FEBRUARY 2005

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ASBMB Today

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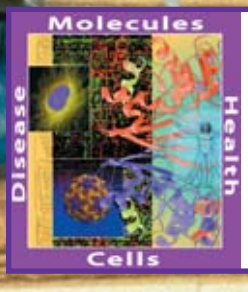
AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

ASBMB Annual Meeting
April 2-6, 2005

See You in San Diego



SAN DIEGO 2005
Call for Late-Breaking Abstracts
see page 14

7th International Symposium on Mass Spectrometry In the Health and Life Sciences:

Molecular and Cellular Proteomics

August 21-25, 2005–Fairmont Hotel, San Francisco

Showcasing current biological discoveries and new techniques in the field of mass spectrometry and proteomics.

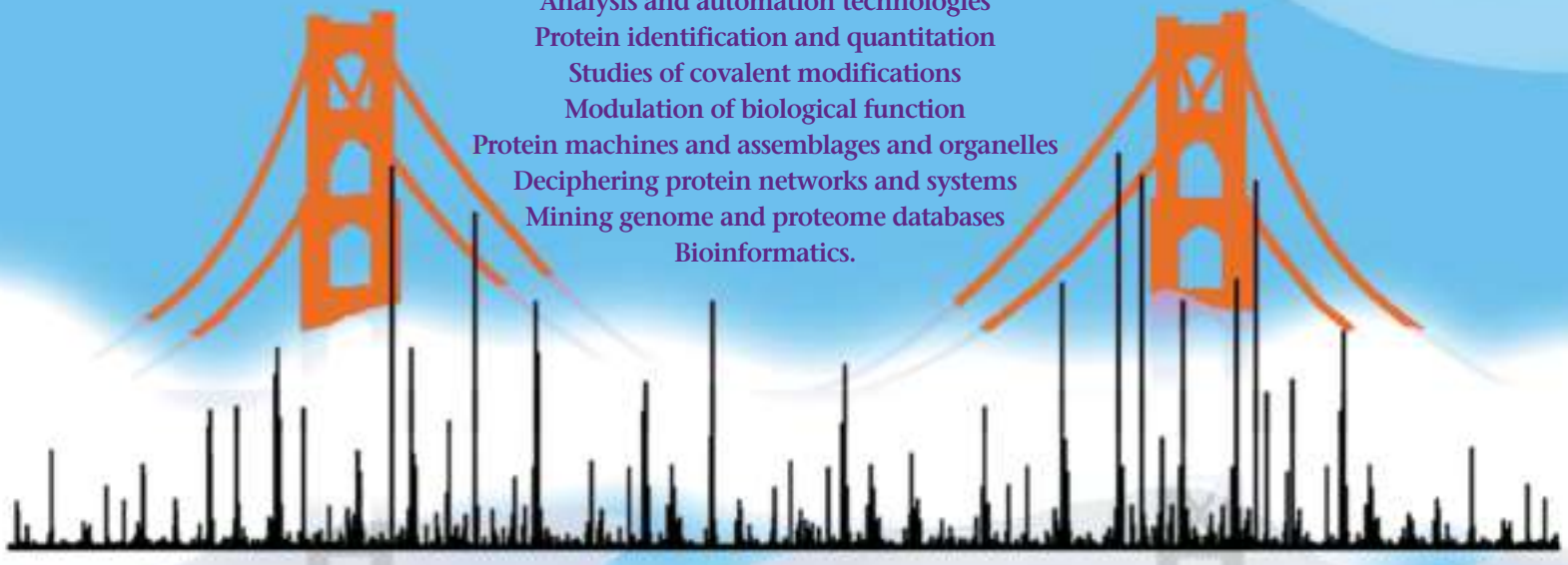
Mass spectrometry technologies now have considerable power to sequence and identify proteins as well as define their sites of posttranslational and xenobiotic covalent modification especially using tandem instruments on proteolytic digests, with ion exchange and capillary chromatographic mixture separations and appropriate bioinformatics tools (database search engines with rigorous match validation).

However, gaining information about function depends on having robust, reproducible separation strategies from cells or tissues, so that complexes are kept together, organelle preps are not contaminated with artifactual components and so on. Affinity methods such as TAP tags and immunoaffinity tags have been very useful here in the last 3-4 years and has led to network walking (iterative TAP tagging-TNF NFkB network for example), but this is just a begining in sorting/identifying and quantitating at the cell communication network level; so more sophisticated strategies are in urgent need of development. Better sample handling is needed to work at lower levels with major losses (attomole sensitivity). Protein quantitation methods must become easier and much more robust; modification stoichiometry is a major challenge.

The program consists of 30 invited plenary and keynote lectures in a single session format as well as posters submitted by participants. The oral sessions will explore developments in sample preparation and mass spectrometric, computer and automation technologies that are revolutionizing strategies for characterization of macromolecules, their molecular transformations, and biologically significant interactions. Discussions will be juxtaposed with presentations from biological perspectives that describe their utility in solving challenging problems in protein biology and proteomics. These themes will focus on the articulation of urgent needs and unsolved problems, as well as potential strategies for dealing with emerging global opportunities in proteomics through genomics, proteomics and bioinformatics.

This symposium will integrate mass spectrometry perspectives with the needs of the biomedical sciences, including:

Sub-cellular separation strategies and sample handling
Analysis and automation technologies
Protein identification and quantitation
Studies of covalent modifications
Modulation of biological function
Protein machines and assemblages and organelles
Deciphering protein networks and systems
Mining genome and proteome databases
Bioinformatics.



For further information please contact the Symposium office:
Phone: (415) 476-4893, Fax: (415) 502-1655, Email: sfms@itsa.ucsf.edu
Website : http://caravaggio.ucsf.edu/symposium/

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ASBMB Today

AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

FEBRUARY 2005,
Volume 3, Issue 11

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ON THE COVER:

See You in San Diego, April 2-6, for the ASBMB Annual Meeting and EB 2005

Photo by Andrew Hudson for the San Diego Convention and Visitors Bureau.

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ASBMB Today
is a monthly publication
of The American Society for
Biochemistry and Molecular Biology

Comments

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Nanotechnology: The Next Medical Revolution?

We published an article, "Nanotechnology: the Next Medical Revolution," in the December 2004 issue of ASBMB Today, and asked readers to let us know what they think the role of biochemists and molecular biologists would be in this "next medical revolution." ASBMB member Robert Gellibolian responded with the letter below. The opinions expressed are those of the author and do not necessarily represent the views of ASBMB.

Dear Editor:

As a scientist and consumer of technology products, I have always had a passion and strong interest in nanotechnology, whether viewed from a MEMS (Micro-Electro Mechanical Systems) point of view or from a biological perspective. As I think more about this issue, I can't help but wonder about how our society has reached a technological inflection point in its evolution. With the turn of the century, countless inventions ranging from the automobile and airplane to more recent advances in computation, internet, fiber optic and cell phones have, in more ways than one, transformed all of our lives. In the midst of all these inventions lies humanity's quest to create yet another 'paradigm shift' by revolutionizing this techno-world with techno-gadgets comprised of smaller and smaller component-parts. This paradigm shift is what constitutes the field of nanotechnology. However, if we stop for a moment and think about it from a universal standpoint, we have already lost this battle to none other than Nature itself, which managed to achieve this very task, eloquently, several billion years ago. As scientists, all we have to do is to look at the fundamental bricks and mortars of any biological system, namely nucleic acids and proteins. Nature has managed to create machines (us) comprised of billions of molecular components (cells), themselves composed of millions of other molecular components (DNA, RNA, and proteins, whether catalytic or structural), all of which work in perfect unison and synchrony (well, most of the time) to make life, as we know it, possible. Millions of years of evolution have gone into creating the highly specific and selective molecular machines needed to create and integrate the intricate pathways for efficient inter- and intra-cellular signaling and communication. AMAZING, to say the least!

The ultimate goal of modern day nanotechnology lies in man's attempt

Continued on page 26

Tell Us What You Think

We appreciate receiving letters that are suitable for publication from ASBMB members regarding issues of importance or commenting on articles appearing in *ASBMB Today*. Letters should be sent to the editor, John Thompson, at the address found at left. Letters must be signed and must contain the writer's address and telephone number. The editor reserves the right to edit all letters.

ASBMB Council meeting, December 11, 2004.

From the Desk of the President:

Collaborative, Interdisciplinary, and Multidisciplinary Research:

Opportunities and Challenges

Calls for more collaborative interdisciplinary research have been heralded by university administrators, industry and funding agencies. The NIH Roadmap sends a clear message that Interdisciplinary research is a priority. There are great opportunities in collaborative, interdisciplinary research, and the case for more of it is compelling. Many of you are familiar with the ancient Indian legend of The Blind Men and the Elephant. Six blind men approach an elephant from different angles and draw very different conclusions as to what this beast looks like – a wall (from touching the side of the elephant), a snake (from touching the truck), a spear (from touching the tusk), etc. It is only by putting all the perspectives and information together that a meaningful picture of the whole emerges. We, as scientists are indeed blind men and women, approaching living systems from different angles, expertise, experience and expectations. It is only when the different approaches and experiences are communicated and integrated that we can put together a valid picture of the 'elephant,' an ultimate goal of our research.

To have high quality interdisciplinary research, however, there is a clear need to have strong disciplinary science. I contend that the best interdisciplinary research teams have individuals with depth in specific disciplines. So, as a biochemist, when I collaborate with a statistician, nephrologist, geneticist, or immunologist, I want to find individuals who have the deepest knowledge in their fields, who have published outstanding work in their fields and who have a much deeper understanding and knowledge base than I have in their fields. This demands that individuals develop depth in their discipline. It also requires that people with a deep understanding in a discipline have the ability to communicate with someone in another discipline.

There are substantial challenges in educating our students for, and in doing, collaborative interdisciplinary research. For example, how do we design graduate programs; how do we evaluate an individual's contribution to the research (especially for hiring, promotion and tenure); how do you evaluate the competency of a collaborator in a different discipline; what happens to a project if a collaborator dies, losses his job or interest in the project; how do you find a collaborator who has the same priorities as you for timely publication and accuracy; how do you establish trust and continuing communication? I am reminded of a story about manufacturing cars in England in the 1980s. There were separate unions for workers that produced various parts of a car; e.g., one for the motor, another of the frame, another for the chaise, etc. However, one union or another was always on strike, so there were never any cars made! Certainly there have to be mechanisms to prevent the total collapse of collaborative research because of a breakdown in one of the parts.

The bottom line is that we need people with strong expertise in disciplines to make up strong interdisciplinary teams. The ideal system would educate individuals in depth, and provide them with the tools to communicate with others and to appreciate a variety of other disciplines. This requires training and development of expertise in specific areas with a broad base of background knowledge in the sciences. Lest we forget, we also need to encourage curiosity, discovery, and individual achievement as well as team accomplishment.

