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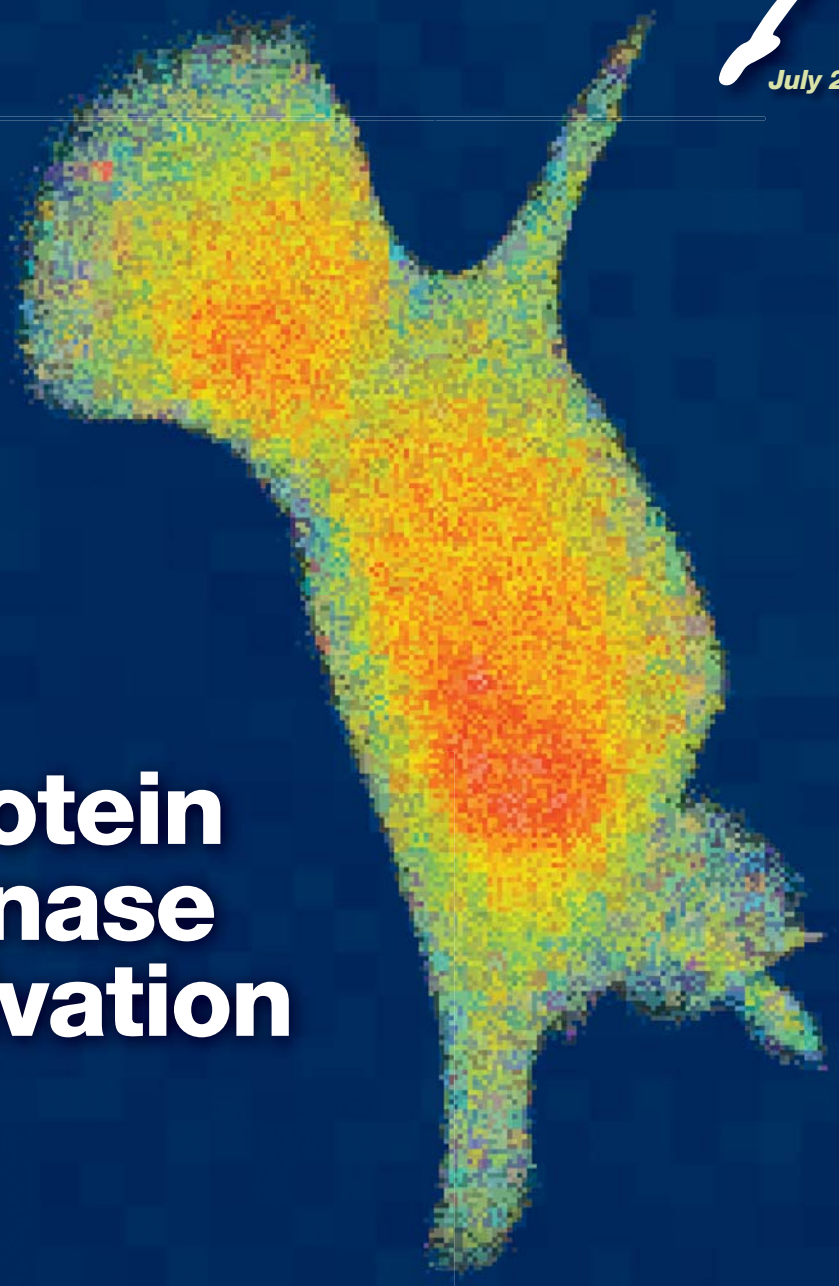
ASBMB today

July 2007



Protein Kinase Activation

American Society for Biochemistry and Molecular Biology

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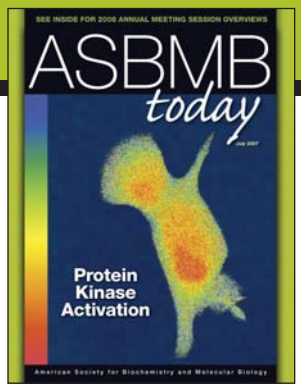

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Activity levels of protein kinase C (high levels in *blue*; low levels in *red*). Activity is highest near the cell membrane where PKC is activated by diacylglycerol. (*Photo courtesy of Alexandra C. Newton, UCSD.*) 27

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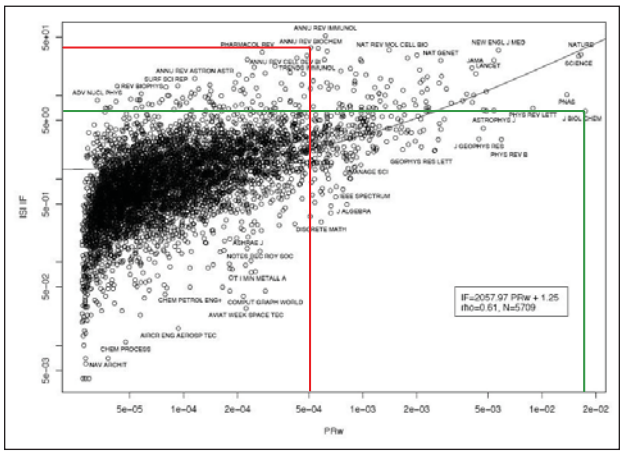

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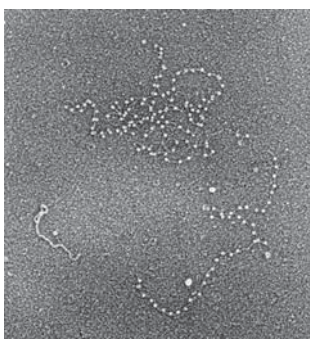

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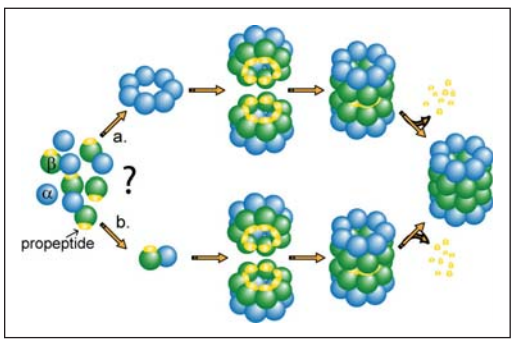

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ASBMB Today

Nicole Kresge *Editor*
nkresge@asbmb.org

Pat Pages *Science Writer*
ppages@asbmb.org

Nancy J. Rodnan *Director of Publications*
nrodnan@asbmb.org

Barbara Gordon *Executive Director*
bgordon@asbmb.org

www.asbmb.org

president's message

A Critical Year—Please Volunteer! Make Your Voices Heard

HEIDI HAMM, PRESIDENT

As reported in the article on page 5 of this issue, the situation is not looking very good for the National Institutes of Health (NIH), although things are looking very good for the National Science Foundation (NSF), which is expecting a 10% increase this year. Those of you who receive grant support from NSF would do well to drop a note to your members of Congress applauding this fine increase and urging them to support it when the bill comes to the House floor.

