozoa of tropical diseases and the blood-clotting elements of human blood."

Although no longer at Illinois, Docampo said he's thrilled that the research will be continuing through the Carver grant to the U. of I. "It's theoretically possible to use this discovery to find ways to help the body's own blood-clotting mechanisms," he said. "It could be potentially very useful to save lives. Many people with severe injuries die from blood loss not directly resulting from their injuries. This research could open doors to helping in that regard."

In his new lab at Georgia, Docampo will continue to study the purification of polyphosphate present in platelets and on the enzymes involved in its metabolism.

** ASBMB members*

Lerner Institute's Williams Takes Australian Post

Bryan R. G. Williams, formerly Chair of the Department of Cancer Biology at Cleveland's Lerner Research Institute, has accepted an appointment as Director of Australia's Monash Institute of Medical Research (MIMR). The Monash network's six campuses in Australia. plus one in Malaysia and one in South Africa, and .centers in London, UK, and Prato, Italy, focus on teaching and biomedical research..

In accepting his new position, Williams said, "I am honored to accept the appointment as Director of the Monash Institute of Medical Research (MIMR). It is a privilege to work with MIMR scientists and staff, as together we take our Institute to the next level of biomedical research."

Williams, an ASBMB member, has served on the editorial boards of the *Journal of Biological Chemistry* and *Journal of Interferon and Cytokine Research*. In 1990, he received the Milstein Award from the International Society for Interferon Research in recognition for outstanding contributions to advancing interferons for treatment of human disease. He is past President of the International Society for Interferon and Cytokine Research and was elected Honorary Fellow, Royal Society of New Zealand in 1997. His scientific achievements are in the fields of interferons, genetics, and molecular biology of tumor suppression.

His work focuses on the role that potential tumor suppressor genes may play in regulating cell growth, differentiation and apoptosis. He uses molecular genetic approaches to understanding the mechanisms of action of interferons, the potent cell growth regulating cytokines and for characterizing the cellular events involved in Wilms tumorigenesis, and has published over 200 peer-reviewed manuscripts that utilize extensive molecular biology and biochemical techniques.

Two-Drug Treatment May Block Source Of Asthma, Chronic Bronchitis

Current treatments for asthma and chronic bronchitis aren't able to address the ultimate source of the problem — they can only alleviate symptoms. But researchers at Washington University School of Medicine in St. Louis have gone to the root of these disorders and found a two-drug treatment that could potentially restore patients' troubled airways to healthy function.

Their study appeared in the February 1, 2006, issue of the *Journal of Clinical Investigation*.

Michael J. Holtzman,* and colleagues discovered that some cells that line the air passages of the lung transform into another cell type in mice and humans with these disorders. This cellular transformation had never before been recognized and is responsible for overproduction of mucus in the airways.

The researchers found that preventing the harmful transformation of lining cells could be accomplished with two drugs, and they assert that these drugs may possibly be used in combination to normalize the airway lining in asthma and chronic bronchitis sufferers.

"In these disorders, shortness of breath and cough are related to hypersecretion of mucus in the airway," says Holtzman, the Selma and Herman Seldin Professor of Medicine and director of pulmonary and critical care medicine. "Physicians prescribe anti-inflammatory steroids and bronchodilators to ease breathing difficulties, but these medications don't specifically reduce mucus production or secretion. Our research addresses this aspect of the problem."

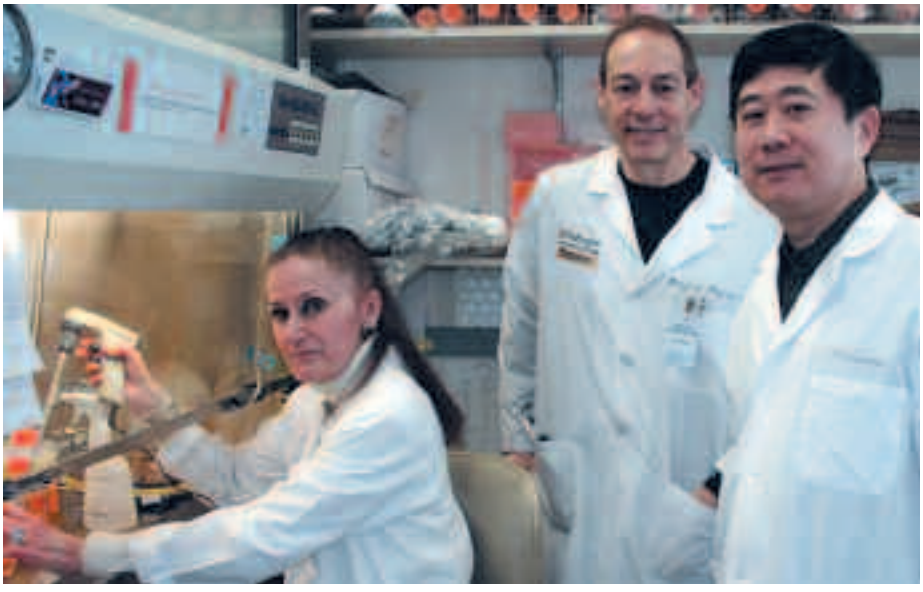
In mice with a chronic lung condition resembling asthma and chronic obstructive pulmonary disease (COPD), the researchers saw that the airway lining maintained an overabundance of mucus-producing cells (called goblet cells for their cup-like shape). Further investigation showed that goblet-cell buildup resulted from two cellular mechanisms. One mechanism allows for the prolonged survival of cells with cilia, tiny hairs that help sweep debris out of the lungs. The other mechanism encourages the ciliated cells to transform into goblet cells.

The researchers were the first to demonstrate this transformation from ciliated to goblet cells in a model of chronic lung disease. They also demonstrated that a similar process may occur in humans with asthma and COPD, a disease classification that includes chronic bronchitis.

"In some people, stimuli such as viral infections seem to cause a chronic excess of goblet cells and lead to persistent breathing disorders," Holtzman says. "We showed that you can block the excess of ciliated and goblet cells using a combination of two types of inhibitors."

The first of these inhibitors is newly developed and is able to impede the activity of epidermal growth factor receptor (EGFR). EGFR was persistently overactive in the ciliated airway cells in mice with the asthma-like condition. This chronic activity protected the ciliated cells from normally programmed cell death and allowed

Holtzman Lab members include, from left, researchers Yael Alevy, Steven Brody, and Yong Zhang.