Judith Bond
President, ASBMB

by Peter Farnham, CAE, ASBMB Public Affairs Officer

Stormy Weather, Rough Seas

"Red sky in morning, sailor take warning," old salts sometimes say. The proverb is a pithy way to describe atmospheric conditions that might indicate difficult weather—and thus greater danger—ahead for ships at sea.

The sky may not be red in Washington this January, but scientists—like sailors—should take plenty of warning from the atmospherics accompanying the opening of the 109th Congress. Stormy weather, rough seas, and dangerous reefs likely lie ahead on both the fiscal and policy fronts.

Cuts Expected in Science Agencies

After a very lean year for funding of scientific research in Fiscal 2005, 2006 is unlikely to be any better (and may very well be worse). The President will release his 2006 budget proposal on February 7, and although no official numbers are available as of early January, word about what to expect has leaked. Many science agencies are expected to receive actual cuts in their budgets in the range of about 2%. If this information is accurate, the news for the agencies we track most closely—the National Institutes of Health (NIH) and the National Science Foundation (NSF)—is not good.

The *New York Times* reported on January 10 that the NIH was going to receive a very modest increase of less than 2% for the coming year. However, this is relatively good news. NIH had been expecting a 2% *reduction* (along with most other science agencies), but HHS Secretary Tommy Thompson appealed the proposed funding level and the Office of Management and Budget backed off. Biomedical inflation is projected to be in the range of 3.5%, so this nominal increase will actually reduce NIH purchasing power for the second year in a row unless Congress is inclined to provide more funding.

Unfortunately, it is not clear that Congress will be able to help NIH much this year. The overall fiscal situation is very bad, with large deficits, an ongoing war in Iraq, and a strong congressional desire to curb spending. Regarding this latter consideration, the recent debate over who would be the new chairman of the House Appropriations Committee (a post won by Rep. Jerry Lewis of California on January 5) hinged on which candidate would do the most to help curb federal spending. To win the chairmanship, Lewis had to promise to work very hard to curb spending, and has publicly stated his commitment to adhere to the House leadership's wishes—more so than any of his predecessors, most of who viewed this key committee as an independent kingdom that the chairman would run as he saw fit.

But more than the woeful fiscal environment is at work, at least regarding NIH. Advocates for the agency have met with what one observer characterizes as "NIH fatigue" on Capitol Hill—the feeling that NIH's problems were solved with the doubling completed in Fiscal 2003, that Congress needs to move on to other issues, and that the agency must learn to live with flat or even slightly declining budgets for at least some period in the future while Congress uses meager resources to address other needs.

In response to this new, less welcoming legislative environment, the biomedical research community has scaled back its proposal for increases this year to the smallest since the late 1990s—about 6%—although even this is characterized by one Hill insider as "completely unrealistic." It remains to be seen if this is the case; however, it is clear that NIH advocates have their work cut out for them in the coming months.

NSF—Even, at Best

NIH at least got an increase last year, however small; NSF actually received a cut of about 2% in FY 2005. For this coming fiscal year, knowledgeable officials tell *ASBMB Today* that the administration initially proposed the agency receive a 5% cut; however, NSF appealed. The appeal was "partially successful." NSF staff now expects the agency to be "about even" (although there is still a small cut) when the President's budget is released—"way better than what had been proposed initially," we were told. Still, if Congress cuts the NSF budget this year, it will be the first time in the agency's history that it has been cut two years in a row. Most other science agencies are expected to suffer fates similar to NIH and NSF, with either flat funding or actual decreases.

Continued on next page

Ahead for Science in 2005

Conflicts of Interests Likely to Heat Up as Well

NIH is up for reauthorization this coming year, and hearings will be held this spring before the House Energy & Commerce Committee, chaired by Texas Republican Joe Barton (authorization bills differ from appropriations bills in that they deal with policy and organizational issues rather than allocate money). Barton, an engineer by training, has taken a strong interest in the conflict of interest issues that surfaced at NIH late in 2003 involving financial relationships between some NIH intramural scientists and pharmaceutical and biotech companies. Barton recently announced that he was personally going to assume the chairmanship of the Oversight & Investigations subcommittee in order to ensure having a role in this and other ongoing investigations.

Unfortunately, congressional focus on NIH-related conflicts of interest has now gone beyond the intramural program. In a December 3, 1004 letter to NIH Director Elias Zerhouni, Reps. Tom Davis (R-VA) and Henry Waxman (D-CA) have asked for information related to conflicts of interest involving the extramural program. Davis and Waxman (the chair and ranking minority member of the House Government Operations Committee, respectively) want to know about "NIH policy for screening researchers who receive NIH grants for potential conflicts of interest" involving relationships with drug companies, as well as "NIH policy for screening scientists who review applications for NIH grants." They also ask NIH to describe how NIH ensures "that researchers who receive or review NIH grants follow appropriate procedure to prevent or disclose potential conflicts of interest."

Stem Cells Will Be on the Table as Well

Finally, the issue of use of embryonic stem cells for research will be back with a vengeance this year. The House handily passed a ban on use of embryonic stem cells for research in each of the past two congresses, and probably will this year as well. Meanwhile, Senator Sam Brownback (R-KS) is also likely to reintroduce his bill to ban such research (as he has done the past two congresses) and will have a better chance of securing its passage this year, since there are four new Republican senators, all of whom are conservatives. Brownback is now thought to be able to muster about 50 votes for a ban on embryonic stem cell research—still short of the 60 needed to end a filibuster, but five more than most vote-counters thought he had in the previous Congress.

So, the biomedical community should expect to be sailing into stormy weather in coming months; the squalls cited above are only a few of the dangers in what are expected to be turbulent legislative and policy waters for science this year.

by Peter Farnham, CAE, ASBMB Public Affairs Officer

Senators Harkin, Specter to Share Schachman Public Service Award

The 2005 recipients of ASBMB's Howard K. Schachman Public Service Award are Senators Tom Harkin (D-IA) and Arlen Specter (R-PA). The Society described the joint award as recognition of the two Senators' long-standing and ongoing advocacy for biomedical research, especially that funded by the National Institutes of Health (NIH).

In a letter to the senators, ASBMB President Judith Bond noted that the Senators "have been…outstanding advocate(s) for biomedical research, and the award is well-deserved. Speaking as a researcher at Pennsylvania State University in Hershey, I believe the Public Affairs Advisory Committee made an excellent choice."

Specter chairs the Senate Appropriations Subcommittee on Labor, Health & Human Services, Education, and Related Agencies, the subcommittee responsible for funding the National Institutes of Health. Harkin is the ranking minority member of the subcommittee and in recent years when the Democratic party controlled the Senate, served as chair. The two senators have a long-standing relationship of mutual cooperation on biomedical research funding, regardless of which of them chairs the subcommittee.

The Shachman Award was established by the ASBMB in 2001, and recognizes individuals who best demonstrate dedication to public service in support of biomedical science, as exemplified by the award's namesake, Howard K. Schachman, who served as chairman of ASBMB's Public Affairs Advisory Committee for more than ten years (1989 - 2000) and continues to make numerous contributions to biomedical research policy as a speaker and thinker on these topics.

Senator Tom Harkin (D-IA)

The Award is given annually, and candidates are considered by the Society's Public Affairs Advisory Committee. The award consists of a permanent keepsake, an honorarium of $5,000, an opportunity to deliver a talk or lecture at the Society's annual meeting, and travel expenses to the meeting. Past recipients are philanthropist and biomedical research advocate John Whitehead (2004); former NIH Director Ruth L. Kirschstein (2003); and former Congressman John Edward Porter (2002).

Senator Arlen Specter (R-PA)

Nominations for ASBMB 2006 Awards

Nominations for the Society's 2006 Awards are now being solicited. The deadline for the receipt of nominations is May 2, 2005. Nomination for all awards should consist of a letter of recommendation, curriculum vitae minus list of publications, a list of not more than 10 of the nominee's most significant publications, and summary, not to exceed two pages, of the nominee's achievements. The Awards for which nominations are sought are:

ASBMB-AMGEN AWARD • ASBMB-MERCK AWARD • SCHERING-PLOUGH RESEARCH INSTITUTE AWARD • WILLIAM C. ROSE AWARD • AVANTI AWARD IN LIPIDS • HERBERT A. SOBER LECTURESHIP •

For more information about the awards check the ASBMB website, www.asbvmb.org. And please make sure to get your nominations to us by May 2, 2005.

Journal of Lipid Research Announces New Thematic Review Series

By Nicole Kresge, Ph.D., Staff Science Writer

The January issue of *The Journal of Lipid Research* (*JLR*) marked the inauguration of a new Thematic Review Series that highlights the role of immune function in atherosclerosis. The first article in the series, written by the editor of the series Dr. Godfrey S. Getz, of the University of Chicago, contained an overview of the Thematic Series along with brief summaries of the current conceptions of atherogenesis, the innate and adaptive immune systems, and the participation of the latter in atherogenesis.

Atherosclerosis is a chronic inflammatory process whereby deposits of macrophages, adaptive immune system cells, smooth muscle cells, matrix components and other substances form plaques on the inner lining of arteries. If these plaques grow large enough, they can significantly reduce blood flow through the artery or they can rupture, causing blood clots that may clog the artery or break off and travel to other parts of the body, leading to heart attack or stroke.

In both human and experimental atherosclerosis, an increase in cholesterol (in the form of LDL or VLDL) is the major factor in the development of vascular lesions. Some of this excess LDL enters the endothelial space where it is oxidized. Components of oxidized LDL can activate endothelial cells and result in the upregulation of adhesion molecules which facilitate the entry of monocytes into the subendothelial space. These monocytes may be converted into macrophages expressing cell surface scavenger receptors which take up the oxidized LDL. The cholesterol from the LDL is then esterified and forms the droplets characteristic of the foam cells that are the hallmark of early and growing atherosclerotic plaques. The foam cells may then produce proinflammatory cytokines which promote further development of the inflammatory response.

The progression of the lesion is characterized by the migration of smooth muscle cells to the plaque and their production of matrix proteins and proteoglycans. The plaque increases in size due to the continued recruitment of monocytes and lymphocytes, the continued migration and proliferation of smooth muscle cells, the death of some cells leading to a necrotic core, and matrix protein synthesis. Thus, atherosclerosis progression represents a chronic inflammatory reaction involving the participation of the innate immune system and modulated by the adaptive immune system.