NIH, however, is experiencing a very different situation. The House appropriations subcommittee on Labor/Heath and Human Services (HHS) and Education, which funds NIH, provided the agency with a $750 million increase in FY2008, to $29.65 billion (a 2.6% increase). However, because the House has agreed with the President's proposal to increase the amount (by $201 million) that NIH is required to transfer to the Global HIV/AIDS program, the House subcommittee actually is proposing that NIH receive an increase in FY 2008 of only $549 million, which translates to a 1.9% increase, barely half the 3.7% rate of inflation for biomedical research. Thus, the proposed increase falls significantly short of the 6.7% increase recommended by ASBMB, FASEB, and the broader medical research community. A 6.7% increase for each of the next three years is needed to erase inflationary losses NIH has suffered since 2003. If this level of funding stands, it would be the fifth year in a row that NIH has received a subinflationary increase, and the erosion of the doubling will thus continue apace.

Flat funding will further discourage the best and brightest young scientists from pursuing a research career in the United States. Another year of failure to provide sustained, strong growth in federal support for medical and health research also exacerbates the flight of innovation overseas, leaving this country far more vulnerable to global competition.

Your voice is needed! I realize that I risk sounding like a broken record, but scientists must take the responsibility to educate their community and their Congressperson how important biomedical research is for the future health of the nation. One way you can assist in efforts to turn this situation around is to contact your member of Congress and urge him or her to support a larger increase in the bill for the NIH. You can do this in several ways. A phone call to the congressional office in Washington is one way. All members of Congress can be reached through the Capitol switchboard at 202-224-3121. You can also write to your member of Congress through the House Web site. Go to www.house.gov

and click on the "Write your representative" link at the top left of the screen. You can also reach your member of Congress through the ASBMB Web site (www.asbmb.org); go to the public affairs page and click on the "Write your Member of Congress" link toward the top of the page.

Another way that you can get involved more permanently, however, is through ASBMB's growing Local Advocates Network. This group, now over 300 strong, is comprised of ASBMB members who have volunteered to become active in their congressional districts as advocates for biomedical and scientific research funding issues. It is not necessary to have a great deal of political experience to participate in this group; all you need to do is agree to contact your member of Congress and Senators occasionally. You will be most effective if you personally meet with your Congressperson and get to know him/her. We will notify you when particularly important issues come up in Congress, but you should not feel limited to responding only to our occasional messages. Taking the initiative to contact your Representative or Senators is important as well.

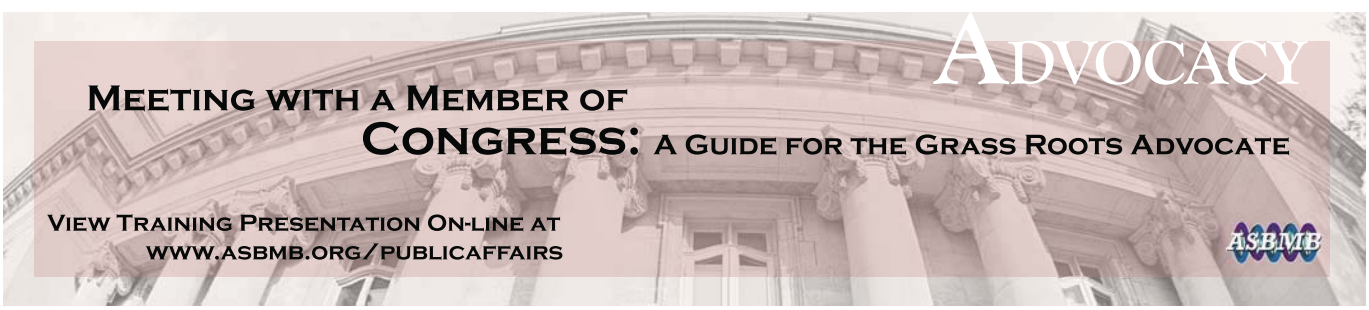
In addition, don't limit yourself to only phone calls or e-mails. A personal visit is a very important tool, particularly if it is done at home in the Congressional district. A large portion of that time at home is spent meeting with constituents at one of their district offices. Members of Congress are home from Thursday evening to Monday morning, pretty much every week. Congress usually takes August off and so your representatives will be in their districts a good bit of the month. August might be a good time to try to meet with them. Why not consider arranging to meet with your representative the next time he or she is home? This can be easily arranged, and our public affairs staff can help you with these appointments if you need advice. Students also make excellent ambassadors for biomedical research. They tend to be young, enthusiastic, and idealistic, and this attitude is usually catching. If you don't want to go to a meeting with your member along, bring a student or two along as guests. They'll find it a very valuable experience.

Another option is to invite your member of Congress to visit your lab or institution and show him or her the great work you do on behalf of the American people. These are usually very nice events, and they pay off big time in the long term. At a minimum, offer the invitation; they surely won't come if they are not invited!

ASBMB has prepared a training DVD on how to conduct a meeting with a member of Congress (see the article about the DVD, also in this issue). It should be up on the ASBMB Web site by the time you receive this issue of *ASBMB Today*, and you can either watch it on the site or download it from the Web site to a DVD and watch it later. We will also have a limited number of copies available to send you if you would like to pursue this option.

To become a member of the Local Advocates Network, send an e-mail to me (hhamm@asbmb.org) or to ASBMB's director of public affairs, Pete Farnham (pfarnham@asbmb.org), and volunteer to join. The critical piece of information Pete needs to get you involved is your 9-digit home Zip code (*i.e.* the Zip code of where you live, and thus, vote). This will allow us to make sure you get placed in the correct congressional district. Of course, if you already know who your member of Congress is, provide that piece of information as well.

In short, this is a very difficult time for biomedical research, and the NIH in particular. The agency needs your help, and anything you can do to assist us in keeping the pressure on the Congress to begin to restore NIH funding levels to what they were in 2003 would be most helpful.