Dr. Michael Holtzman

the cells to accumulate to higher than normal levels. By blocking EGFR, the inhibitor prevented the buildup of ciliated cells.

The second inhibitor the researchers tested interferes with signaling pathways activated by an immune-system protein known as interleukin-13 (IL-13). They found that IL-13 elicited the crucial change from ciliated to goblet cells in mouse airways and human airway cells in culture. Interfering with IL-13 prevented this transformation from one cell type to the other—a process known as transdifferentiation.

"Finding this sequence of events—the increase in the level of ciliated cells and then the transdifferentiation of these cells to goblet cells—opens up new treatment options that may be more effective than those tried in the past," Holtzman says. "We've shown that if you combine the EGFR and IL-13 inhibitors in a rational way, you can restore the normal architecture of the airway lining. But you have to use the combination to fully correct the abnormalities."

Holtzman believes the study's findings could readily translate into clinical treatments for asthma, COPD and other chronic airway diseases because EGFR antagonists and IL-13 inhibitors are now undergoing separate testing in the treatment of chronic airway diseases by several drug companies. The present study results should allow for better design and assessment of these inhibitors when used either alone or in combination.

** ASBMB member.*

Cancer Trigger Arrested by Molecular Handcuffs

A molecule that promotes cell growth, and is frequently increased in different types of tumours, can possibly be restrained by a molecular version of handcuffs, raising the prospect of a new way of treating the disease according to research published February 15, 2005.*

Cancer Research UK-funded scientists were able to lock up a protein called IGF2,** which helps control growth in all normal cells but when overproduced makes cells grow too large and too fast. In humans, increased levels of IGF2 are associated with a higher relative risk of bowel cancer. The scientists, based at Bristol University, took mice with a genetic predisposition to bowel polyps, which can lead on to cancer, and used a molecule that binds strongly to IGF2 to capture it and rescue the mouse cells from its effects.

This research demonstrates that the principle of using this method to 'trap' cancer-driving molecules works. The next step will be to develop clinical drugs that take advantage of similarly natural and non-toxic traps. If successful, such drugs could make a major difference to the lives of many people with cancer.

Professor Bass Hassan, senior author of the report, said: "We knew that having too much IGF2 in cells promotes the development of tumours, and wanted to find out if we could just stop the molecule from working rather than destroying it.

"We took part of another protein that binds exclusively to IGF2 and found it blocked IGF2's action, leaving other molecules free to go about their business. We are already in the process of modifying the trap to make it even better for use as a therapeutic drug. If all goes well we will be able to start early clinical trials in the next two or three years."

Professor John Toy, medical director of Cancer Research UK, said: "We are constantly searching for ways to halt cancer-promoting agents. When they are in the body, this has to be done without affecting important molecular processes that keep us healthy.

"Prof Hassan's team has shown a viable and potent method of blocking IGF2's effects in mice. But, of course, it is too early to predict whether it will work as a treatment for cancer patients. However, every successful drug has had to start at the stage of showing it works in principle. Many years of further research are now needed to reveal the true potential of this approach."

**Harper et al. (2006) Cancer Research 66 (4)*
***IGF2 – Insulin-like growth factor 2*

Biologists Cite Way to Multiply Blood Stem Cells; Research May Aid Bone Marrow Transplants

Biologists at the Whitehead Institute for Biomedical Research in Cambridge recently announced a way to dramatically expand populations of blood stem cells, a discovery that could improve bone marrow transplants and make them available to more patients.

Bone marrow transplants save the lives of thousands of Americans every year, mainly cancer patients, but many others are denied treatment because the cells that give the transplants their regenerative power–blood stem cells–are quite rare, and doctors have no way of substantially increasing their number before giving a transplant to a patient.

The new technique, discovered in mouse experiments by biologists at the Whitehead Institute, uses a cocktail of growth factors to multiply the stem cells up to thirtyfold. If the discovery can be adapted to humans, scientists said, it would transform the field, saving patients who can't be helped today, in part because of a shortage of bone marrow donors.

''This is a very significant step forward," said Dr. Guy Sauvageau, who was not involved in the Whitehead work and is scientific director of the Institute for Research in Immunology and Cancer in Montreal.

The discovery is also a boon for the field of adult stem-cell research, which has labored in the shadow of its controversial cousin, embryonic stem-cell research. Adult stem cells, such as those that form the blood, do not have the ability to become any cell in the body–the hallmark of embryonic stem cells, which are totipotent. Yet adult stem cells, unlike embryonic ones, are already used to treat patients.

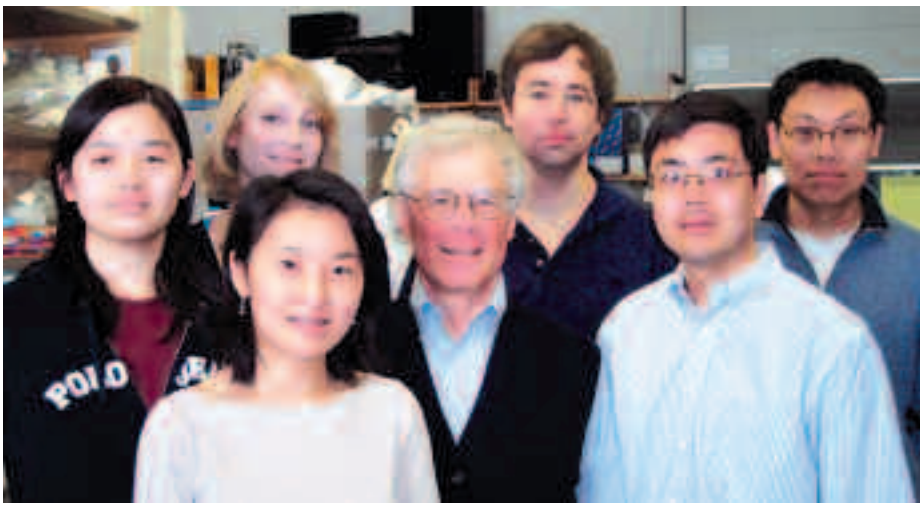
The new research, published in the February 2006 *Nature Medicine*, could expand the relatively limited medical uses for adult stem cells. To find a way to multiply the blood stem cells, the researchers began with nature, according to Cheng Cheng Zhang, a postdoctoral fellow at the Whitehead and first author of the paper. When a mouse is developing in the womb, there is a dramatic expansion in the number of blood stem cells near the liver. The same thing happens in humans.