The new *JLR* Thematic Review Series will consist of eight substantial reviews dealing with important aspects of immune function in relation to atherosclerosis. Four reviews will be devoted to the innate immune system and the others will deal with the bridge between innate immunity and the adaptive immune response. Some examples of upcoming Review article topics include the scavenger receptors expressed on the macrophage and dendritic cell surface, the toll like receptors, the natural antibodies recognizing modified lipoproteins and apoptotic cells, the contributions of the different lymphocyte subclasses to atherogenesis, and the role of cytokines on target cells within the plaque.

The current and future thematic reviews can be found both on the *JLR* website (www.jlr.org) and in the journal itself.

Topics in the *Journal of Lipid Research* Series

Immune function in atherogenesis.
Author: Godfrey Getz
(Published January 2005)

Recent insights into the biology of macrophage scavenger receptors.
Authors: David R. Greaves and Saimon Gordon
(Published January 2005)

Acute-phase response proteins: markers or mediators of inflammatory cardiovascular disease?
Authors: Alan Chait, Chang Yeop Han, John F. Oram, and Jay Heinecke

Paying the price for pathogen protection: toll receptors in atherogenesis.
Author: Peter Tobias and Linda Curtiss

Bridge to the adaptive immune system.
Author: Godfrey Getz

Natural antibodies.
Authors: Peter Shaw, Christoph Binder, and Joe Witztum

Unusual lymphocyte suspects.
Author: Catherine Reardon and Paul VanderLaan

Cytokines affecting endothelial and smooth muscle cells.
Author: Elaine Raines

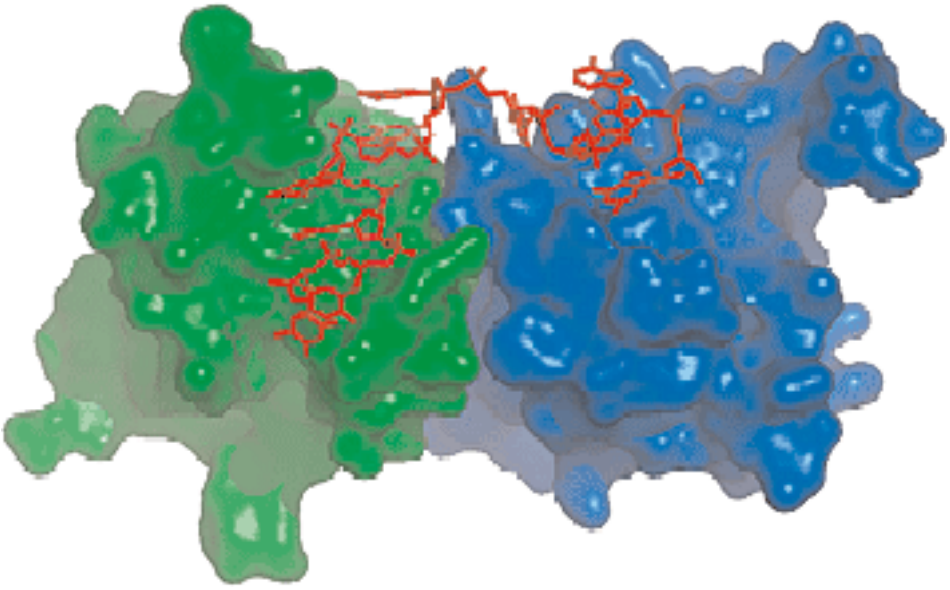
Cytokines affecting macrophages and leukocytes. Author: Alan Daugherty

Monocyte chemotaxis and atherogenesis.
Author: Oswald Quehenberger

Visualizing the End of

Scientists have glimpsed the three-dimensional structure of a protein that protects the ends of human chromosomes, a function that is essential for normal cell division and survival. By visualizing the protein as it surrounds the end of a chromosome, the scientists have learned how the protein homes in on a specific DNA sequence and acts like a protective cap to prevent erosion of chromosome ends.

The researchers, led by Howard Hughes Medical Institute President Thomas R. Cech,* whose laboratory is at the University of Colorado at Boulder, published their findings in an advance online publication of Nature Structural and Molecular Biology on November 21, 2004. Ming Lei and Elaine R. Podell in Cech's lab were co-authors. According to Dr. Cech, the findings raise new questions about essential cellular functions taking place at the end of the chromosome.



The POT1 protein binds to the end of a human chromosome by way of two oligonucleotide/ oligosaccharide-binding folds, shown here in green and blue. Single-stranded telomeric DNA is represented in red.

"There may be other states of the telomere as well, but we think this is right where the action is."

—Thomas R. Cech

During normal DNA replication, the very ends of a DNA molecule are lost. In order to prevent erosion, chromosomes are capped with a specialized region of DNA known as a telomere–a short, repetitious DNA sequence that does not code for any protein. In humans, an entire telomere is thousands of base pairs long, and is made up of a repeating sequence of six nucleotides. The final 100 to 300 nucleotides at the very end extend beyond the double helix as a single-stranded DNA "tail." The telomeres of normal cells gradually become shorter and shorter with each cell division, a characteristic sign of cellular aging.

Cells, however, also possess a unique enzyme known as telomerase that can lengthen telomeres by adding DNA to the ends of the chromosome using its own RNA template. In most cells, telomerase activity is very low after embryonic development, and regulation of telomerase is critical, because too much telomerase activity can promote tumor development.

In 2001, Dr. Peter Baumann in Cech's laboratory discovered POT1 (for "protection of telomeres"), the only protein known to bind to human telomeric DNA tails. POT1 plays an important role in capping the ends of chromosomes and in regulating telomere length. "Before that discovery," he said, "people weren't even in agreement that there was a protein at the very ends of human chromosomes." At the same time, Cech's team found a version of the POT1 protein in fission yeast. Other versions of POT1 have since been found in plants and mice—each recognizing a telomeric sequence that is unique to that organism.

the Human Genome

POT1 is critical to normal cell division and survival; experiments in fission yeast have shown that without it, most cells die immediately. Cells that do manage to survive quickly lose their telomeres, which interferes with normal cell division and eventually leads to massive DNA errors and abnormal, circular chromosomes. In human cells grown in the laboratory, too much POT1 can be disruptive, causing abnormal lengthening or shortening of telomeres.

Prior to determining the structure of human POT1, the researchers' prediction of what it might look like was based on their understanding of the yeast version of the protein. In yeast, POT1 wraps around the end of a chromosome via a region known as an oligonucleotide/oligosaccharide-binding fold (OB-fold)—a shape found in many proteins that recognize and bind to DNA or RNA. The repeating six-nucleotide telomeric unit fits precisely within this fold, with many POT1 molecules binding to each chromosome end.

The HHMI President and his colleagues expected human POT1 to have a similar design, but the results of their biochemical analyses of the protein did not fit easily with this model. For example, when the scientists added the protein to short pieces of DNA containing the six nucleotides that make up a human telomeric repeat, the human POT1 protein bound poorly.

To their surprise, they found that POT1 required a stretch of telomeric DNA containing at least ten nucleotides for efficient recognition and binding of DNA. "We were confused about how ten nucleotides was even a binding site, because it wasn't a multiple of six." Dr. Cech said. "If you need to coat something that has a repeating motif of six, you need to bind some multiple of six."

To understand how human POT1 recognized and bound to the telomere, the researchers crystallized a form of POT1 bound to the critical ten-nucleotide segment of DNA. They then used x-ray diffraction to reveal the structure of the complex. Unexpectedly, they found that unlike the yeast version of the protein, human POT1 contained two distinct OB-folds. The grooves of the two folds align with one another, forming a continuous channel where the telomeric DNA can fit.

They also learned that while the protein would bind to a ten-nucleotide sequence, the structure could also accommodate twelve nucleotides. "So it turns out it doesn't bind one six, it binds two times six," commented Dr. Cech. On a single chromosome end, he noted, there might be eight to 24 POT1 molecules coating the DNA tail.

The structure of the complex suggests that the end of the chromosome is tightly protected by POT1, and the researchers were able to verify this with additional biochemical experiments. When the POT1-DNA complex was treated with a solution that would normally modify the DNA at specific sites, no such changes occurred - indicating that those sites were completely enclosed by the POT1 protein.

Photo by Paul Fetters for HHMI

HHMI President Thomas R. Cech

According to Dr. Cech, the findings raise important questions about the regulation of telomerase. When telomeric DNA is buried within POT1, telomerase cannot access the DNA to elongate the telomere. "This is something that could keep the cell from making telomeres all day long," he said. "We think this is one level at which telomerase is regulated." Therefore, he said, an important next step will be to determine the cellular mechanism that switches the telomere to the on state so that elongation can occur.

"This is the end of the human genome. If you march out to the ends of human chromosome, what's there? Now we know what is there—at least part of the time," he summed up. "There may be other states of the telomere, as well, but we think this is right where the action is."

**ASBMB member*

Blocking Cell Suicide Switch Fails To

Researchers knew that prions, the misfolded proteins that cause mad cow disease and other brain disorders, were killing off a class of important brain cells in a transgenic mouse model. But when they found a way to rescue those cells, they were astonished to discover the mice still became sick.

Now they believe previous efforts to find the beginnings of the mouse disorder may have been focused on the wrong part of the brain cell and are plotting new directions for research.

In a study that appeared in the January 1, 2005, issue of the *Proceedings of the National Academy of Sciences*, scientists report evidence that clinical symptoms in the mice are produced by damage to synapses, the areas where nerve cell branches come together for communication.

"This could have important therapeutic implications," says senior author David Harris,* Professor of Cell Biology and Physiology at Washington University School of Medicine in St. Louis. "There's a great deal of effort being put into developing treatments for neurodegenerative disorders that would inhibit neuron death. Our results suggest that if we just prevent cell death without doing something to maintain the functionality of the synapse, patients may still get sick."

Dr. Harris noted that the findings also link prion diseases, which are relatively rare, to more common neurodegenerative disorders such as Alzheimer's disease, where recent evidence has also elevated the importance of damage to synapses.

Because of the bizarre methods by which prions spread and cause disease, they have only recently gained widespread acceptance as the source of several disorders that rapidly devastate the brains of humans, cows, deer and sheep.

In these disorders, the most infamous of which is mad cow disease, copies of a normal brain protein, PrP, fold themselves into abnormal shapes, dramatically altering the proteins' properties. Genetic mutations can increase chances that copies of the PrP protein will misfold into the prion form. Proximity to prions also can increase the chances that normally folded copies of PrP will misfold and become prions.

Human prion disorders can be caused by inherited mutations, through contamination during a medical procedure or, in very rare instances, from consumption of infected animals. In addition, some "spontaneous" cases of human prion disease currently can't be tracked to any genetic or environmental cause. Human prion disorders have no treatment and are fatal in months to several years.