ASBMB Today Welcomes New Editorial Board Members

As part of an ongoing effort to make *ASBMB Today* the highest quality magazine for our members in the U.S. and around the world, we have recently expanded the magazine's Editorial Advisory Board to more closely reflect the Society's members and interests. These new members include representatives from Europe and Asia, the biotech community, and the National Postdoctoral Association. We have also added editors from ASBMB's three journals–the *Journal of Biological Chemistry* (*JBC*), *Molecular & Cellular Proteomics* (*MCP*), and the *Journal of Lipid Research* (*JLR*).

This newly-expanded *ASBMB Today* Editorial Advisory Board is comprised of:

- **Mike Autry,** postdoctoral fellow at the University of Minnesota, president of the University of Minnesota Postdoctoral Association, and member of the National Postdoctoral Association Policy Committee.
- ASBMB Education and Professional Development Committee member **Greg P. Bertenshaw** of Correlogic Systems, Inc.
- **Craig E. Cameron,** Paul Berg Professor of Biochemistry and Molecular Biology at Pennsylvania State University, *JBC* Editorial Board member and member of the A SBMB Minority Affairs Committee.
- **Irwin Fridovich,** Emeritus James B. Duke Professor of Biochemistry at the Duke University Medical Center.
- ASBMB Past President and current *JBC* Associate Editor **Richard Hanson** of Case Western Reserve University School of Medicine.
- *MCP* Editorial Board member **Elizabeth A. Komives,** professor of Chemistry and Biochemistry at the University of California, San Diego.
- ASBMB Past President **Bettie Sue Masters** of the University of Texas Health Science Center at San Antonio.
- *JBC* Associate Editor **Luke A. O'Neill** of Trinity College, Dublin.
- *JBC* Editorial Board member **Duanqing Pei,** professor and deputy director general at the Guangzhou Institute of Biomedicine and Health.
- *JLR* Associate Editor **Carol C. Shoulders** of the Medical Research Council Clinical Sciences Centre, London, England.
- ASBMB Past President **Robert D. Wells,** Robert A. Welch Endowed Chair in Chemistry at Texas A&M University.

The Editorial Advisory Board will be chaired by *ASBMB Today* Consulting Editor Alex Toker of Harvard Medical School. These board members will act as a primary source of material for Science Focus articles and will also be involved in generating other types of articles of interest to ASBMB members.

This issue of the magazine also marks the launch of a new format for our Science Focus articles. These articles will now feature high profile scientists, with in-depth interviews about their work and their contributions to the field. Some of these featured scientists will be prominent researchers, whereas others will be new and emerging "hot" junior scientists who will shape biomedical research and emerge as the leaders of tomorrow. From time to time we will also feature articles based on recent journal articles as we have in past issues of *ASBMB Today*.

Nicole Kresge, Editor


Robert D. Wells


Carol C. Shoulders

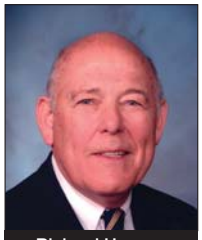

Duanquing Pei


Mike Autry


Greg P. Bertenshaw


Craig E. Cameron


Irwin Fridovich


Richard Hanson


Elizabeth A. Komives


Bettie Sue Masters


Luke A. O'Neill

2008 Appropriations Bills Begin to Move

BY PETER FARNHAM

Early June found several appropriations bills starting to move in the House, and, in marked contrast to previous years, the Labor/Health and Human Services (L/HHS) bill, which covers the National Institutes of Health (NIH), was one of the first out of the gate. In recent Congresses, the L/HHS bill was always one of the last. Unfortunately, the news for NIH—at least so far—is not as good as we had hoped.

NIH Appropriations Fall Short of Inflation—Again

The relevant appropriations subcommittee marked up the L/HHS bill on June 7 and was able to provide only an additional $750 million for NIH, translating to a 2.6% increase over the fiscal year (FY) 2007 level. This was not related to any displeasure with NIH among subcommittee members; rather, under the budget resolution, the subcommittee received an allocation that, while better than last year's, still did not allow for overly generous funding increases for the agencies under its jurisdiction.

Under the bill, NIH received $29.65 billion, which is about $750 million above the 2007 level. However, the bill also increases the amount of the transfer from NIH to the Global HIV/AIDS fund from the $99 million in FY 2007 to $300 million in FY 2008, which means the net increase in the NIH budget is $549 million (1.9%) over FY 2007. Subcommittee Chairman Dave Obey (D-WI) claimed—somewhat debatably—that the $750 million increase is the largest NIH increase in four years, although it is significantly below the ASBMB's request of $1.9 billion, or a 6.7% increase. The allocation is also below biomedical inflation (usually in the 3–4% range). You may remember that 6.7% increases for each of the next three years are needed to erase NIH's losses since the doubling was completed in 2003 and NIH began to suffer inflation-fueled cuts.

Obey noted that the bill falls short of the FY 2005 funding levels, adjusted for inflation and population growth. He pointed out that the programs funded by the L/HHS appropriations bill are "the last best hope for people without means and without advantage" and cited several "deficits" in health, education, and labor programs, admitting, "We can't erase those deficits in a single year."

The full House Appropriations Committee was tentatively scheduled to consider the bill on June 14, with House floor action planned for late June. In the past, the bill has been contentious because it presents an opportunity for both parties to highlight their differences over social issues, complicating debate. Obey has tried to steer clear of those issues so far, so there is a chance that debate on the bill will move smoothly, allowing the ambitious schedule of completing work on all appropriations bills by the end of July to be met.

Speaking on behalf of FASEB, President Leo Furcht said "This is the fourth year we've seen a proposal for NIH funding that fails to keep pace with inflation. The proposal is significantly lower than the 6.7% increase recommended by FASEB and the broader biomedical research community. The flat funding we have experienced over the past several years has had a devastating effect on the scientific enterprise. Our best and brightest young scientists are being discouraged from pursuing research careers, the pace of discovery has slowed, and we have eroded our ability to take advantage of the wealth of scientific opportunities produced by our investment in NIH."

Furcht explained that the scientific community ultimately would like a sustainable model for research funding. "To continue our astonishing progress in science and medicine, we need to recoup the losses caused by inflation during the period of flat funding," he said. "Our message is simple: a 6.7% increase each year for the next three years would get NIH back on track to restoring the erosion due to inflationary losses. FASEB feels

strongly that the best messengers to explain the value of biomedical research and why it is so necessary to provide sustainable funding are the scientists working in labs, making breakthrough discoveries."