Zhang's team, working under the direction of Whitehead scientist Harvey F. Lodish,* suspected that there are cells in the liver that help the blood stem cells multiply. Zhang tried growing blood stem cells next to different types of liver cells, until he found cells that prompted the blood stem cells to multiply, according to the paper, which was published online.

Stem cells have become the focus of intense research because of their regenerative power. Stem cells can make copies of themselves, and also become more specialized cells, meaning that they can replace damaged tissues. Bone marrow transplants give a patient new blood stem cells, which can then replace red, white, and other blood cells destroyed by chemotherapy or radiation therapy. The transplants are used to treat leukemia, or blood cancer, as well as lymphoma and other blood disorders.

One of the most immediate applications of multiplying blood stem cells would be to make the blood taken from umbilical cords at birth more widely usable as an alternative source of stem cells for patients awaiting bone marrow transplants, said Dr. Eva Guinan, Associate Director for Clinical and Translational Research at the Dana-Farber Cancer Institute. Cord blood contains blood stem cells, but not in sufficient numbers to help many adults. Thousands of Americans die every year waiting for a bone marrow transplant.

The technology could also have a wide range of other applications, improving the safety of current procedures and making new ones possible, said Guinan, who is also a bone marrow transplant doctor at Children's Hospital Boston.



From left are Lodish Lab members Kathleen Xie, Megan Kaba, Wei Tong, Harvey Lodish, Christopher Hug, Chengcheng Zhang, and Guangtao Ge.

For example, it could make it easier to perform gene therapy, in which doctors correct genetic problems in hematopoietic cells and put the repaired cells in a patient. This could be done, for example, in patients who have severe, inherited diseases of the immune system.

The discovery is also important, scientists said, because it provides new clues into the basic biology of the stem cells. Although these transplants have been used for decades, and blood stem cells are the most intensively studied stem cell, biologists have not been able to accomplish one of the most basic tasks: keeping them alive and healthy outside the body for long periods. This has made them more difficult to study, preventing the expansion of their medical applications, scientists said. The new finding, which coaxed the cells to multiply in laboratory dishes over the course of a week or more, suggests that the field may be approaching a solution to this problem.

To find out what makes these cells special, he compared them with other cells in the liver. He found that these cells were churning out proteins that the other cells were not. He then did another round of experiments, which showed that these proteins, called growth factors, made the blood stem cells multiply.

The most successful cocktail of proteins caused a thirty-fold increase in the number of stem cells, substantially more than similar attempts by other researchers in the past. Some scientists have achieved higher levels by genetically engineering the blood stem cells, but this technique poses a threat of cancer, so would not likely be used by doctors.

Similar growth factors are found in human livers, and the Whitehead team is organizing a study to see whether they can be used to make human blood stem cells multiply in the lab. The work is far from any commercial application because these experiments are difficult and time-consuming. (The team declared no financial interests in the research, according to the paper.) But if the experiments are successful, the next step would be to make sure that all of the growth factors could be used in human cells, without posing any kind of threat. Zhang said he has started new experiments to find more growth factors, with the hope that he can boost the numbers of stem cells even more.

"The more the better," he said.

** ASBMB member.*

George Mason University Scientists Discover New Archive of Potential Disease Markers in Blood

A new study by Lance Liotta* and Emanuel Petricoin III, Co-Directors of George Mason University's Center for Applied Proteomics and Molecular Medicine, has identified an archive of protein fragments in human blood that may be markers for early disease detection, prognosis and treatment. The study was performed

Dr. Emanuel Petrocoin III.

in collaboration with scientists at the National Cancer Institute and New York University.

While previous studies by these and other scientists have predicted the existence of these fragments, this is the first conclusive evidence that the information they contain can be identified, measured and analyzed in the context of specific diseases.

Their findings, which resulted from an ovarian cancer study set of 110 patients, were published in the October 2005 issue of *Clinical Chemistry*. Confirmatory research trials are under way, and validation of these results through large-scale clinical trials begins soon.

"Albumin and other large proteins are abundant in blood serum and plasma," says Petricoin. "Our concept is that these high-abundance proteins act as molecular magnets that mop up fragments of other proteins. This albumin-bound material contains a treasure-trove of information that no one ever knew existed in the blood." "This archive has been hidden from scientific analysis until now because the fragments were stuck to proteins that were routinely discarded as unimportant," he added. "Although we have suspected the existence of these fragments in the past, this is the first study in which we have actually identified and named the molecules," Liotta says. "This gives us an untapped archive of proteins from diverse tissue and cellular origins that may offer vital disease-related information."

One of the proteins identified in the study is a specific fragment of BRCA2, a gene associated with an inherited risk for ovarian and breast cancer. Liotta and Petricoin plan to investigate the fragment to determine if it may be useful for risk assessment, as well as early detection of ovarian cancer.

Scientists at Boston-based PerkinElmer Life and Analytical Sciences utilized Liotta's and Petricoin's molecular mop concept to explore a new approach for studying blood-borne markers for Alzheimer's disease. Their findings also were published in the October 2005 issue of *Clinical Chemistry.*

"Liotta's and Petricoin's concept that molecules like albumin can harvest previously unknown, important diagnostic information could be a real breakthrough and offers an exciting new opportunity for the diagnostic market," said Mary Lopez, PerkinElmer's strategic collaborations leader, molecular medicine. "We agree that the carrier protein binding archive represents a tremendous source of fresh diagnostic lnformation."

** ASBMB Member*

Dr. Lance Liotta.(at right) and research colleague Virginia Espina.

ASBMB Supports American Competitiveness Initiative

By Peter Farnham, CAE, ASBMB Public Affairs Officer

ASBMB added its name to a 35-member list of organizations supporting the American Competitiveness Initiative (ACI), announced by President Bush during his State of the Union address in early February. A letter supporting the ACI notes that "we support both the President's American Competitiveness Initiative and the new Congressional focus on ensuring future U.S. competitiveness." The letter was sent to the top congressional leadership in both parties in late February. The organizations supporting the letter include professional scientific societies, industrial associations, teacher groups and private companies.

The letter points out that the ACI "encompasses a ten-year agenda to address the challenges of math and science education and to expand funding at the National Science Foundation, the Department of Energy Office of Science, and the National Institute of Standards and Technology core programs. The President highlighted that 'preparing our nation to compete in the world is a goal that all of us can share." We agree, and we urge you—our nation's political leaders—to support the initiative and work together to legislate a comprehensive innovation policy that will assure our nation's future success."