"There's a great deal of effort being put into developing treatments for neurodegenerative disorders. ...if we just prevent cell death without doing something to maintain the functionality of the synapse, patients may still get sick."

—Dr. David Harris

Dr. David Harris

Dr. Harris has created nearly 50 genetically modified lines of mice to study prion diseases. The mouse model that he and his colleagues used for the most recent study has a mutation in PrP that causes it to misfold, leading to difficulty in movement and other symptoms similar to those seen in human prion diseases.

Scientists previously found that the mouse mutation kills off a class of brain cells known as cerebellar granule neurons. They form an important part of the structure of the cerebellum, an area in the back of the brain involved in motor coordination and other functions.

"The die-off is very dramatic—it's massive and occurs at roughly the same time among all the granule neurons, and it leads to visible shrinkage of the cerebellum," Dr. Harris says. "That had us thinking these cellular deaths had to be related to the onset of symptoms."

Stop Prion Damage In Mouse Brains

To further understand what was happening, he began to look into proteins involved in a cellular suicide process called apoptosis. He became interested in a protein called Bax that other scientists had previously identified as a trigger of apoptosis in central nervous system cells.

Dr. Harris and his colleagues crossbred the mouse prion model with a line of mice where the Bax gene had been deleted. As they expected, cerebellar granule neurons survived in mice that both had the prion mutation and lacked the Bax gene.

"That's important by itself, because it tells us that Bax is involved in the cell death pathway," he noted. "There are other options for self-destruction that the cells could have been using, but now we know that the Bax pathway is the one to focus on."

Although the neurons survived, the clinical symptoms persisted. Microscopic examinations of the brains of mice from the original prion model had previously revealed clumps of prion protein in brain areas heavy with synapses, so researchers decided to look at the health of synapses in the new crossbred line of mice.

A test for synaptophysin, a protein found at synapses, revealed widespread loss of synapses in the new line of mice.

"The neurons were still alive, but their connections were damaged or missing," says Dr. Harris. "This discovery really has changed the way we think about future directions for our work."

He says future research will include studies of how prions damage the synapse and whether the clumps of prion protein are involved in that damage.

** ASBMB member.*

Wnt Protein Prevents Obesity by Inhibiting Fat Cell Development

Genetically engineered mice, created at the University of Michigan Medical School, are living every dieter's dream. They eat unlimited amounts of high-fat food but have about 50 percent less body fat than normal mice on a low-fat diet. And, they show no signs of diabetes or other metabolic disorders, which are common in animals with too little fat.

However, the genetically altered mice also have some less-than-desirable characteristics—such as underdeveloped mammary glands, an inability to generate body heat, and skin that's twice as thick as normal.

All these changes appear to be caused by a protein called Wnt10b, which is present in artificially high amounts in fat tissue from the experimental mice. Wnt10b is part of a family of 19 secreted proteins. The Wnts act through autocrine and paracrine mechanisms to influence essentially all aspects of cell biology, including development, replication, and apoptosis. Although the function of Wnt10b is unknown, its expression in preadipocytes suggests a role in regulating adipogenesis. Previously, Ormond A. MacDougald,* an Associate Professor in the U-M Medical School, showed that Wnt10b gene activity repressed fat cell development in tissue cultures.

Now, Dr. MacDougald and Kenneth A. Longo, a U-M research fellow, have demonstrated that Wnt10b has the same effect on fatty tissue in mice. They reported their findings in the August 8, 2004, issue of the *Journal of Biological Chemistry.*

To determine the effect of the gene on adipose tissue development, the researchers created transgenic mice that express the Wnt10b gene specifically in adipose tissue. The fatty tissue in the transgenic mice contained 50 times the amount of Wnt10b found in adipose tissue from normal mice.

The Longo and MacDougald team discovered that Wnt10b had a different effect on the two types of fat found

in normal mice. White fat is a storage reservoir for excess energy. Brown fat is a specialized form of adipose tissue, found in small mammals and human newborns, which generates heat to keep the animal warm. The transgenic mice in the study had half as much white fat as normal mice and virtually no brown fat at all. This made it impossible for them to maintain their core body temperature, leaving them very vulnerable to cold.

For reasons the scientists do not understand, the transgenic mice had skin that was twice as thick and much heavier than normal mice. Dr. MacDougald speculates it "could be due to increased replication or decreased apoptosis of collagen-secreting cells within the dermis. Alternatively, Wnt might be causing a dramatic increase in collagen secretion from individual cells."

Perhaps the most surprising thing about the transgenic mice was their general state of robust good health.

"When we started making these animals, we thought they would have reduced amounts of fat, and thus suffer from metabolic complications, including diabetes," Dr. Longo explained. "Adipose tissue produces proteins, such as leptin and adiponectin, which affect the body's ability to respond to insulin. Reduced insulin sensitivity is one of the first symptoms of diabetes. So having little or no white fat is just as devastating to your health as having too much fat."

"Even though the Wnt10b transgenic mice had half as much adipose tissue and produced half the normal amount of leptin, they had none of the metabolic consequences we expected," Dr. MacDougald said. "In fact, the insulin sensitivity and glucose tolerance of transgenic mice on a high-fat diet was better than that of normal mice on a low-fat diet. We don't know why, but additional research should provide some answers."

**ASBMB Member*

Om Bahl Dies at 77, Research Led to Home Pregnancy Tests

ASBMB member Om Parkash Bahl, Professor in the State University of New York, Buffalo, Department of Biological Sciences, who in the 1970s published, in the *Journal of Biological Chemistry*, the structure of hCG, the basis for the development of the home pregnancy test, the fundamental research that led to the development of the home pregnancy test, died on December 10 in Buffalo's Millard Fillmore Hospital following a stroke. He was 77. Following a memorial service to be held on the UB campus in the spring, his family will travel to India to scatter his ashes in the Ganges River.

Dr. Bahl is best known for his research into the pregnancy hormone, human chorionic gonadotropin, or hCG. Early-pregnancy tests used today are designed to detect hCG in urine and are based on the results of Bahl's research in the 1970s, determining the hormone's complete structure. His research later was licensed from UB by Carter-Wallace, Inc.

He received many awards and honors, including the Padma Bhushan, the highest civilian award conferred by the government of India. The award, presented to him by Prime Minister Indira Gandhi, was in recognition of his scientific achievement in the fields of reproductive biology and pregnancy control.

Dr. Bahl served on a variety of editorial boards for scientific journals. He also was an advisor to the Population Council, the World Health Organization and the Population Research Committee of the National Institutes of Health.

Bahl joined the UB faculty as an assistant professor of biochemistry in 1966 and was named a professor in 1971. He was the first Chair of the UB Department of Biological Sciences from 1976-83, advancing the department's national reputation for research and teaching.

National Conference Puts Students in the Spotlight

By Nicole Kresge, Ph.D., Science Writer

Some 1,600 minority undergraduate and graduate student researchers and 900 faculty and administrators gathered at the Hyatt Regency in Dallas, Texas, November 10-13, 2004, for the Annual Biomedical Research Conference for Minority Students (ABRCMS). Now in its fourth year, ABRCMS is the largest biomedical student conference in the nation.

"ABRCMS is the only conference of its type that attracts a large number of minority science students from all ethnic groups who are underrepresented in sciences and gives them the opportunity to be the center of attention," explains Dr. Juliette Bell, chair of the ASBMB Minority Affairs Committee. "I think it is very important for students to attend conferences such as ABRCMS so that they will have the opportunity to meet and interact with other minority students who are actively engaged in research and to see that they are competitive with students from all types of institutions."

Formerly known as the MARC/MBRS Symposium, ABRCMS is sponsored by the National Institute of General Medical Sciences (NIGMS), Division of Minority Opportunities in Research Program (MORE), and managed by the American Society for Microbiology (ASM).

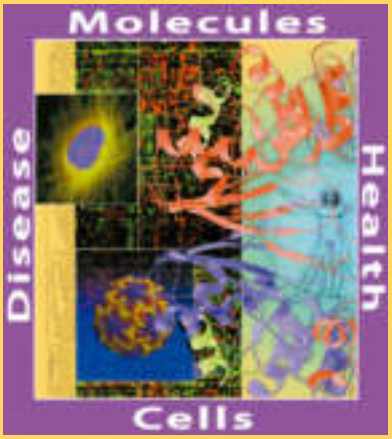
The conference is unique in that it is designed to encourage students to pursue advanced training in the biomedical sciences or behavioral sciences, including mathematics. The focus of the conference is entirely on the students, with sessions covering subjects such as applying to graduate school, career pathways in the biomedical sciences, time management, and strategies for taking the MCAT and GRE.

"At most other types of conferences, such as the annual meetings of professional societies, the focus is on the world renowned researchers," notes Dr. Bell. "While still providing top-notch research presentations, ABRCMS focuses on student presentations, mentoring, and professional development. ABRCMS also provides the opportunity for minority students to showcase their talents and interests and to interact with representatives from graduate schools. Many of these interactions lead to summer internships, scholarships, and graduate school opportunities."

Scientific sessions at ABRCMS were limited to two mornings: one for faculty members to present their research and one for students to present theirs. The student's oral presentations covered a wide variety of topics in molecular biology and biochemistry, from the identification of drug-resistant strains of HIV by mass spectrometry to using functional genomics to discover genes involved in cicardian rhythms to the determination of the crystal structure of a superoxide dismutase mutant. Students who didn't give talks were able to present posters in sessions covering nine different scientific categories: biochemistry, cell and developmental biology, molecular biology, chemistry, microbiology, neuroscience, physiology, quantitative science, and social and behavioral sciences.

During the three-day conference, 809 out of 902 students who presented their research, from sophomores through seniors, competed for awards. Seventy-two undergraduate students were recognized for their scientific presentations during the closing awards banquet, including seven who won awards in the Biochemical Sciences sponsored by ASBMB.

The conference also provided plenty of opportunity for students to network with over 300 representatives from graduate schools, government agencies, and scientific societies and foundations. "I tell my students that the most important thing that they can learn from a conference such as ABRCMS is how to network with people," explains Dr. Bell. "This includes interacting with representatives from graduate schools, speakers and presenters, faculty from other universities, and peers. Such interactions often lead to opportunities far exceeding the expectations of the students."



Proteolysis and Disease

Organizer: Charles Craik, Univ. of California, San Francisco

2005 ASBMB Annual Meeting
Held in conjunction with EB 2005
April 2-6, 2005, San Diego, CA

Additional Speakers will be chosen from the abstracts submitted.

Abstract Deadline:
February 9, 2005

Travel Awards Available for Undergraduates, Graduates, Postdoctoral Fellows, and Undergraduate Faculty.