Several reasons have been offered as to why the increase for NIH is less than we had expected. First, President Bush recommended significant increases for two programs that are very important to Democrats–a $2.5 billion increase for Pell Grants in FY 2008 and a $1 billion increase for the No Child Left Behind program. The House put significant money into these programs in order not to be outdone by the President's spending proposals—$2 billion more for Pell Grants in FY 2008 and $2 billion more for the No Child Left Behind program in FY 2008. Therefore, essentially the first $4 billion of the new money the subcommittee received under the budget resolution over FY 2007 levels was taken up by those two programs.

Second, House appropriators expect Sens. Tom Harkin (D-IA) and Arlen Specter (R-PA) to provide a significant increase for NIH when the L/HHS bill is taken up in the Senate. If the Senate does so, it is not likely to provide comparable increases for many of the programs the House regards as priorities. Thus, during conference negotiations, the House will be able to advocate for those programs for which it recommended higher funding levels (when compared to the Senate) as well as (we hope) support the expected higher Senate number for NIH. During conference negotiations in previous years, the House has been willing to accede to the higher Senate number for NIH as a way to provide additional funds to the agency.

It is important to keep in mind that we are only at the start of the appropriations process for FY 2008, and we hope that we can improve the House number as the summer continues.

NSF Numbers Looking Good

In sharp contrast to the early outlook for NIH, the National Science Foundation (NSF) has done quite well at the subcommittee level. Markup in the Commerce, Justice, Science, and Related Agencies subcommittee occurred on June 11, and NSF was treated very well. The overall total for the agency is $6.509 billion, an increase of $80 million over President Bush's request and close to $600 million over FY 2007 (about 10%). The Research and Related Activities account, which funds most of the core research at the agency, received $5.139 billion, 7.9% over last year. The Education and Human Resources account received $822.6 million, an increase of $124.6 million over FY 2007. The other major accounts at NSF—Major Research Equipment and Facilities Construction, Agency Operations, the National Science Board, and the Office of Inspector General—were all funded at the President's requested level. Full Committee markup is scheduled for mid-June.

Peter Farnham, CAE, is ASBMB's public affairs officer.

Training DVD on Meeting with Members of Congress

The ASBMB Public Affairs Advisory Committee (PAAC) has produced a training DVD called "*Meeting with Your Congressman: A Guide for the Grass Roots Advocate.*" The DVD, less than 20 minutes long, was filmed in March and debuted at the ASBMB annual meeting in Washington, D.C., in early May.

The PAAC decided to produce the DVD because of feedback it had received from many ASBMB members, who said that while they were interested in helping advocate for ASBMB interests as well as those of biomedical research, they had no idea how to go about meeting with a member of Congress and needed some guidance. The committee thus decided that a DVD showing how a meeting with a member of Congress should go would be useful.

The DVD shows two meetings between a fictional member of Congress and a delegation of biochemists from the fictional Eastern Virginia State University. In the first meeting, the visiting scientists make just about every common mistake that a group can make, including showing up late, failing to introduce themselves, behaving discourteously, not having a specific request, and arguing. Following this meeting, a narrator walks the viewer through a critique of the many mistakes made. Then, a second meeting is shown where everything goes much more smoothly. Again, the narrator critiques the second meeting, pointing out what was done properly.

The DVD was filmed on location at ASBMB headquarters and features actors from the ASBMB and FASEB public affairs staffs, as well as PAAC members Robert Palazzo and Robert D. Wells. The DVD was produced by Bayou City Productions in Houston, Texas. It is available for viewing and downloading on the ASBMB Web site under the "What's New" column. A limited number of copies of the DVD are also available; please let us know if you would like to receive one.

We hope all of you will take 20 minutes to view the DVD, particularly if you are planning on getting involved in advocacy issues.

House Version of Farm Bill Proposes Major Changes for USDA Research

BY CARRIE D. WOLINETZ

The House Agriculture Subcommittee on Conservation, Credit, Energy, and Research marked up four titles of the 2007 Farm Bill, including the research title. Oddly, the House bill appeared to be a hybrid of several proposals to restructure agricultural research at the U.S. Department of Agriculture (USDA) that had been put before Congress. Although this proposal itself is likely to undergo tremendous modification, it does illustrate the potential for increasing, changing, or improving the competitive research portfolio at the USDA. FASEB is working with society members to develop a position on the Farm Bill and to keep the research community apprised of changes. Some of the details of the House bill are included below:

- **Requires President Bush to submit a single line item in the annual budget for all agriculture research, extension, and related activities:** It is unclear whether this is government-wide, agriculture-related research or only at USDA; would nutrition research at the National Institutes of Health (NIH) count, for example? Also uncertain is the motive behind this; is this an attempt to gather difficult information or an effort to hide programs behind one large item?
- **Restructuring of USDA research:** This bill would create a new Agriculture Research Institute, which is actually a collective of six topic-specific institutes whose staff is limited to 30 positions total (not per institute) including six high profile institute directors. Although tasked with coordinating and directing all research activities of the USDA in an "integrated, multidisciplinary, interdisciplinary, interagency, and interinstitutional manner," apparently this doesn't include extramural, competitive, earmarked, or new research programs because the bill also creates a National Institute for Food and Agriculture (NIFA), an initiative supported in other venues by FASEB. Although the bill says NIFA shall administer "all competitive grants," it also reauthorizes the National Research Initiative Competitive Grants Program and earmarks quite a few separate competitive research programs (bioenergy, specialty crops, etc.).
- **An eighth institute or a sneaky way to fund IFAFS?** It's unclear whether the section authorizing the "Institute for Future Food and Agricultural Systems" is simply a mistype of "Initiative for Future Agricultural and Food Systems" (IFAFS), which currently exists, or a new entity. Although IFAFS has been authorized for a long time, it has essentially never been funded because it is not supported by appropriators. This section takes 30% of appropriated funds from National Research Initiative (NRI) and uses it to fund IFAFS activities while taking the authorized money for IFAFS and giving it to NRI. Essentially, this would result in real money being lost from competitive research at NRI and replaced with non-existent dollars. What's especially odd about this is that transfer is not reflected in the reauthorization level for NRI listed in the staff summary as the same $500 million (although no number is cited in the actual bill).
- **Confusing authorization levels:** The research title is striking in its lack of authorization levels, despite creating a host of new entities and programs. There is either no funding level mentioned or odd language such as "shall fund each research institute through appropriations available to the various agencies within the mission area." Only earmarks for targeted programs, reauthorized programs, or what appears to be an inserted stand-alone bill on viruses (see next bullet) list authorization levels.
- **Live virus bill:** Based on its structure, it seems that this section is a non-introduced stand-alone bill that has been inserted. It gives the Secretary of Agriculture the authority to create a list of viruses that could cause harm to livestock and prohibit their transportation, storage, importation, use, etc. without special permission. Although there is language to prevent this bill from applying to viruses on the USDA's select agent list, it does make one wonder: If we already have a select agent law and list that does this, why do we need another?