Innovation and competitiveness have become subjects of keen congressional interest in the months since the National Research Council's report, *"Rising Above the Gathering Storm"* was released. The ACI was directly aimed at addressing shortcomings discussed in that report, and House Republicans and Democrats have competitiveness initiatives either under development or already introduced.

In remarks made on March 1, House Science Committee chairman Sherwood Boehlert (R-NY) said, "there truly is no more important task before the Congress than ensuring the long-term competitiveness of the United States. We have to act now or we will pay later. We will not be able to maintain our levels of prosperity or employment over the long term if we do not have the best educated, most innovative population on the planet. The competition is catching up. It's no time to rest on our laurels."

Boehlert also said that the Science Committee—largely responsible for legislation on this subject in the House—will be holding hearings this spring to develop "a targeted, affordable set of real solutions, not a laundry list of buzzwords" (Boehlert is the 2006 recipient of the ASBMB's Howard K. Schachman Public Service Award).

Ever a Biochemist!

By Theodore L. Sourkes, O.C., Ph.D., F .R.S.C. Professor emeritus, Departments of Psychiatry, Biochemistry, and Pharmacology and Therapeutics, McGill University, Montreal, Canada

As part of our Centennial Celebration, we asked members to contribute reminiscences of their early thoughts about becoming a scientist, their experience as postdocs, their first paper published, their first lecture at an ASBMB Meeting, the friendships and connections they formed with other ASBMB members, their impressions of the first ASBMB meeting they attended, and anything else they thought pertinent. Here is another contribution. We believe you will find it interesting, and we look forward to receiving and publishing more reminiscences. Please send to them to editor@asbmb.org.

I grew up in Montreal and Quebec, where I had good schooling, but not until my final years of high school did I have any contact with science. It was then that excellent teachers introduced me to chemistry and physics. This experience was so exciting that it decided me to register in the science faculty at McGill University in 1935. The combination of chemistry and biology offered by biochemistry appealed to me, and in my second year I opted for that subject.

Upon graduation I took ajob in what is now Canada's Health Protection Branch in Ottawa. The work dealt with bioassay of sex hormones, so that I had an education in biostatistics and the design of experiments, all of which stood me in good stead in succeeding years. I followed this with a year at Queen's University in Kingston, Ontario, studying pharmacology. We were now well into the Second World War and, ineligible for the army, I proceeded to take jobs in essential industry.

In August 1945 I returned to McGill to take the M.Sc. course in animal nutrition and chemistry, working under Earle Crampton, Canada's leading nutritionist at the time. At the end of the year he recommended me for Ph.D. studies at Cornell, and in the fall of 1946 I entered the Department of Biochemistry there. Because I now wished to focus on enzymology, I chose Professor James Batcheller Sumner as my research director. Shortly after arriving in Ithaca I learned that Sumner had just won the Nobel Prize in Chemistry.

My years at Cornell were an exciting period in my life. I had left what was at that time a small university in Canada's major metropolitan center, and had come to a very large university in a small American town. I was impressed in my new surroundings by the diversity of the university population, the availability of cultural pursuits, and the beauty of the Cornell campus. What an environment in which to study hard and carry on research!

Armed with a Ph.D. I took a teaching post at Georgetown Medical School in Washington, D.C. for two years. I had developed an interest in the biochemical mode of action of drugs, so that when an opening became available at the Merck Institute for Therapeutic Research in Rahway, New Jersey, for an enzyme chemist with knowledge of pharmacology, I applied, and was successful. I was directed to the department headed by Wayne Umbreit, an outstanding bacterial physiologist-biochemist. One of the problems I was given was the search for potential antihypertensive compounds. At that time the antimetabolite hypothesis was especially prominent in the drug field, and accordingly the Merck chemists had synthesised a series of analogues of dihydroxyphenylalanine (DOPA), one of which, it was

Theodore L. Sourkes, in the Nutrition Laboratory of Macdonald College McGIll University, 1946. Photograph by E. W. Crampton.

hoped, might inhibit DOPA decarboxylase, and reduce the production of norepinephrine. Out of this work came the finding that alpha-methyl-DOPA (Aldomet) is clinically effective in hypertension, and for many years it was the treatment of choice for that disorder.

In 1953 I returned to McGill University, now as a member of the research-oriented Department of Psychiatry. My program gradually expanded to embrace many topics in neurochemistry and biological psychiatry, and included the writing of a book, "Biochemistry of Mental Disease." Collaborations with experts in other fields led to the detection of dopamine dysfunction and the ameliorative action of L-DOPA in Parkinson's disease. This was followed by our discovery of the dopaminergic nigrostriatal tract in the brain, whose function gradually fails in that disorder. These fundamental findings led to the widespread reorientation of research on Parkinson's disease, and to its successful treatment.

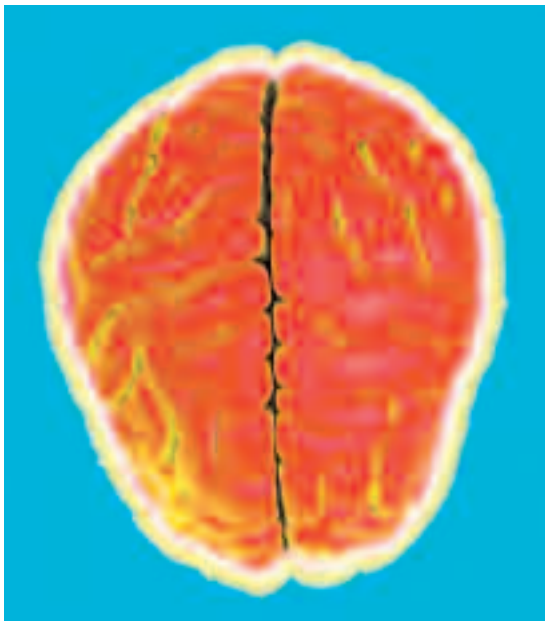
My research on biochemical activities of the nervous system, registered in numerous publications, continued until 1991 when I retired. As professor emeritus, I continue investigating and publishing, but now on neurochemical history, a subject that I find eminently satisfying.

Mad Cow Protein Aids

Few conditions are more detrimental to human brains than the one popularly referred to as mad cow disease. But now there's reason to suspect that the protein which, when malformed, causes bovine spongiform encephalopathy in cows and Creutzfeldt-Jakob disease in people, might also be necessary for healthy brain function. Researchers from Whitehead Institute for Biomedical Research and Harvard Medical School/Massachusetts General Hospital have discovered that the normal form of this detrimental protein may actually help the brain create neurons, those electricity-conducting cells that make cognition possible.