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Intramembrane Proteolysis

Title TBD
Chair, Bruno Martoglio, Inst. of Biochemistry, Zurich

Title TBD
Michael Brown, Univ. of Texas Southwestern Medical Center

Proteases in Infectious Diseases

Title TBD
Chair, Charles S. Craik, Univ. of California, San Francisco

Parasite proteases: Lessons in evolution, biochemistry and drug design
James H. McKerrow, Univ. of California, San Francisco

Proteases in Neoplasia and Angiogenesis

Title TBD
Chair, Luisa Iruela-Arispe, Univ. of California, Los Angeles

Protein Inhibitors Therapeutics and Drug Design

Proteases as Therapeutic Targets
Chair, Nancy Thornberry, Merck

New chemical tools to study proteases
John Ellman, Univ. of California, Berkeley

Probing allosteric transitions with tethering
James Wells, Sunesis Pharmaceutical

Experimental Biology 2005

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Proteolysis and Disease

Organizer: Professor Charles S. Craik,
University of California San Francisco, San Francisco, CA

Virtually any biological process, from development to apoptosis, can be linked to a proteolytic event.

Most of the proteolytic enzymes studied to date belong to either the metallo, serine, cysteine, threonine or aspartyl proteases. The wealth of structural, mechanistic, and regulatory information that exists on representative members of these families provides a rich database for developing selective inhibitors of enzyme activity.

In cases where there is a direct link between the proteolytic event and disease, significant opportunities exist for therapeutic intervention. For these reasons, there has been a great deal of interest in dissecting the complex regulation, localization and activation of protease function.

This meeting will focus on a small but highly important subset of proteolysis to provide a window into this rich area of research. Biologists and chemists from academia and industry will be brought together to focus their interdisciplinary efforts on understanding the mechanism of proteolysis in a biological context and in several cases, the relationship between proteolysis and disease.

Intramembrane Proteolysis

Chair, Bruno Martoglio, *Novartis Pharma AG, Basel, Switzerland*

This symposium will address the role of intramembrane proteolysis in events ranging from the proteolytic processing of Notch to the processing events involved in cholesterol metabolism. The human genome encodes seven intramembrane-cleaving GXGD aspartic proteases: two presenilins, signal peptide peptidase (SPP), and four SPP-like candidate proteases (SPPLs).

Dr. Bruno Martoglio will discuss potential substrates for the SPPLs and show that they promote activation of signaling molecules through regulated intramembrane proteolysis. Dr. Michael Brown will discuss the paradigm of intramembrane proteolysis, namely regulation of lipid biosynthesis and how membranes can function as molecular sensors that respond to changes in the metabolic condition of the cell through the concerted action of proteases. Lastly, Dr. Raphael Kopan will discuss Notch intramembrane proteolysis and its role in a conserved signal transduction pathway involved in cell fate selection.

Proteases in Neoplasia and Angiogenesis

Chair, Luisa Iruela-Arispe, *University of California, Los Angeles*

This symposium will highlight the role that proteolysis plays in oncogenesis. As the current model of cancer shifts from the simplified one in which cancer is the result cellular behavior dysregulation to a more refined one in which cancer evolves out of careful and specific alterations of cellular behavior, the role of proteolysis becomes paramount. This is particularly the case when the new balance of cellular processes includes signaling, growth, angiogenesis, migration and death—all involving the actions of proteases.

Dr. Luisa Iruela-Arispe will describe the modulation of angiogenic signals by matrix metalloproteases (MMPs). Dr. Zena Werb will discuss the emerging importance of stromal cells in tumorigenesis. And lastly, Dr. Guy Salvesen will present newly emerging principles of proteolysis that have resulted from dissecting the proteolytic components of the intracellular pathway that leads to apoptotic cell death.

Proteases in Infectious Diseases

Chair, Charles Craik, *University of California, San Francisco*

There is more than one way to cleave a peptide bond and nowhere is that more evident than in proteases from viruses and parasitic organisms. New information on the structures and functions of these proteases has revealed unexpected protein folds and highly unique control mechanisms which may prove to be their Achilles' heel and could lead to novel antivirals. Dr. Charles Craik, will describe efforts to understand the complex interplay between the quaternary structure of a herpes virus protease and its active site. Dr. James McKer-

From his office, Dr. Craik looks out over the new UCSF Mission Bay campus and, in background to the east, a slice of San Francisco Bay.

row will discuss eukaryotic parasite proteases. Several of these organisms depend on cysteine proteases for many aspects their lifecycle, making them targets for therapy based upon differences relative to their mammalian counterparts. Dr. Jack Dixon and Feng Shao will discuss bacterial pathogens, in particular, AvrPphB, an avirulence protein from the plant pathogen Pseudomonas syringae that can trigger a disease-resistance response in a number of host plants by hijacking eukaryotic signal transduction systems.

Protease Inhibitors, Therapeutics and Drug Design

Chair, Nancy Thornberry, *Merck Research Labs, Rahway, New Jersey*

Proteases have long provided a testing ground for rational efforts to develop effective therapeutics. Since the development of inhibitors to angiotensin converting enzyme for regulation of blood pressure, proteases have served as tantalizing but often elusive targets for drug design. Dr. Jon Ellman will describe his various tools to study the extended substrate specificity of a protease and how to use that information to develop combinatorial libraries to identify highly selective inhibitors for the different classes of proteases. Dr. James Wells will present a powerful method to identify allosteric sites in proteases that can be used to regulate their activity using caspases as an example. Dr. Nancy Thornberry will provide data on what may be the next success story for anti-proteolytic therapy in the inhibition of dipeptidyl peptidase IV for the treatment of type 2 diabetes mellitus.

Fred Guengerich to Receive William C. Rose Award

Frederick P. Guengerich, Professor of Biochemistry at the School of Medicine, Vanderbilt University, has been selected to receive the William C. Rose Award. This Award recognizes outstanding contributions to biochemical and molecular biological research and a demonstrated commitment to the training of younger scientists, as epitomized by the late Dr. Rose. Recent recipients of the Award were Sunney I. Chan in 2004, Jack E. Dixon in 2003, Gordon Hammes in 2002, Marc W. Kirschner in 2001, and Rowena G. Matthews in 2000.

The Award consists of a plaque, transportation to the ASBMB Annual Meeting, April 2-6 in San Diego, to present a lecture, and reimbursement for travel, hotel accommodations, meals, and ground transportation. Dr. Guengerich's lecture will be at 8:30 a.m., Wednesday, April 6.

In nominating Dr. Guengerich for the Award, Dr. Minor J. Coon, of the University of Michigan Medical Center, recalled, "Fred joined my laboratory as a Postdoctoral Fellow in 1973, following completion of his Ph.D. studies at Vanderbilt University, and I have followed his career closely ever since. Because of our common research interests I hear his presentations frequently at national and international meetings and read his outstanding and frequent publications. He is almost unmatched in his dedication to science, his insight into the mechanistic aspects of cytochrome P450, and his excellent contributions to the overlapping fields of biochemistry, toxicology, and chemical carcinogenesis."

Initially, Dr. Guengerich's laboratory was focused on the purification and characterization of human cytochrome P450s. His research led to the identification of the major cytochrome P450s involved in human drug metabolism and made a significant impact in the pharmaceutical industry. It allowed his lab to set up specific assays to determine whether compounds were inhibitors and/or substrates for human cytochrome P450s. These assays are used now to eliminate compounds early in the drug discovery process that may produce significant drug-to-drug interactions in people.

Dr. Guengerich's research helped define the molecular basis for individual variability in human drug metabolism. As a consequence of this research the analysis of individual variability in human drug metabolism has been integrated in most drug development programs in the industry. I cannot think of another individual whose research has made a greater impact on the understanding of human drug metabolism and its translation to drug discovery and development.

In addition to this pioneering work on the purification and characterization of human cytochrome P450s, his laboratory has been instrumental in defining the catalytic mechanisms of cytochrome p450 mediated reactions, the enzymology of glutathione S-transferases, particularly mechanism of reactions and genotoxicity, and mechanism of mutagenesis.

He has also used P450s from various species to elucidate the reactions of chemicals with DNA bases, and with his associates has characterized more than 20 new adducts and their mechanism of formation. Since 1981 he has served as Director of the Center in Molecular Toxicology at Vanderbilt University and has built this unit into one of the preeminent such academic programs in the world. He is regarded as one of the leading investigators of his generation in the fields of xenobiotic biochemistry and molecular toxicology as related to environmental health.

Dr. Frederick P. Guengerich

Dr. Guengerich's research interests in the biochemistry of toxicology reaches beyond P450 enzymes and he has made important contributions to our understanding of NADPH-cytochrome P450 reductase, glutathione transferases and expoxide hydrolases. These studies have led his laboratory into investigation of adducts between carcinogens and DNA. His laboratory continues to characterize different DNA adducts formed by these enzymes and has established general procedures for their identification and structural characterization.

Dr. Guengerich, who has served three terms on *The Journal of Biological Chemistry* Editorial Board, is considered one of the two or three leading scientists in the world in the study of P450 enzymes, and continues to make seminal contributions in this area and in the study of carcinogen-DNA adducts. As expected of a Rose Award recipient, he shares Dr. Rose's enthusiasm for training young investigators. Those trainees carry with them his appreciation of the basic principles of biochemistry in their daily activities, and the general area of toxicology and drug metabolism is much richer thanks to his training of young scientists.

Biochem4schools: A New Online UK Resource For Teachers and Students

Biochem4schools, a new free web-portal, developed by the Biochemical Society for use by teachers and students at all levels, was launched at the Association for Science Education's Annual Meeting, January 6-8, in Leeds. Biochem4schools can be accessed at http://www.biochem4schools.org.

This new portal is free to use, user friendly, visually attractive, saves time and effort searching for biochemistry resources and is accessible for everyone. Biochem4schools guides users to relevant bresources already on the web. The Biochemical Society has pulled together over 300 resources from web sites worldwide providing access for teachers and students to information according to the stages of learning, the curriculum being studied, and the topic of interest.

The 16 topic areas range from genes to biotechnology and the site reflects the fast pace of change in biochemical research. Resources are added as they become available, and can be reviewed by users, who will be able to see the top sites to visit in each topic. Each resource site has icon labels to explain their suitability for different age groups, and curriculum links as well as a description of and comment on the content with extensive cross-referencing to help you find what you are looking for.

Biochemistry is a fast-expanding field, represented increasingly in school curricula and in the world of undergraduate learning and research. Current 'hot topics' such as cloning make biochemistry education important and relevant, and with a choice of search options and a wide-ranging collection of resources, biochem4schools gives educators and pupils access to the most up-to-date information.