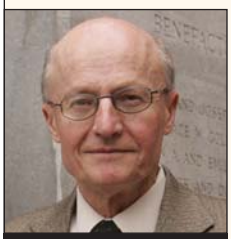
Carrie D. Wolinetz is with the FASEB Office of Public Affairs.

Biomolecular Catalysis

BY VERN SCHRAMM AND SUSAN MARQUSEE

Protein-protein interactions, macromolecular dynamics, protein and nucleic acid folding patterns, and dynamics in catalysis are the leading edge of the broadly defined field of biomolecular catalysis, one of the 15 session themes to be featured at the 2008 ASBMB Meeting in San Diego, April 5-9. Molecular dynamics occur at all size and time scales in the atomic organization of biological molecules. Functional macromolecules have evolved to harness this dynamic at both macro- and microscales to optimize biological organization and function.

Susan Marqusee



Vern Schramm

Organizers Susan Marqusee, professor of Molecular & Cell Biology, University of California, Berkeley, and Vern L. Schramm, professor of Biochemistry at the Albert Einstein College of Medicine, have assembled leaders in diverse areas of this fundamentally critical aspect of biochemistry and molecular biology.

Protein-protein interactions and multifunctional proteins have arisen from the biological need to cross water-insoluble barriers, protect reactive metabolic intermediates, eliminate toxins, and regulate protein function. In the session "Protein Interactions in Catalysis," Ruma Banerjee, University of Michigan, will describe "protein escorts" for vitamin B_{12} assimilation, an essential dietary cofactor. Susan M. Miller, University of California, San Francisco, will describe the unusual reactions catalyzed by mercuric reductase, essential for converting toxic oxidation states of mercury to less toxic forms. Protein-protein interactions are essential in the pathway of purine *de novo* synthesis, and new advances in understanding the function of these multifunctional proteins will be described by Steven J. Benkovic of the Pennsylvania State University.

The essential role of protein catalysts in disease states has made enzymes essential targets both for academic research and the pharmaceutical industry. In the session "Enzymes as Drug Targets," Chi-Huey Wong, Scripps Research Institute, will share his studies on glycoproteomic mapping for drug discovery. Synthesis of DNA in all organisms requires a balanced supply of deoxyribonucleotides, and Joanne Stubbe, Massachusetts Institute of Technology, will emphasize a new paradigm for inhibition of ribonucleotide reductases by altering subunit interactions. Computational chemistry, mutational analysis, and applications of transition state theory to enzymatic catalysis lead to the inescapable conclusion that both global and local dynamic motions of proteins are essential in enzymatic catalysis. Schramm will describe an intersection of dynamics and thermodynamics in transition state formation and inhibitor design. Several of the transition state analogues from this research program are in clinical trials for cancer and autoimmune diseases.

Perhaps no field has matured more in the past decade than that of signal transduction. The realization that protein-protein transient interactions dominate most of the interactions controlling cell division, development, differentiation, and growth has generated intense interest in exploring protein interfaces. In the session "Energetics and Design," Tanja Kortemme, University of California, San Francisco, will discuss the novel design features of protein-protein interface contacts. Vincent J. Hilser, University of Texas Medical Branch, will describe the design implications for an ensemble-based view of proteins. Susan Marqusee, University of California, Berkeley, will explain how to manipulate and detect the protein energy landscape as a protein folds to stable or not so stable states.

Protein and nucleic acid folding trajectories are problems of near infinite complexity, yet folding occurs along specific energetic landscapes controlling the specific ensembles and their dynamics. These topics are explored in the fourth session of this meeting theme with a focus on "Macromolecular Folding and Fluctuations." A. Joshua Wand from the University of Pennsylvania will discuss the surprising role for conformational entropy in molecular recognition by proteins. Dynamics and folding in nucleic acids have been probed with ever increasing molecular resolution, and Michael Brenowitz from the Albert Einstein College of Medicine will describe rapid footprint

technology as a step towards single nucleotide resolution in the RNA folding problem. Our perspective on protein folding is often clouded by the differences in using defined experimental conditions compared to those in the cell. Lila M. Gierasch from the University of Massachusetts, Amherst, will explore her findings with us in her studies on the influence of the cellular environment on protein folding and stability.

It will not escape the prudent reader that the meeting theme of Biomolecular Catalysis is tightly interconnected with other themes of the meeting. Chemical Biology, RNA, Metabolism, Signaling, and Molecular Dynamics are all represented here as well as being the focus of other themes for the 2008 ASBMB Meeting. This structure provides high quality scientific sessions throughout the meeting. We look forward to seeing you in San Diego.

Biomolecular Catalysis, Folding, and Design Thematic Meeting

Organizers: Susan Marqusee, University of California, Berkeley, and Vern Schramm, Albert Einstein College of Medicine

Symposium: Protein Interactions in Catalysis

- *Enzyme and Escort Service in B12 Assimilation*, Ruma Banerjee
- *The Mercuric Reductase System*, Susan M. Miller
- *Protein Interactions in de novo Purine Synthesis*, Steven J. Benkovic

Symposium: Enzymes as Drug Targets

- *Glycosyltransfer Enzymes as Targets for Glycoproteomic Mapping and Drug Discovery*, Chi-Huey Wong
- *A New Paradigm for Inhibition of Ribonucleotide Reductases: Enhanced Subunit Interactions with Substoichiometric amounts of Gemzar 5'- diphosphate*, Joanne Stubbe
- *Targeting Purine Salvage in Cancer and Malaria*, Vern L. Schramm

Symposium: Energetics and Design

- *Design of Selective and Multispecific Protein Interfaces*, Tanja Kortemme
- *Design Implications for an Ensemble-based View of Proteins*, Vincent J. Hilser
- *Manipulating and Detecting a Protein's Energy Landscape*, Susan Marqusee

Symposium: Macromolecular Folding and Fluctuations

- *A Surprising Role for Conformational Entropy in Molecular Recognition by Proteins*, A. Joshua Wand
- *A Step Toward Solution of the RNA Folding Problem*, Michael Brenowitz
- *The Influence of the Cellular Environment on Protein Folding and Stability*, Lila M. Gierasch

Genome Dynamics: Replication, Recombination, and Damage Response

BY PETER BURGERS AND TOM ELLENBERGER

Mutational drift of the genome is held in check by accurate replication and DNA repair mechanisms. These essential functions are in turn regulated by cell cycle checkpoints and other DNA damage responses that mobilize repair enzymes or trigger programmed cell death when irreparable damage ensues. Although DNA damage can result from exposure to environmental toxins, reactions with endogenous metabolites and the stalling of replication forks can cause more pervasive problems, resulting in covalent modifications and DNA strand breaks. The genome dynamics theme of the 2008 ASBMB Meeting will feature a rich menu of talks covering structures, enzymatic mechanisms, and regulation of DNA replication and repair proteins, complexes, and pathways.