"It's been difficult to understand why this prion protein, which when malformed subjects us to this horrible disease, is so abundant in our brains in the first place," says Whitehead Member Susan Lindquist,* who is also a Professor of Biology at MIT. Along with Jeffrey Macklis of Harvard Medical School and Massachusetts General Hospital, she is co-senior author on this *Proceedings of the National Academy of Sciences* paper, published the week of February 13, 2005. "We've known for years what happens when this protein goes wrong. Now we're starting to see what its normal form does right."

For over 10 years, researchers have known that a protein called PrP causes mad cow disease and its human equivalent, Creutzfeld-Jakob disease, when it forms incorrectly. PrP is a prion, a class of proteins that has the unusual ability to recruit other proteins to change their shape. (PrP is shorthand for "prion protein".) This is significant, because a protein's form determines its function. When a prion changes shape, or "misfolds," it creates a cascade where neighboring proteins all assume that particular conformation. In some organisms, such as yeast cells, this process can be harmless or even beneficial. But in mammals, it can lead to the fatal brain lesions that characterize diseases such as Creutzfeld-Jakob.



Curiously, however, PrP can be found throughout healthy human bodies, particularly in the brain. In fact, it's found in many mammalian species, and only on the rarest occasions does it misfold and cause disease. Clearly, scientists have reasoned, such a widely conserved protein also must play a beneficial role.

In 1993, scientists created a line of mice in which the gene that codes for PrP was knocked out, preventing the mice from expressing the prion in any tissues. Surprisingly, the mice showed no sign of any ill effect. The only difference between these mice and the control mice was that the knock-out animals were incapable of contracting prion-related neurodegenerative disease when infected. Researchers knew then that PrP was necessary for mad-cow type diseases; any other kind of normal function remained unknown.

Recently, researchers from the labs of Lindquist and Whitehead Member Harvey Lodish* discovered that PrP helps preserve stem cells in the blood. Because of this, Lindquist teamed up with Macklis to see if there might also be a similar connection between PrP and cells in the brain, where the prion protein is far more abundant.

Andrew Steele, a graduate student from the Lindquist lab, teamed up with Jason Emsley and Hande Ozdinler, postdoctoral researchers in the Macklis lab, to investigate the effects PrP might have on neurogenesis. (Neurogenesis is the process by which the brain creates new neurons in the developing embryonic brain and, to a limited extent, even in the adult brain.) To do this they studied embryonic brain tissue from three kinds of mice: those in which the PrP gene was permanently disabled, or knocked out; those in which the gene was over-expressed, producing an unusually large amount of PrP; and normal control mice.

Steele and Emsley isolated neural precursor cells—early stage cells that

Creation of Brain Cells

give rise to mature neurons and so-called glial support cells. (These precursor cells are often referred to as neural stem cells, though they lack certain properties that are characteristic of broader stem cells.) After placing these embryonic precursor cells under culture conditions that enabled them to grow and differentiate, they noticed striking differences. Cells from the knock-out mouse remained in the precursor stage for a long time, compared to the control mice. But cells in which PrP was over-expressed began forming mature neurons almost immediately.

"The more PrP you have, the faster you become a neuron. The less you have, the longer you'll stay in a precursor state," says Steele.

In addition, the researchers discovered that in adult mouse brains, PrP is only expressed in neurons, but not in the glial cells, cells that form the brain's connective tissue. They also found that while the amount of PrP does affect the speed with which neurons were produced in the adult brain, ultimately the different mice ended up with the same number of neurons. In order to further investigate these findings, the researchers are currently placing these different groups of mice in stimulation-rich environments that will require the quick production of new neurons. The idea is to observe the mice and see if there are any significant differences in how they perform and behave.

"We now see that the normal form of this prion protein is one of many key players in the fascinating and important process of neurogenesis," says Macklis, also a member of the Harvard Stem Cell Institute.

**ASBMB Members*

by John D. Thompson, Editor

Take Your Pills, All Your Pills

"Here comes the doctor, here comes the nurse, here comes the lady with the alligator purse." That ancient bit of doggerel chanted by children, who viewed the nurse as a lady with an alligator purse chock full of bitter-tasting medicine, has long been passé. Now, for an increasing number of grown-ups, the nurse may well be a voice on the telephone reminding them patients to do what's best for themselves and take their medicine, for the benefit of their health—and also for the sake of a big pharmaceutical company's financial health.

An article in the March 13th New York Times, told of a man whose weekly self-injections of a drug to treat hepatitis C left him so feverish and fatigued, that he often thought of quitting. He didn't though, thanks to a nurse who urged him by phone to stay the course and take his medicine. That nurse, however did not work for the patient's doctor. Instead, she was paid by the drug's maker, Roche, and its distributor, McKesson. Each month that the hepatitis C patient took his medicine as prescribed meant $3,000 in sales for those companies.

Stimulating sales this way is the focus of other industry initiatives, including television advertisements like one by AstraZeneca in which a doctor asks a series of patients if they are taking their Toprol-XL hypertension pills daily. "You can't forget," the doctor gently scolds. "High blood pressure can make your heart work harder than it should, every day."

Lending credence to such efforts are studies showing that failure to take medicines as prescribed can cause patients to develop more serious and costly complications later. Still, these efforts draw some criticism. The *Times* article quoted one critic of pharmaceutical marketing, Dr. Jerry Avorn, a professor at Harvard Medical School, as saying, "They're about brand loyalty and not about public health."

He acknowledged however that patients' failure to take their medicine is a big problem for both industry and the public health. "I'm often surprised to hear drug companies worry about increasing their market share from 7% to 9% for a particular disease, when the 500-pound gorilla issue is that half the people who were prescribed those drugs aren't taking anything. A ton of money is wasted on paying for drugs which people use so irregularly that they get no clinical benefit."

Top Aussie Scientist Favors Genetically Modified Food

Australia's new chief scientist is an award-winning molecular plant science expert who preaches the benefits of genetically modified foods. Commonwealth Scientific and Industrial Research Organization (CSIRO) Scientist Jim Peacock, 68, will cap a nine-month search by taking on the role of the nation's top adviser on science. His predecessor, Robin Batterham, resigned in May 2005 after a storm of controversy over his part-time role, and claims of a conflict of interest with his private-sector employment as chief technologist at mining giant Rio Tinto. Peacock is seen as nearly certain to take on the job full-time after having been an ardent critic of Batterham's part-time role.