Biochem4schools has been developed for use in the classroom as well as on a PC. The increase in the use of data projectors and interactive whiteboards in classrooms makes web-based classroom learning an ideal resource for both teachers and their students, and the high proportion of PC ownership means that these resources can be used for homework, projects, and coursework.

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Study Finds First Molecular Target to Halt Spread of HPV

Pennsylvania State College of Medicine researchers have discovered the first molecular therapy to target cancer-causing components and thereby destroy a bona fide human papillomavirus (HPV) infection.

"Our results suggest that targeting therapies to the RNA that encodes a specific pair of proteins in HPV may break a chain that, left unhindered, promotes cellular proliferation and, potentially, cervical cancer," said Gary Clawson,* Professor of Pathology, and Biochemistry and Molecular Biology. "Until now, there have been no effective and specific molecular treatments reported for HPV infections or for related papillomavirus infections."

The study was published July 1, 2004, in the online version of the journal *Gene Therapy*.

Dr. Gary Clawson

HPV is one of the most common causes of sexually-transmitted infection in the world. Types of HPV can cause fast-growing lesions such as genital and planter warts, and a number of HPV types are considered to be "high-risk" for development of cervical dysplasia, a known precursor to cervical cancer. According to the Department of Health and Human Services, 20 million Americans are already infected with HPV.

HPV-infected cells require continued production of two proteins, E6 and E7, to survive and proliferate. The proteins assist HPV by binding to tumor suppressors pRb andp53, respectively, and deregulating the cell cycle. Since E6 and E7 are produced by overlapping mRNAs, the Clawson supposed that by destroying the common RNA used for production of the proteins, the virus would no longer be able to trigger cellular proliferation.

"There are some unique characteristics of E6 and E7 which make them good targets, most importantly, their critical role in overcoming cell growth control pathways," said Dr. Clawson.

His team first used library selection to find accessible sites on the surface of the E6/E7 RNA for the genital wart-causing HPV 11. They then targeted the sites with two types of nucleic

Continued next page

Anita Roberts to Deliver FASEB Excellence in Science Lecture

ASBMB member Anita Roberts has been selected to receive the FASEB Excellence in Science Award and deliver a lecture at EB 2003 in San Diego. Her lecture, TGF-β-Journey of Discovery and Promise, will be at 8:30 a.m., Tuesday, April 5.

Dr. Roberts joined the National Cancer Institute in 1976. She has achieved international acclaim for her work in growth factor research, having discovered and characterized, together with Dr. Michael Sporn, the cytokine transforming growth factor-β (TGF-β). Her research has established roles for this peptide in autoimmune disease, fibrogenesis, carcinogenesis, and wound healing which are leading to the development of new therapies for these diseases.

From 1995 to 2004 Dr. Roberts served as Chief of the Laboratory of Cell Regulation and Carcinogenesis at the National Cancer Institute. She was recently named the 49th most cited scientist, worldwide, for the period 1982-2002 by the Institute for Scientific Information, making her the second most highly cited woman scientist.

Dr. Anita Roberts

She was among the first group of NIH scientists elected to the Senior Biomedical Research Service and was a past president of the Wound Healing Society. Dr. Roberts has authored over 330 articles and serves on numerous scientific advisory and editorial boards. Her present research interests are focused on identification of the roles of specific downstream signaling pathways of TGF-β in disease pathogenesis and on the possibility of applying this knowledge to design of novel therapies.

Dr. Roberts obtained her Ph.D. from the University of Wisconsin for the study of the metabolism of retinoic acid with Dr. Hector DeLuca followed by a postdoctoral fellowship at Harvard University Medical School.

acids which bind to RNA and render it useless. The first was a small stretch of nucleic acid or antisense nucleotide called ASO407, and the second was a short, catalytic, single-stranded DNA molecule called a DNAzyme. Both were tested in an animal model in which human foreskin was infected with HPV 11 and then grafted onto immunodeficient mice. Five of 11 grafts treated with ASO407 showed eradication of the virus. Of seven small papillomas treated with ASO407 four were negative for the virus.

"If this can be regarded as a cure rate, this rate is comparable or even superior to that achieved with a currently-available therapy, called imiquimod, and other therapies," Dr. Clawson said.

In larger papillomas, one of four treated with ASO407 was negative, suggesting that ASO407 may be most useful clinically for treatment of early HPV-associated lesions. DNAzymes were less effective than ASO407, showing therapeutic effects in only three of 10 samples. Their effects appeared to be limited to the upper levels of the lesion.

"Despite an increase in our understanding of the relationship between HPV and cancer, few advances have been made in the treatment of HPV-associated lesions," commented Dr. Clawson. "In this study we managed to design and test reagents targeted to the RNA that encodes E6 and E7 proteins of HPV 11. This may lead to alternative treatments to suppress HPV lesion progression."

The team is currently working on a similar treatment for HPV 16, which is the most important high-risk HPV and is involved in cervical dysplasias and cervical carcinoma.

**ASBMB Member*

Correction: The photo above should have appeared instead of Dr. Clawson's in conjunction with the article, 3-D Structure of Anthrax Toxin Complex Solved, on page 6 of the December issue of ASBMB Today. Those in the photo are Dr. Robert C. Liddington of the Burnham Institute (left) and coauthors Eugenio Santelli (middle) and Laurie Bankston.

Researchers Report Early Success Using Saliva to Detect Oral Cancer

Scientists funded by the National Institute of Dental and Craniofacial Research have taken a major step forward in using saliva to detect oral cancer. As published in the December 2004 issue of Clinical Cancer Research, they found they could measure for elevated levels of four distinct cancer-associated molecules in saliva and distinguish with 91% accuracy between healthy people and those diagnosed with oral squamous cell carcinoma.

This "proof-of-principle" study marks the first report in the scientific literature that distinct patterns of "messenger RNA (mRNA) not only are measurable in saliva but can indicate a developing tumor.

According to Dr. David Wong, of the University of California at Los Angeles School of Dentistry and senior author on the paper, it may be possible to further refine the test, possibly by including additional cancer-linked mRNAs, to attain the necessary 99% to 100% accuracy of commercial diagnostic tests for oral squamous cell carcinoma. Currently no biochemical or genetic diagnostic tests are commercially available for oral cancer.

With these baseline data as their scientific anchor, the researchers could begin to test whether saliva contains distinct mRNA patterns. "We obtained saliva and blood from 32 people who had been recently diagnosed with oral squamous cell carcinoma but not treated," said Yang Li, D.D.S., Ph.D., lead author on the study and a researcher in Wong's laboratory.

The scientists extracted the mRNA from the saliva of the cancer patients and soon discovered 1,679 genes were expressed at significantly different levels in the cancer patients compared to healthy individuals. Seven mRNAs in particular were present at a 3.5-fold higher level in the cancer patients. Among them was the mRNA for the gene IL-8, whose protein Dr. St. John had originally searched for in saliva.

The researchers then whittled down their list of signature mRNAs to four, based on statistical models that indicated the synchronized rise in expression of these four molecules increased the probability that the saliva belonged to a cancer patient. These four mRNAs are from the following genes: Interleukin 1-beta (IL1B), Ornithine decarboxylase antizyme 1 (OAZ1), spermidine/spermine N1-acetyl transferase (SAT), and interleukin 8 (IL-8).

They screened the saliva again, and could identify the saliva from cancer patients in nine out of 10 samples. "This was primarily an exploratory study to validate our initial finding of a unique molecular signature of mRNAs in people with oral squamous cell carcinoma," Dr. Wong explained. "We will follow up with a larger cohort of about 200 patients in the near future, and this study will hopefully allow us to distinguish in saliva between the various stages of the cancer and ultimately push our accuracy up to as close to 100 percent as possible."

2005 NIH Director's Pioneer Award Program

NIH has just announced the 2005 NIH Director's Pioneer Award, a key component of the NIH Roadmap for Medical Research. The award supports scientists of exceptional creativity who propose pioneering approaches to major challenges in biomedical research. The program is open to scientists at all career levels who are currently engaged in any field of research, interested in exploring biomedically relevant topics, and willing to commit the major portion of their effort to Pioneer Award research. Women, members of groups that are underrepresented in biomedical research, and individuals in the early to middle stages of their careers are especially encouraged to nominate themselves.

Awardees must be U.S. citizens, non-citizen nationals, or permanent residents. In September 2005, NIH expects to make 5 to 10 new Pioneer Awards of up to $500,000 in direct costs per year for 5 years.

The streamlined self-nomination process includes a 3- to 5-page essay, a biographical sketch, a list of current research support, and the names of 3 references. Nominations may be submitted on the Pioneer Award Web site, http://nihroadmap.nih.gov/pioneer, between March 1 and April 1, 2005.

Study Finds Acupuncture Relieves Pain, Improves Function in Knee Osteoarthritis

A study was funded by the National Center for Complementary and Alternative Medicine (NCCAM) and the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) has found that acupuncture can relieve pain and improve function for people with osteoarthritis of the knee, and serves as an effective complement to standard care. This landmark study, the longest and largest randomized, controlled phase III clinical trial of acupuncture ever conducted, was published in the December 21, 2004, issue of the *Annals of Internal Medicine*.

The multi-site study team, including rheumatologists and licensed acupuncturists, enrolled 570 patients, aged 50 or older with osteoarthritis of the knee. Participants had significant pain in their knee the month before joining the study, had never experienced acupuncture, had not had knee surgery in the previous six months or used steroid or similar injections. They were randomly assigned to receive acupuncture, sham acupuncture, or participation in a control group that followed the Arthritis Foundation's self-help course for managing their condition. Patients continued to receive standard medical care from their primary physicians, including anti-inflammatory medications, such as COX-2 selective inhibitors, nonsteroidal anti-inflammatory drugs, and opioid pain relievers.

"For the first time, a clinical trial with sufficient rigor, size, and duration has shown that acupuncture reduces the pain and functional impairment of osteoarthritis of the knee," said Stephen E. Straus, NCCAM Director. "These results also indicate that acupuncture can serve as an effective addition to a standard regimen of care and improve quality of life for knee osteoarthritis sufferers. NCCAM has been building a portfolio of basic and clinical research that is now revealing the power and promise of applying stringent research methods to ancient practices like acupuncture."

"More than 20 million Americans have osteoarthritis. This disease is one of the most frequent causes of physical disability among adults," said Stephen I. Katz, M.D., Ph.D., NIAMS Director. "Seeking an effective means of decreasing osteoarthritis pain and increasing function is of critical importance."