Tom Ellenberger (*left*) and Peter Burgers.

The "DNA Replication Mechanisms" session will focus on factors that function in the regulation of initiation and termination of DNA replication. Anja Bielinsky (University of Minnesota) will discuss how the eukaryotic replication initiation protein Mcm10 is switched from an initiation mode into an elongation mode by ubiquitination. While unmodified Mcm10 binds DNA polymerase α and promotes initial primer formation, its ubiquitinated form binds proliferating cell nuclear antigen (PCNA), and this form may recruit PCNA to the primer terminus during lagging strand DNA replication. Nicholas Dixon (Wollongong University) has determined how the polarity of binding of the *Escherichia coli* replication termination protein Tus to its *ter* sequence allows it to block a replication fork traveling in one direction but not in the opposite direction. Polar binding of Tus makes it operate as a "molecular mousetrap" capturing single-stranded DNA as it is being unwound during fork movement. Laurie Kaguni (Michigan State University) will describe a close-up view of the mitochondrial DNA replication fork, including the interactions that govern high fidelity mitochondrial DNA replication and molecular defects associated with dysfunction of the mitochondrial replication apparatus.

The "DNA Damage Response and the Cell Cycle" session will focus on DNA damage response mechanisms in eukaryotic cells that alter the functionality of the replication fork or cause a temporary inhibition of cell cycle progression for repair of DNA damage to be completed before advancing to the next phase in the cell cycle. David Orren (University of Kentucky) is interested in the function of the WRN and BLM DNA helicases. Patients with Werner or Bloom syndrome are defective for helicase function, show defects in genome stability, and are cancer-prone. He will discuss the roles of these DNA helicases in the stabilization of stalled replication forks, in the resolution of replication blockage, and in the maintenance of telomeres. Two talks in this session will discuss the biochemical function of checkpoint proteins that link DNA damage to progression of the cell cycle. Peter Burgers (Washington University) will discuss how the PCNA-like checkpoint clamp recognizes DNA structures that are formed during DNA repair. Loading of the checkpoint clamp onto these DNA structures causes activation of the ATR kinase that propagates the signal downstream leading to inhibition of the CDK kinases that drive the cell cycle. Karlene Cimprich (Stanford University) has studied checkpoint function in Xenopus extracts. Such extracts faithfully reproduce DNA replication and its control and are amenable to biochemical analysis. She will present studies elucidating the DNA structures that link damaged replication forks to cell cycle checkpoints.

The "DNA Repair Mechanisms" session will feature the biochemical mechanisms of DNA repair reactions in a broad variety of damage-specific responses. Tom Ellenberger (Washington University, St. Louis) will describe several protein-protein interactions in the nucleotide excision repair (NER) pathway that are essential for the removal of helix distorting lesions. Small molecule inhibitors of these interactions are being developed to dissect alternative repair pathways that share components of the NER pathway. Repair proteins that participate in multiple pathways of excision repair may represent control nodes

for differential regulation of alternative pathways. Manju Hingorani (Wesleyan University) is examining how mutations resulting from replication errors are corrected in *E. coli* and *Saccharomyces cerevisiae* by mismatch repair (MSH) proteins. The MSH proteins recognize defects in DNA base pairs and bind to MLH proteins that signal downstream events ultimately resulting in DNA repair. Steady-state and presteady-state kinetic studies of DNA damage recognition and processing events will be described, addressing the dynamics of binding and signaling during the repair of mismatched base pairs. John Hunt (Columbia University) will describe crystallographic and biochemical studies of *E. coli* AlkB, which was recently shown to remove aberrant methyl groups from DNA in a multistep reaction coupled to the oxidation of 2-oxoglutarate. His work has demonstrated a structural plasticity of the enzyme that accommodates a diverse group of methylated bases as substrates. The functions of eight mammalian paralogues of AlkB (ABH1-8) are being explored.

In the "Double-stranded Breaks and DNA Recombination" session, Michael Cox (University of Wisconsin) will describe the mutational spectra of *E. coli* strains that were selected for extreme resistance to ionizing radiation (enough to introduce more than 100 double strand breaks per genome). The full genomics sequences of independent strains exhibiting 2,000- to 10,000-fold resistance reveal a surprising diversity of independent mutations, some of which are likely to enhance the processing of double-strand DNA breaks. In collaboration with John Battista (Louisiana State University), the functionally important genes are being identified, which should reveal the complexity of cellular responses to this potentially lethal form of DNA damage. Tanya Paull (University of Texas, Austin) is studying the mechanisms of DNA double-strand break repair and break induced signaling pathways in eukaryotic cells. Her talk will focus on the Mre11/Rad50/Nbs1 (MRN) complex, which plays a central role in recognizing and repairing DNA breaks. The MRN complex also recruits and activates ATM, the protein kinase that activates a damage-induced cell cycle checkpoint that leads to apoptosis. Biochemical studies that reveal the molecular basis of MRN and ATM functions and their interactions will be related to observations of DNA repair and signaling in eukaryotic cells. Homologous recombination is a high fidelity strategy for the templated repair of complex forms of DNA damage, including double-stranded DNA breaks and interstrand cross-links. Moreover, recombination supports DNA replication in the recovery of broken replication forks and the repair of gaps caused by fork stalling. Wolf-Dietrich Heyer (University of California, Davis) will describe studies of the transition between the central reaction of recombination—the search for homology search and DNA strand invasion—and the priming of DNA synthesis by the invading DNA 3'-end. The Snf2 family motor protein Rad54 promotes DNA strand invasion and the subsequent turnover of the Rad51 recombinase, exposing the end of the invading DNA strand for DNA synthesis. This transition to DNA synthesis is critical and should only occur when the strand invasion occurred at the correct site, increasing the fidelity of DNA repair by homology-dependent recombination pathways.

These principal talks will be complemented with short talks selected from submitted abstracts in these areas. We look forward to many fruitful discussions in the ever developing field of genome dynamics.