Described as one of Australia's "living treasures," Peacock led one of CSIRO's most successful sections, the plant industry division, for 25 years. He has scotched arguments that GM crops could become eco-vandals by rejecting claims genes could "jump the fence" and infect neighboring crops with GM-modified genes. One of his major interests is the secrets behind the genes that control when a plant flowers, the key to developing GM crops. Peacock warned last year that state government bans on the planting of GM canola crops were costing the economy hundreds of millions of dollars worth of exports.

"We can change our foods so our most common staples will help guard against the onset of these diseases and will make a significant contribution to reducing the enormous expenditure on therapeutic medicine," he recently told a meeting of the National Press Club. "Diabetes is the epidemic of the 21st century. If the important starch component of these cereals had a low glycemic index, we would be a long way to reducing the incidence and severity of diabetes."

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by John D. Thompson, Editor

Monsanto Settles Lawsuit With University of California

Monsanto Co. has agreed to pay the University of California more than $100 million to settle the school's claim, in a suit filed in 2004, that the biotechnology company infringed on its patent related to a hormone that makes cows produce more milk. The university's Board of Regents and Monsanto made a joint announcement in March as the bovine growth hormone case was scheduled to go to trial.

St. Louis-based Monsanto agreed to pay the school $100 million in upfront royalties plus pay 15 cents a dose, or at least $5 million annually, to license the patented technology, commonly called BST, in the future. The university's patent rights expire in 2023.

At issue was the genetically engineered bovine somatotropin hormone, sold under the brand name Posilac. Monsanto says injections of the hormone help dairy cows produce 10% to 15% more milk. The university alleges in its lawsuit that three researchers at UC-San Francisco first isolated the DNA that is used to make the hormone. The lawsuit said Monsanto knew about the research as early as 1985, but sold the product anyway.

While researchers might have developed the technology decades ago, the school did not win a patent until 2004, said UC spokesman Trey Davis. The school filed its lawsuit that year. Monsanto spokesman Andrew Burchett said the company was the first to produce the product commercially and it patented the production process.

Monsanto said the agreement will give it the exclusive commercial license to use the university's patented hormone. The university will have the right to use the hormone in noncommercial research, and the U.S. government will retain some rights because federal funding was used to develop the technology.

Next Alliance for GlycoFi: Merck

Just a few weeks after announcing a major collaboration and equity investment from Eli Lilly, glycan specialist GlycoFi trumpeted another big catch?a multi-year research collaboration and strategic alliance with pharmaceutical giant Merck & Co.

Exact financial terms of the deal were not released, however, as with Lilly, Merck is expected to make an equity investment in GlycoFi, provide an upfront payment, and fund continuing research efforts taking place under the agreement. GlycoFi could also receive milestone payments and royalties on the sale of any commercial products that result from their work.

"This alliance along with our earlier one with Lilly will keep us funded for a number of years," according to James Posada, Senior VP of Business and Market Development at GlycoFi.

J. Craig Venter's Next Project

J. Craig Venter wants to cure our addiction to oil. To do so, he proposes creating a designer microbe—the heart of a biological engine, and then adding genes culled from the sea to turn crops such as switch grass and cornstalks into ethanol. While he's doing that, he wants to modify or devise microorganisms to produce a steady stream of hydrogen. Either of his ideas could prompt a major shift in the economics of the energy industry.

"We are on a crusade as much as it is an economic goal," Venter told *The Washington Post*. "This is one of those crusades that only works if it becomes really profitable."

"Craig confronts," Alfonso Romo Garza, a Mexican billionaire, controller of a decent chunk of the world's commercial vegetable seeds and backer of Venter's latest undertaking told *The Post*. "Of course, he's antagonistic. He's controversial. But I love controversial people because those are the people who change the world."

Back from a three-year, yacht trip around the world, Venter now sports an extensive collection of genetic material scooped from the sea, and that is to be the raw material for his alternative fuel project. With $15 million from Garza, he has launched a new company, Synthetic Genomics Inc., in Rockville, Maryland..

A number of other companies claim to be ahead of Venter in the quest to use biotechnology to make energy, and they contend that they have more near-term and less complicated methods. Vinod Khosla, co-founder of Sun Microsystems Inc. and a prominent Silicon Valley venture capitalist who has turned his investment focus to new energy, said of Venter's new company, "There are too many technical risks cascading together."

Career Opportunities

Univ of Alaska

Institute of Arctic Biology

University of Alaska Fairbanks

Post Doctoral Fellow

The Institute of Arctic Biology at the University of Alaska Fairbanks is seeking a postdoctoral fellow to work on a team oriented research project to study molecular mechanisms of neuroprotection in hibernation. The successful applicant should have a Ph.D. in neuroscience, cell biology or a related field and have experience with acute brain slices or cell culture techniques, western blotting, immunohistochemistry and/or calcium imaging. Experience in signal transduction research is an asset.

The funding for this position is currently available for 1 – 2 years, depending on the exact position and available funding. If this appointment extends beyond one year, in subsequent years, for purposes of collective bargaining, this position will be represented by a union. At that time, the successful candidate will be obligated to pay to the union an agency fee as a condition of employment.

To apply, go to https://www.uakjobs.com/applicants/jsp/shared/frameset/Frameset.jsp?time=1138678945192
A complete job description can be downloaded from our web site at http://www.uakjobs.com, or touch the quicklink www.uakjobs.com/applicants/Central?quickFind=54152. If you need any assistance please contact UAF Human Resources at 907-474-7700.

Massachussetts General Hospital

Res Assoc / Lab Manager wanted. Must have Masters degree in Mol or Cell Biol, Biochem, or related field and 2 yrs. exp in same type of pos or 2 yrs. mol biol lab exp, incl. exp with cultured cells & protein expression in mammalian and/or insect cells, bact transformation, and protein expression and co-precipitation, & also including at least 1 yr. lab. management or senior technologist exper. Experience can be pre- or post-degree. Send resume to Tod Gulick, MD, Asst. Biochemist, MGH Diabetes Research Lab, Building 149, CNY 8, 13th St., Charlestown, >MA 02129.