During the course of the study, led by Brian M. Berman, Director of the Center for Integrative Medicine and Professor of Family Medicine at the University of Maryland School of Medicine, Baltimore, 190 patients received true acupuncture and 191 patients received sham acupuncture for 24 treatment sessions over 26 weeks. In both the sham and true acupuncture procedures, a screen prevented patients from seeing the knee treatment area and learning which treatment they received. In the education control group, 189 participants attended six, 2-hour group sessions over 12 weeks based on the Arthritis Foundation's Arthritis Self-Help Course—a proven, effective model.

On joining the study, patients' pain and knee function were assessed using standard arthritis research survey instruments and measurement tools, such as the Western Ontario McMasters Osteoarthritis Index (WOMAC). Patients' progress was assessed at 4, 8, 14, and 26 weeks. By week 8, participants receiving acupuncture were showing a significant increase in function and by week 14 a significant decrease in pain, compared with the sham and control groups. These results, shown by declining scores on the WOMAC index, held through week 26. Overall, those who received acupuncture had a 40 percent decrease in pain and a nearly 40 percent improvement in function compared to baseline assessments.

For the first time, a clinical trial with sufficient rigor, size, and duration has shown that acupuncture reduces the pain and functional impairment of osteoarthritis of the knee.

"This trial, which builds upon our previous NCCAM-funded research, establishes that acupuncture is an effective complement to conventional arthritis treatment and can be successfully employed as part of a multidisciplinary approach to treating the symptoms of osteoarthritis," said Dr. Berman.

by John D. Thompson, Editor

Venture Capital Focuses on Healthcare, Biopharma in 2004's Third Quarter

U.S. venture-capital investment reported its typical slowdown in the third quarter of 2004, with $4.56 billion invested in 467 deals, according to the Quarterly Venture Capital Report released by Ernst & Young LLP and VentureOne, a unit of Dow Jones Newswires. Compared with the third quarter of last year, both the number of deals and the amount invested were down 4%.

Within the healthcare industry, the biopharmaceutical segment offered one of the positive notes, with 61 deals and $966.9 million invested, representing 25% more deals and 16% more money than last quarter. For the venture-capital market as a whole, healthcare deals made up 25% of the quarterly deal-flow, the industry's highest percentage this year. Healthcare also received 32% of the total amount invested. Among the largest healthcare deals was the $48 million deal in Sopherion Therapeutics (New Haven, Connecticut), a developer of targeted pharmaceuticals using biosynthetic modules.

"Early-stage healthcare companies fared particularly well in the third quarter, with 40 deals raising a total of $357.9 million, the most raised for healthcare company formations since mid-2002," said Jeff Fialko, Ernst & Young's venture capital advisory group leader for the mid-Atlantic area. "Early-stage healthcare investors were likely encouraged by the ability of the life-science companies with strong pipelines to find IPO exits in today's highly selective capital markets. Thirty-two of the 48 venture-backed IPOs through the third quarter of 2004 occurred in healthcare segments.

"Health-care start-ups also received larger infusions of venture capital to get them off the ground. The median amount raised in a first-round healthcare investment was $7.3 million in the third quarter, the highest amount on record."

Serologicals Corp. Names Aaron Shatkin To Board Of Directors

Serologicals Corporation has elected Aaron J. Shatkin to the company's Board of Directors. Dr. Shatkin, is a member of ASBMB, the National Academy of Sciences and American Academy of Arts and Sciences. He currently serves as the Director for the Center for Advanced Biotechnology and Medicine, as well as a Professor of Molecular Genetics and Microbiology at the Robert W. Johnson Medical School in Piscataway, New Jersey, and also as Professor of Molecular Biology at Rutgers University. Dr. Shatkin began his professional career with the National Institutes of Health (NIH) in 1961, and his teaching career at the Georgetown University Medical School in 1968.

"Serologicals Corporation is proud that Dr. Shatkin has agreed to join our Board of Directors," said Desmond H. O'Connell, Jr., Chairman of the Board of Directors for Serologicals. "His worldwide expertise in the field of molecular genetics and microbiology, as well as his renown as one of the world's leading authorities on biotechnology will prove beneficial to Serologicals as we continue to implement our ongoing growth strategy."

Serologicals,, headquartered in Atlanta, Georgia, is a global provider of biological products, enabling technologies and custom services to life science companies. The company's customer base includes major life science companies and leading research institutions, and its products are used as tools for research in oncology, hematology, immunology, cardiology, neurology, proteomics, infectious diseases, cell signaling and stem cell research. In addition, the company is a leading manufacturer of monoclonal antibodies for the blood typing industry.

Dr. Aaron J. Shatkin

UK Urged to Focus on Marine Biotechnology

A new report on marine biotechnology in the UK has called for a more coordinated approach to maximize the benefits of this rapidly developing sector.

The report, commissioned by the Foresight Marine Panel Marine Biotechnology Group and funded by the UK Department of Trade and Industry (DTI), found that the sector has already developed a wide range of applications, such as the extraction of anti-cancer and anti-viral compounds from marine organisms; the use of coral-derived materials as bone replacements; and the development of bioluminescent sensors to detect environmental pollution and toxins.

'This report brings to the fore the exciting opportunities offered by harnessing our increasing knowledge of marine biotechnology," said UK Science and Innovation Minister Lord Sainsbury. "It points the way to how UK industry can develop innovative products and processes that will bring wider benefits to the UK. The DTI's five year program sets out how we will champion science, innovation and technology in the UK. We need to invest in these areas if we are to compete successfully in the global knowledge economy."

According to the report, The Prospects of Marine Biotechnology Development in the UK, marine biotechnology represents one of the most exciting emerging technology sectors, with a global market valued at $2.4 billion U.S. and a predicted growth rate exceeding 10% per year. The sector is expected to contribute to nearly every industry sector, from healthcare to bioremediation and from cosmetics to nutraceuticals.

"The time to invest in underpinning the science, knowledge networks, and public understanding of this major biotechnology field has now arrived," states the report, calling for a more coordinated approach between the research base, entrepreneurial enterprise and the large pharmaceutical, biochemical and food multinational companies.

The report also encourages the use of UK Research Council funding and the new initiatives offered by the UK government to promote and encourage innovation. The Technology Strategy published in November 2004 provides $148.7 million U.S. for research and development of the latest innovative technologies. The strategy has already identified bio-based industrial products as one if its nine high priority technology areas.

Indian pharmaceutical sector 'lacks trained personnel'

India's ambitions to emerge as a pharmaceutical giant could be thwarted if it does not address its lack of trained workforce and improve the quality of related courses, drug researchers warn.

Bansi Lal, head of the privately funded Nicholas Piramal Research Centre, warned delegates at the 92nd Indian Science Congress in Ahmedabad in early January that despite India's potential for, and confidence in, emerging as a hub for pharmaceutical research and development, it lacks trained personnel.

"It is a myth that we have abundance of manpower," said Lal. "We do not have the right quality of experts." He said India should introduce pharmacology at an earlier stage in education and also set up regional drug research centers. Currently, the earliest courses in pharmacology are offered at the undergraduate level.

Lal said India is "reasonably strong" in chemistry but its performance in identifying new lead molecules for drugs is a concern. India's other weak points include poor facilities for testing drugs on animals, and not having enough manufacturers of scientific instruments.

Chittar Mal Gupta, director of the public sector Central Drug Research Institute (CDRI) in Lucknow, agrees that India faces a shortage of skilled personnel for research and development of new drugs.

Gupta told SciDev.Net, which focuses on pharmaceutical news in Africa, Asia, and Latin American, that unlike the West, where most pharmaceutical research is in the private sector, in India it is mostly done in government-owned laboratories, which do not operate with the speed essential for drug development and delivery. India is, however, changing its strategy and publicly-funded laboratories like CDRI now link up with the Indian private sector at an early stage to accelerate drug development and trials soon after potential new drug molecules are discovered, he added.

Nanotechnology letter continued...

Continued from page 2

to emulate Nature and create his own microcosm of molecular evolution by engineering 'artificial' molecular machines that can manufacture almost any material from the atom up. This level of atomic accuracy requires detailed knowledge of not only the product that one is trying to make, but also the molecular machines (or as Erik Drexler termed them, the assemblers) that we are trying to engineer to catalyze the formation of the product.

So, what role can biochemists and molecular biologists play in Nanotechnology? Well, we have been playing an important role in this quest for a very long time. Biochemists have been studying and purifying enzymes in an effort to understand how they achieve high specificity and selectivity in the reactions that they catalyze. The regulation of such enzymatic catalysis is also another important field of study by biochemists. Molecular biologists help in this process by developing DNA recombinant technologies to express and purify these molecular machines. For example, in vitro evolution has been and is currently being used by many companies such as Diversa and BioCatalytics to create new and sometimes highly efficient enzymes that can catalyze the synthesis of new materials such as difficult to make new drugs whose conventional synthesis would otherwise be close to impossible with currently available technologies.

Mastering the creation of such novel proteins requires the creative cooperation and dedicated efforts of biochemists and molecular biologists. It isn't hard to imagine that such technologies will soon find their way into the development of new 'artificial' enzymes, perhaps with engineered artificial amino acids in their active sites, that can catalyze the synthesis of novel materials that do not yet exist today. This is one of many examples of what the field of nanotechnology can achieve. Other examples include the creation of novel nanosensors that can detect the levels and activity of certain enzymes in the cell. These nanosensors can be used in the diagnosis and progression of diseases involving aberrations in levels and/or activity of these enzymes. Armed with such information, pharmaceutical companies can develop highly effective medicines targeting these very enzymes, modulating their levels and/or activities inside the cell.

However, we should not delude ourselves into thinking that any one of these fields will, in and of itself, be sufficient to define the field of nanotechnology. Such a gargantuan task requires the merging and multidisciplinary cooperation of a number of fields including biochemistry, molecular biology, chemistry, physics, and computer science.

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Business Fails Science in UK

Government statistics for 2003, the latest year available, show that business spending on R&D in the UK is largely stagnant. It represented 1.2% of GDP, as it has since 1996.

The number of industry scientists and engineers decreased 2% from 2002, and there was a worrying 11% drop in technician numbers, according to a report in Research Fortnight.

Anne Campbell, Member of Parliament, plans to bring a Private Members Bill during the current parliament that requires government departments and agencies to spend 2.5% of their R&D budgets with small businesses. Similar legislation in the U.S. has successfully fostered new science-based start-up companies.

The UK's Small Business Research Initiative in the UK has not been so successful, partly because participation is not mandatory for government departments and few have chosen to participate and partly because the current procurement processes are seen as too time-consuming and bureaucratic.

But if business is ignoring universities, universities are not neglecting the world of business. A survey by the Universities Companies Association showed that total licensing income of UK universities in 2003 increased nearly 40% to £31.3 million ($59 million U.S.). Although, at 151, the number of new UK spin-off companies remained about the same as in 2002.