Genome Dynamics: Replication, Recombination, and Damage Response Thematic Meeting

Organizers: Peter Burgers, Washington University, and Tom Ellenberger, Washington University

Symposium: DNA Replication Mechanisms

- *Dynamics of the Mitochondrial Replication Fork,* Laurie Kaguni
- *Termination of DNA Replication in E. coli,* Nick Dixon
- *Role of Mcm10 in Yeast DNA Replication,* Anja Bielinsky

Symposium: DNA Damage Response and the Cell Cycle

- *Clamp-ATR Kinase Interactions in Checkpoint Function,* Peter Burgers
- *Role for the Werner Syndrome Protein (WRN) in Replication Fork Regression,* David Orren
- *DNA Damage Checkpoints in Xenopus Extracts,* Karlene Cimprich

Symposium: Double-Stranded Breaks and DNA Recombination

- *Rapid Evolution of Radiation Resistance in Escherichia coli,* Michael Cox
- *Mechanism of Recombination in Eukaryotes: Some Remodeling Required,* Wolf-Dietrich Heyer
- *MRE11-RAD50-NBS1 Complex and Double Strand Break Repair,* Tanya Paull

Symposium: DNA Repair Mechanisms

- *Structural Insights in Nucleotide Excision Repair,* Tom Ellenberger
- *Mopping Up after Messy Polymerases,* Manju Hingorani
- *Oxidative DNA Repair by AlkB Family Metalloenzymes,* John Hunt

Dynamic Chromatin—Chromosomes in Action

BY BRAD CAIRNS AND DANESH MOAZED

In recent years, remarkable progress has been made in our understanding of chromatin dynamics–the construction and remodeling of specialized chromosomal domains to regulate diverse chromosomal processes. Researchers leading this progress will be featured during the "Dynamic Chromatin and Gene Expression" theme at the 2008 ASBMB Meeting.

Chromosomes are complex and dynamic and are partitioned into domains of differing chromatin character through multiple mechanisms. First, in addition to canonical nucleosomes, histone variant nucleosomes are placed at particular locations such as centromeres to confer specialized functions. Second, covalent modifications (such as acetylation or methylation) on nucleosomes attract proteins important for establishing the composition and character (silent or active) of the gene or region. Third, nucleosomes are mobilized and/or ejected by complexes termed "remodelers" to assume the correct positions and density on the DNA, which can facilitate or impede processes such as transcription. Additionally, the process of transcription itself, as well as noncoding RNA molecules derived from transcription, can directly affect the chromatin structure in a region. These four processes work together to both build and alter particular chromatin domains: to help form centromeres/kinetochores, to protect DNA at chromosome ends (telomeres), to facilitate recombination, to regulate transcription, and to localize and assist DNA repair machinery.

Brad Cairns

Danesh Moazed

Current research in chromatin dynamics is focused on understanding how chromatin regulatory factors work together (or antagonistically) to establish and maintain chromatin domains, to form boundaries between chromatin domains, and to coordinate transitions between alternative chromatin states. The chromatin dynamics theme addresses these areas and will be divided into four sessions: 1) "Chromatin Regulation of DNA Repair, Recombination, and Genome Stability" (chair: Xuetong Shen, University of Texas M. D. Anderson Cancer Center); 2) "Chromatin Structure in Gene Activation" (chair: Yang Shi, Harvard Medical School); 3) "Chromatin Changes in Development" (chair: Brad Cairns, University of Utah/ Howard Hughes Medical Institute); 4) "Non-coding RNAs in Gene Regulation and Chromosome Structure" (chair: Danesh Moazed, Harvard Medical School).

The session "Chromatin Regulation of DNA Repair, Recombination, and Genome Stability" will address how DNA repair systems find sites of DNA damage within repressive chromatin, alter chromatin to facilitate repair, and halt the cell cycle to enable repair. Shen will discuss how nucleosome remodeling factors alter chromatin structure during DNA repair. Jim Haber (Brandeis University) will discuss how the cell cycle and the DNA repair process are coordinated through checkpoint pathways. Jennifer Gerton (Stowers Institute for Medical Research) will discuss machinery that helps chromosomes associate to facilitate recombination and DNA repair.

How genes transition between repressed and active states will be addresses in the session "Chromatin Structure in Gene Activation." An important part of this transition involves the methylation and demethylation of histone proteins, which guides the binding of transcriptional regulatory factors. Shi will discuss the identification and characterization of histone demethylases and their roles in transcriptional regulation. Nucleosomes are assembled at gene promoters to facilitate repression and ejected to facilitate activation. Jessica Tyler (Colorado State University) will describe new insights on the factors that regulate the dynamic nucleosome assembly and disassembly at genes. A key question in transcriptional regulation is how chromatin modifications help guide transcriptional states. Richard Young (Massachusetts Institute of Technology) will discuss new data on how particular chromatin modifications help poise genes for different future transcriptional

states, a process of particular importance in embryonic stem cells, which are pluripotent.

How chromatin structures help guide development is featured in the session "Chromatin Changes in Development." One of the most fascinating examples of chromatin specialization during development involves the establishment and maintenance of the X chromosome inactivation in female mammals. Jeannie Lee (Massachusetts General Hospital) will report new information on the function of noncoding RNAs and chromatin regulators in the X inactivation process. During meiosis, homologous chromosomes must be intimately paired to ensure proper chromosome segregation. Abby Dernburg (University of California, Berkeley) will discuss recent breakthroughs involving the identification of pairing sequences and associate proteins that orchestrate meiotic chromosome dynamics. Other key questions at the chromatin development interface include the chromatin packaging and DNA methylation status of germ cells (sperm and eggs) and how these states change during fertilization and early development. Cairns will discuss recent progress in this area using zebrafish as a model system.

Talks in the session "Non-coding RNA in Gene Regulation and Chromosome Structure" will focus on the roles of both large and small noncoding RNAs in regulation of gene expression and chromatin structure. In fission yeast, components of the RNA interference (RNAi) are required for the assembly of large heterochromatic domains at repetitive DNA regions that surround centromeres. Moazed will present data on biochemical analysis of RNAi and heterochromatin complexes that work together to assemble and maintain heterochromatin. Plants have perhaps the most remarkable and extensive noncoding RNA regulatory system with well established roles for small RNAs (sRNAs) in regulation of both DNA and histone methylation. Craig Pikaard (Washington University) will speak about the role of sRNAs in silencing of large chromosome domains involved in nucleolar dominance in Arabidopsis. The reverse transcriptase telomerase adds simple repetitive DNA elements to chromosome ends using a non-coding RNA cofactor as the template to compensate for DNA loss during replication. Kathleen Collins (University of California, Berkeley) will report new progress on understanding how the telomerase ribonucleoprotein complex is assembled and regulated.