New York Medical College

Postdoctoral positions available immediately to study the mechanism of bacterial DNA topoisomerase I and analyze/model interactions with novel antibacterial compounds (J. Biol. Chem. 280:38489, 2005). The research will combine HTS, chemical modification and mutagenesis. Demonstrated expertise in fluorescence spectroscopy, enzyme kinetics, protein purification, molecular modeling or bacterial genetics is desirable. Our campus is located 30 minutes north of New York City. Send CV, contact information for three references to: Prof. Y.-C. Tse-Dinh Department of Biochemistry & Molecular Biology New York Medical College Valhalla, NY 10595 Email: yuk-ching_tse-dinh@nymc.edu

Columbia University

Positions are available in the laboratory of Dr. Stephen L. Sturley at Columbia University, New York, at the level of postdoctoral fellow and require a Ph.D. / MD, with experience in molecular biology and preferably but not essentially some knowledge of yeast genetics or lipid metabolism. The successful candidate will work on a project studying an aspect of our studies on lipid homeostasis. In particular we are searching for committed and motivated individuals for our studies on sterol transport and sphingolipid homeostasis and its role in neuro-degeneration. Salaries are of course commensurate with experience. Contact Steve Sturley at (212) 305 6304 or sls37@columbia.edu for further details. In addition, several members of the lab including Dr. Sturley will be at the San Francisco ASBMB meeting in April 2006.

Calendar of Scientific Meetings

APRIL 2006

American Society for Biochemistry and Molecular Biology Centennial Meeting in Conjunction with Experimental Biology 2006

April 1–5 • San Francisco
For information contact: www.asbmb.org/meetings
Email: meetings@asbmb.org
Ph: 301-634-7145; Website: www.asbmb.org/meetings

Recomb 2006—The Tenth Annual International Conference on Research in Computational Molecular Biology

April 2–5 • Venice, Italy
For information contact:Email: info@veneziacongressi.com
Ph: +39 0415238995; Website: http://recomb06.dei.unipd.it/

Bio 2006 Chicago—Annual International Convention of the Biotechnology Industry Organization

April 8–12 • McCormick Place, Chicago, Illinois
Register on or before February 23 to take advantage of early discounted rate. For internet registration and wire payment instructions: www.bio.org
To register by mail: BIO c/o SunTrust Bank, P.O. Box 79532 Baltimore, MD 21279-0532
Note: Faxed forms are no longer accepted.

47th ENC Experimental Nuclear Magnetic Resonance

April 23–28 • Asilomar Conference Ctr., Pacific Grove, CA
Contact: ENC, 2019 Galisteo Street, Building I-1
Santa Fe, New Mexico 87505; Ph: 505-89-4573
Fx: 505-989-1073; Email: enc@enc-conference.org
Web page: http://www.enc-conference.org

MAY 2006

Canadian Proteomics Initiative—The Sixth Annual International Conference

May 10–12 • University of Alberta, Edmonton, Canada
The program developed for CPI 2006 offers something for everyone with an interest in proteomics, bioinformatics, and structural biology. CPI will offer three post-conference workshops on May 13-14: Bioinformatics for Proteomics, Practical Proteomics, and Introduction to Transcriptomics.
Co-Chairs: Joel H. Weiner and David Wishart, University of Alberta Contact: Steven Leard, steven@marketwhys.ca
phone: 780-414-1663; fax: 780-414-1664; Website: cpicanada.org

FEBS Special Meeting on Cellular Signaling -

May 26–June 1 • Dubrovnik, Croatia
www.dubrovnik-conference.org

CSBMCB International Meeting on Membrane Proteins in Health and Disease

May 31–June 4 • Niagara-on-the-Lake, Ontario, Canada
This Canadian Society of Biochemistry, Molecular and Cellular Biology sponsored meeting, held in Canada's wine country close to Niagara Falls, will feature cutting-edge sessions on Structural Biology of Membrane Proteins, Regulating Membrane Permeability, Dynamics of Membrane Proteins, Transporters and Disease, Trafficking Defects in Membrane Proteins, and Assembly and Disassembly of Membrane Proteins. Meeting organizer: Dr. Reinhart Reithmeier
Email: r.reithmeier@utoronto.ca
Website: www.csbmcb.ca/e_index.html

JUNE 2006

20th IUBMB International Congress of Biochemistry and Molecular Biology and 11th FAOBMB Congress in conjunction with 79th Annual Meeting of the Japanese Biochemical Society and 29th Annual Meeting of the Molecular Biology Society of Japan

June 16–23 • Kyoto, Japan
Deadline for On-line Registration: May 18, 2006
Website: www.congre.co.jp/iubmb/registration.html

Bacterial Cell Surfaces
A Gordon Research Conference

June 25–30 • Colby-Sawyer College
New London, New Hampshire
Chairs: Ry Young and Arnold J. Driessen
Vice Chairs: Anne H. Delcour and Jeff Errington

4th Annual Meeting of the International Society for Stem Cell Research

June 29–July 1 • Metro Toronto Convention Centre
Toronto, Ontario, Canada
For information on the ISSCR Annual Meeting, contact ISSCR Headquarters: Ph: 847-509-1944; E-mail: isscr@isscr.org
Conference Administrator: Deb Pederson dpederson@isscr.org
Press Inquiries: Heather Gagnon hgagnon@isscr.org
Conference Director: Liz Freyn lfreyn@isscr.org

JULY 2006

Third Annual World Congress on Industrial Biotechnology and Bioprocessing,

July 11–14 • Toronto, Canada
Sponsored by the Biotechnology Industry Organization (BIO), American Chemical Society (ACS), National Agriculture Biotechnology Council (NABC), Agri-Food Innovation Forum, and BIOTECanada.
Email: worldcongress@bio.org; Ph: 202-962-9200

17th International Symposium on Plant Lipids

July 16–21 • Michigan State University Campus, East Lansing
Organizer: Christoph Benning
For registration information, preliminary program, instructions for submitting abstracts, and for information on financial aid available for young scientists to attend the meeting, go to: www.ispl2006.msu.edu/. Members of underrepresented groups are especially encouraged to apply for financial aid.