An editorial in a recent issue of the Times Higher Educational Supplement considered that a year after the Lambert review of business-university interaction, little has changed to help "third-stream" activities in universities. Lambert "muddied the waters" by calling for changes to the RAE to reward more applied work. Higher Education, said the editorial, needs a funding stream for business interaction on a par with the RAE rather than the latter becoming "an afterthought in an exercise with different objectives."

New NSF Center Will Transform Evolutionary Biology

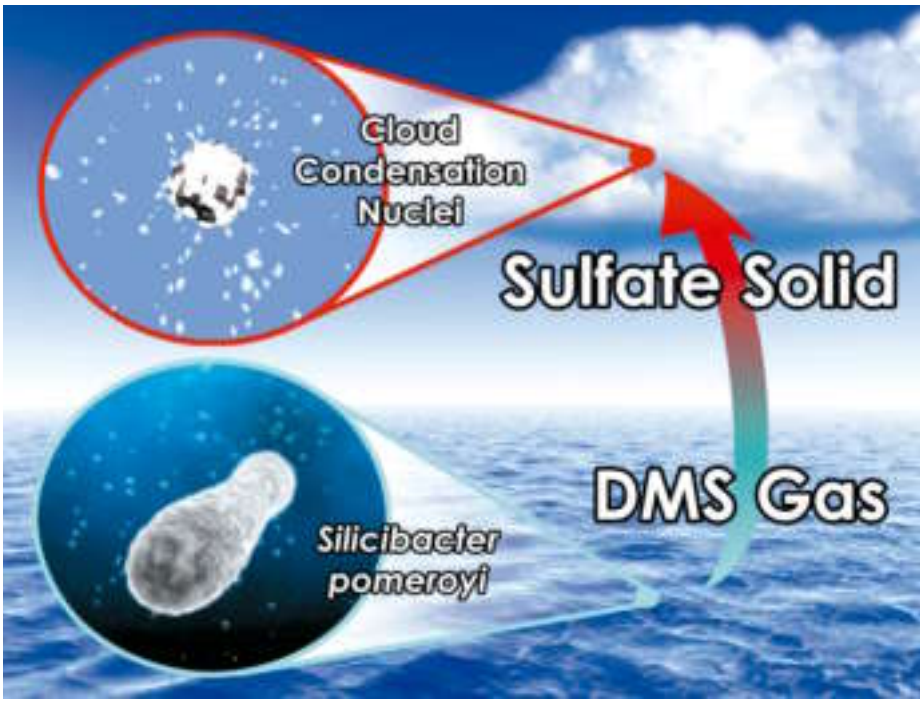
A modest building will soon bring together millions of algae, bacteria, insects, sea slugs, worms, birds, mice, plants, people and a host of other creatures, in the form of masses of data on their genetics, behavior and structure.

The building will house the new National Evolutionary Synthesis Center (NESCent), established in Durham, North Carolina, with a $15 million grant from the National Science Foundation (NSF). The evolution center is a result of collaborations among Duke University, North Carolina State University, and the University of North Carolina (UNC) at Chapel Hill.

"This new center will transform evolutionary biology by tackling long-standing questions in a new way through science that is collaborative, and that synthesizes results," said Sam Scheiner, program director in NSF's Emerging Frontiers Division, which funded the center.

"Information about biological evolution has exploded in the past several decades, fueled by advances in biodiversity, computation, genomics and many other fields," said Joel Kingsolver, a biologist at UNC and the center's associate director for science and synthesis. "Now is the time for synthesizing this information to gain a new level of scientific understanding about evolution, and to apply this understanding to important societal issues."

Until now, said the center's director, Clifford Cunningham, a Duke biologist, different scientific disciplines have too often concentrated only on their own pieces of the puzzle. The center's aim, he said, will be to help scientists assemble those pieces to see the broad picture of evolution. In a sense, according to Cunningham, each kind of researcher speaks a different scientific language, and the challenge will be to get them to learn each other's languages so they can collaborate to make advances in evolution.



The center will develop a common "language" to enable communication among disparate scientific information databases on the large number of organisms important in the study of evolution. "The scientific challenges of the 21st century involve coordination and management of data," said Dan Reed, leader of the center's computing strategy and a computer scientist at UNC. "The explosive growth of scientific data, captured by research collaborators around the world, necessitates new approaches to data storage, mining and presentation. By coordinating data, researchers will be better able to answer long-standing questions."

"Studies at the center will have applications that impact individuals in many ways, including forensics and agriculture," said the center's associate director for education and outreach, Greg Gibson, a geneticist at North Carolina State University. "Designing strategies for prevention of insecticide resistance, finding new approaches to environmental protection and developing a better understanding of humans' shared genetic heritage are objectives that require a new understanding of evolutionary processes."

The center will emphasize educational programs in which scientists will communicate their results to policymakers. The educational programs will also help teachers develop lesson plans on evolution and interest students at historically minority colleges and universities in studying evolution. A network of educators and extension agents throughout the state will work to keep the public informed about the outcome of center activities.

Calendar of Scientific Meetings

MARCH 2005

FEBS Advanced Lecture Course

March 12–17 • Wildbad Kreuth, Germany
Origin and Evolution of Mitochondria and Chloroplasts
Deadline for application and abstract submission: January 31, 2005; Contact: Prof. J. Soll, Botanik, LMU, München
Menzinger Straße 6780638, München, Germany
Ph: +49 89 17861 244; Fax: +49 89 17861 185
Email: evo05@lrz.uni-muenchen.de

CSBMCB Sponsored Meeting on Cellular Dynamics

March 16–20 • Banff Centre, Banff, Alberta, Canada
This Canadian Society of Biochemistry, Molecular and Cellular Biology sponsored meeting will feature cutting-edge sessions on Nuclear structure, Organelle Inheritance, Imaging Technologies, Protein Folding, mRNA Localization, Organelles of the Secretory Pathway and Systems Approaches to Cell Biology. Keynote Speaker will be Günter Blobel.
Meeting organizer: Email: rick.wozniak@ualberta.ca
Website: www.csbmcb.ca/2004Meeting/index.html

Horizons in Molecular Biology Decoding Nature: Hierarchy of Interactions

March 17–19 • Max-Planck Institute for Biophysical Chemistry in Göttingen, Germany
Email gpmolbio@gwdg.de
Website: www.horizons.uni-goettingen.de

Experimental Biology 2005 and the Congress of the International Union of Physiological Sciences Joint Meeting

March 31–April 6 • San Diego Convention Center
Experimental Biology 2005 meets April 2 - 6. The IUPS Congress meets March 31 - April 5. In addition, a number of IUPS satellite symposia will be held within a 150-mile radius of San Diego immediately before or after the larger meeting.
Website: www.faseb.org/meetings/eb2005/call/default.htm

APRIL 2005

American Society for Biochemistry and Molecular Biology Annual Meeting in Conjunction with EB2005

April 2–6 • San Diego
Nobel Laureates Michael S. Brown and Joseph L. Goldstein will open the ASBMB Annual Meeting with the Herbert Tabor/Journal of Biological Chemistry Lecture.
Contact: ASBMB 2005, 9650 Rockville Pike, Bethesda, MD 20814-3008; Ph: 301-634-7145; Email: meetings@asbmb.org
Website: www.asbmb.org/meetings

The 46th ENC Experimental Nuclear Magnetic Resonance

April 10–15 • Rhode Island Convention Center, Providence, RI
Contact: ENC, 2019 Galisteo Street, Building I
Santa Fe, New Mexico 87505 (USA); Ph: 505-989-4573
Fx: (505-989-1073; E-mail: enc@enc-conference.org
Website: www.enc-conference.org

MAY 2005

Bone Quality: What Is It and Can We Measure It?

May 2–3 • Hyatt Regency Bethesda, Maryland
A Scientific Meeting Sponsored by the National Institute of Arthritis and Musculoskeletal Skin Diseases (NIAMS) and the American Society for Bone and Mineral Research (ASBMR)
Abstract Submission Deadline: February 8, 2005, at 5:00 p.m. EST.
For more information, call (202) 367-1161
Email: asbmr@smithbucklin.com
Website: www.asbmr.org/bonequality.cfm

EuroMedLab 2005—16th IFCC-FESCC European Congress of Clinical Chemistry and Laboratory Medicine

May 8–12 • EuroMedLab, Glasgow, UK
Contact: Jordanhill Campus Southbrae Drive Glasgow 2, UK
Email: euromedlab2005@meetingmakers.co.uk
URL http://www.glasgow2005.org

From Gene to Genome: Heredity and Society

May 26–28 • Palais de Congrès, La Grande Motte, France
Contact: Christophe Schwob
Ph: +33 4 95 09 38 00; Fx : +33 4 95 09 38 01
Email: c.schwob@mcocongres.com
Website: www.genetogenome.org

JUNE 2005

7th Annual Plant Sciences Institute Symposium; Meristems 2005

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

International Society For Stem Cell Research 3rd Annual Meeting

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

Glycoproteomics—Protein Modifications for Versatile Functions

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

JULY 2005

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

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

7th International Symposium on Biocatalysis and Biotransformations

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

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

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

BioScience2005 — From Genes to Systems

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

Gordon Research Conference on Molecular & Cellular Biology of Lipids

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

AUGUST 2005

Ninth International Congress on Amino Acids and Proteins

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

SEPTEMBER 2005

Second World Congress on Synthetic Receptors

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

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

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

International Conference on Enzyme Technology RELATENZ 2005

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

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

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

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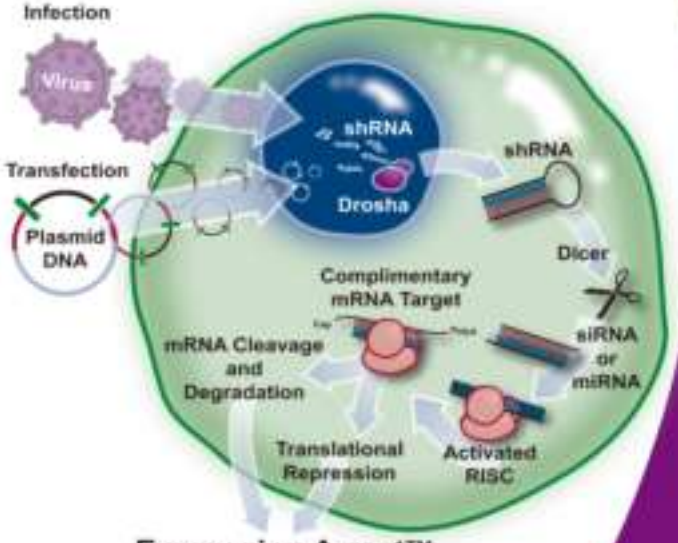

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