Bioscience 2006: Bioscience for the 21st Century

July 23–27 • Glasgow, Scotland
Abstract Submission Deadline: April 13, 2006
Early Registration Deadline: May 22, 2006
For information: www.BioScience2006.org

Biochemical Journal Symposium Literature, Legacy, Life

July 24 • Glasgow, Scotland
Celebrating 100 Years of Biochemistry
For information: www.BioScience2006.org

AUGUST 2006

ISPMB 2006 – 8th International Congress of Plant Molecular Biology

August 20–25 • Adelaide Convention Centre, South Australia
Abstract And Early Registration Deadline: Friday, March 3.
Online registration and abstract submission pages:
www.sallyjayconferences.com.au/ispmb2006/registration.htm
www.sallyjayconferences.com.au/ispmb2006/abstract.htm
Abstracts cannot be accepted without registration and payment. All abstracts must be submitted online, abstracts sent as attachments will not be accepted.
www.sallyjayconferences.com.au/ispmb2006/program.htm

SEPTEMBER 2006

5th European Congress of Biogerontology

September 16-20 • Istanbul, Turkey
Tel: +90 216 347 35 35 Pbx; Fax: +90 216 347 78 50
Email: okarabel@symcon.com.tr; Website: www.symcon.com.tr
Congress President Prof. Serif Akman, Etlik, Ankara , Turkey
Tel: +90 312 304 3306; Fax: +90 312 304 3300
E-mail: sakman@gata.edu.tr

The 33rd Annual Conference of the Federation of Analytical Chemistry and Spectroscopy Societies (FACSS)

September 24–28 • Disney's Contemporary Resort, Lake Buena Vista, FL
Contact: FACSS, PO Box 24379, Santa Fe, NM 87502
Phone: 505-820-1648; Fax: 505-989-1073
Email: facss@facss.org; Web Page: www.facss.org

OCTOBER 2006

International Conference of Immunogenomics and Immunomics

October 8–12 • Budapest, Hungary
A joint meeting of 2nd Basic and Clinical Immunogenomics and 3rd Immunoinformatics (Immunomics) Conferences
Email: diamond@diamond-congress.hu
Website: www.bcii2006.org

4th International Conference on Structural Genomics

October 22 – 26 • Beijing, China
Website: http://www.sino-meetings.com/icsg2006/

NOVEMBER 2006

Transcriptional Regulation by Chromatin and RNA Polymerase I I

November 2–6 • Kiawah Island, South Carolina
Organizer: Ali Shilatifard, Saint Louis, University School of Medicine, Email: shilatia@slu.edu

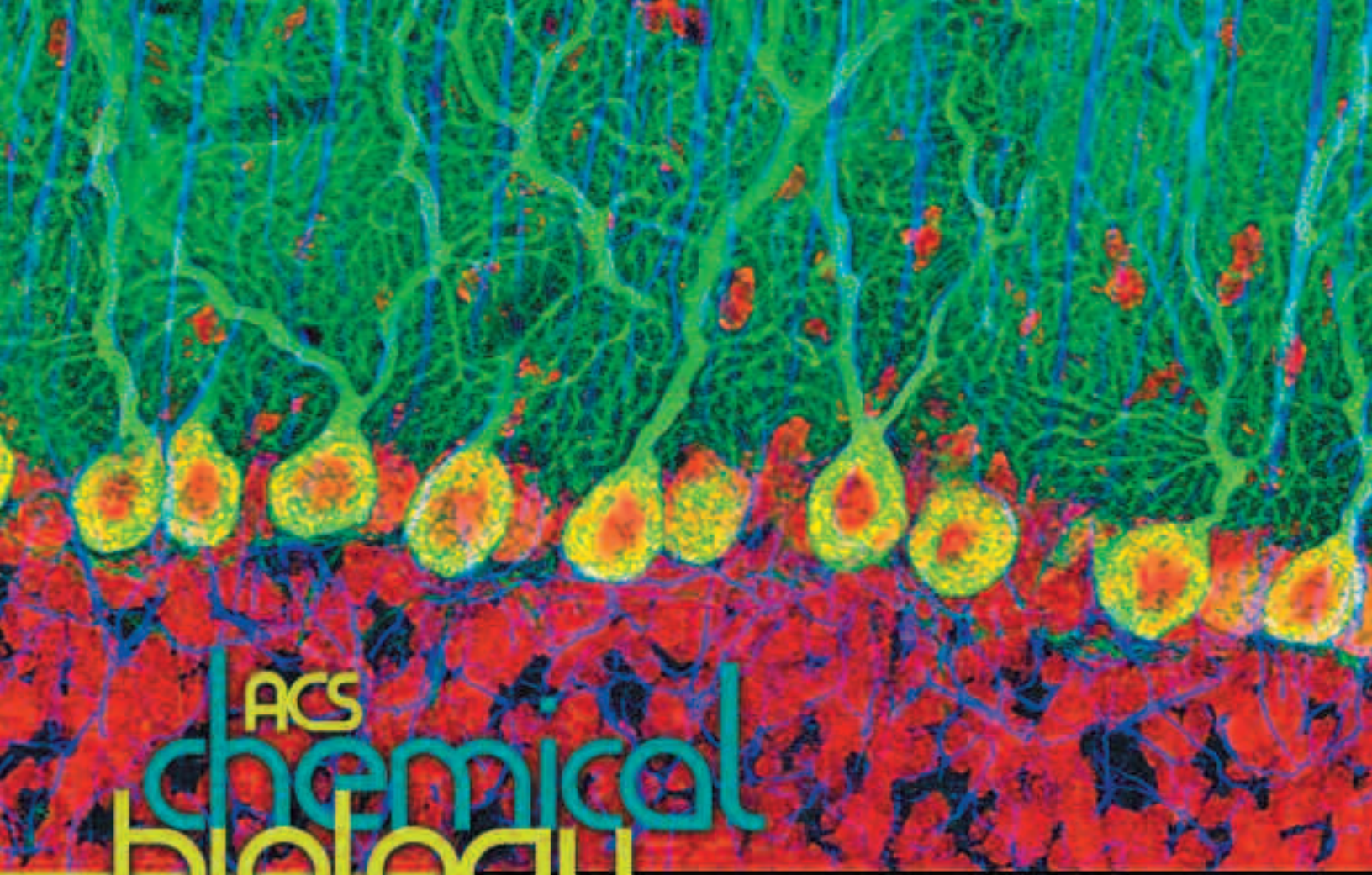
Annual meeting of the Society for Glycobiology

November 15-18 • Los Angeles
Contacts: Linda Baum, President; lbaum@mednet.ucla.edu
Kelley Moremen, Secretary; moremen@uga.edu
Website: www.glycobiology.org

OCTOBER 2007

34th Annual Conference of the Federation of Analytical Chemistry and Spectroscopy Societies (FACSS)

October 12–18 • Memphis Convention Center, Memphis, TN
Contact: FACSS, PO Box 24379, Santa Fe, NM 87502.
Ph: 505-820-1648; Fax: (505) 989-1073
Email: facss@facss.org; Web Page: www.facss.org



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