Dynamic Chromatin and Gene Expression Thematic Meeting

Organizers: Brad Cairns, Howard Hughes Medical Institute/ University of Utah School of Medicine, and Danesh Moazed, Harvard Medical School

Symposium: Chromatin Regulation of DNA Repair, Recombination, and Genome Stability

- *Chromatin Responses in DNA Repair,* Xuetong Shen
- *Chromatin and DNA Damage Checkpoints,* Jim Haber
- *Chromatin Cohesion and Recombination,* Jennifer Gerton

Symposium: Chromatin Structure in Gene Activation

- *Histone Methylation and Demethylation in Gene Regulation,* Yang Shi
- *Transcriptional Regulation by Chromatin Assembly and Disassembly,* Jessica Tyler
- *ES Cell Pluripotency and Chromatin,* Richard Young

Symposium: Chromatin Changes in Development

- *Chromosome Pairing during Meiosis,* Abby Dernburg
- *Chromosome Marking and Modification during Zebrafish Development,* Brad Cairns
- *X Chromosome Inactivation,* Jeannie Lee

Symposium: Non-coding RNAs in Gene Regulation and Chromosome Structure

- *Non-coding RNAs in S. pombe,* Danesh Moazed
- *siRNA Involvement in Multi-megabase Chromosomal Silencing in Nucleolar Dominance,* Craig Pikaard
- *Telomerase Ribonucleoprotein Assembly and Activity,* Kathleen Collins

Chemical Biology

BY ANNA MAPP AND LAURA KIESSLING

Defining the rapidly evolving field of chemical biology is challenging. Perhaps the difficulty arises because of the prevalence of interdisciplinary research that interweaves ideas and methods from biology and chemistry. Therefore it is appropriate that the chemical biology theme of the 2008 ASBMB session focuses on neither a general research topic nor the application of a key method—rather, it showcases a broad array of research at the interface of chemistry and biology. The topics of the individual sessions range from imaging to neuroscience to small molecule control of cellular processes. The common thread linking these areas and the individual presentations is the ability to explore biological questions using molecules (and assemblies) not found in nature.

Anna Mapp

Laura Kiessling

The contributions of chemical biology to imaging cellular processes have been dramatic and wide ranging. Since the introduction of the fluorescent calcium ion sensors, appreciation of the value of using designed compound to visualize key signaling pathways has grown. Chemical biology continues to make critical contributions to this area, and the chemical biology session, entitled "New Strategies for Imaging Protein Localization and Dynamics," highlights some recent developments. One challenge is the ability to selectively illuminate proteins based upon their conformation and/or functional state. Jin Zhang (Johns Hopkins University) has developed a novel approach to visualizing kinase activity in living cells. Her method combines protein engineering and Forster Resonance Energy Transfer to report on the activity of those enzymes. Ron Raines (University of Wisconsin, Madison) has developed another type of probe for imaging; his group has designed a new class of "latent" fluorophores that are unmasked upon cellular uptake. These can be used to follow internalization, as illustrated by his studies exploring the cellular toxicity of ribonucleases. The research of Jay Groves (University of California, Berkeley) is focused on combining imaging and nanoscience methods to explore how the spatial arrangement of signaling receptors controls output responses. He uses nanopatterned substrates to organize the signaling molecules inside living cells into defined geometries. With new developments in surface science, he can control the number of receptors in a signaling cluster, which makes it possible dissect mechanisms of signal amplification.

A forefront area of biology is understanding the molecular details underlying nervous system function. Chemical biology approaches to the problem can address fundamental questions in this area from a new perspective. The second session, "Chemical Perspectives in Neurobiology," highlights the benefits of this approach. Baldomero Olivera (University of Utah) takes advantage of the potent and selective venom peptides from cone snails that show remarkable selectivity for individual neuroreceptor classes. These peptides are then used to decipher the physiological roles of the receptors in signaling and, ultimately, to develop novel drug candidates. Rather than using peptides or proteins from nature, Dennis Dougherty (Caltech) incorporates unnatural amino acid residues into specific neuroreceptors to probe the structures and mechanisms of ion channels. In contrast, Ehud Isacoff (University of California, Berkeley) uses environmentally sensitive fluorescent dyes attached in a site-directed manner to membrane proteins to report local protein motion during functional rearrangements. He applies this method to ion channels to understand the mechanism by which they sense physiological signals and gate.

The use of bioactive small molecules to study protein structure and function has a long and storied history in chemical biology, and the third session, "Small Molecule Control of Protein Folding and Assembly," spotlights new directions in this arena. Two of the speakers, Aseem Z. Ansari (University of Wisconsin-Madison) and Anna Mapp (University of Michigan), use small molecules to control the assembly of multiprotein complexes. Ansari has identified minimal interaction motifs from developmentally important transcription factors that can be used to nucleate and stabilize transcription factor complexes at gene promoters. Mapp has developed small organic molecules that mimic natural transcriptional activators and, depending upon the context,

can be used to up- or down-regulate targeted genes in cellular systems by affecting transcriptional machinery assembly. The final speaker, Tom Muir (Rockefeller University), has developed a general strategy for controlling the timing of protein production within cells. His approach triggers rapid production of the protein of interest because it relies on small molecule responsive protein splicing.

The final session, "Chemical Probes and Their Use in Identifying New Therapeutic Targets," is focused on the types of studies that are identified with chemical biology—the use of small molecule probes to explore biological systems. The speakers in this session will discuss how small molecule probes can illuminate and validate pathways with potential therapeutic value. Randy Peterson (Harvard Medical School) takes advantage of high throughput small molecule screens in zebrafish to identify modifiers of organismal processes, ranging from those in developmental biology to adult disease. Such screens have been used to identify novel small molecules that modify the *in vivo* development of blood and blood vessels and that serve as powerful tools to explore the biology of blood and vascular diseases. Helen Blackwell (University of Wisconsin, Madison) also studies signaling, but she focuses on bacteria. She is investigating quorum sensing (the process by which bacteria sense their population density) by creating her own language of small molecule modulators. Compounds that interfere with bacterial communication could lead to the development of new classes of antibiotics. Laura Kiessling (University of Wisconsin-Madison) is using synthetic molecules to elucidate and inhibit key steps in the biosynthesis of the mycobacterial cell wall. Her studies are providing insight into the synthesis of biological polymers in the absence of a template. They also suggest new targets for treatment of tuberculosis.

The strategies and interdisciplinary approaches that will be described in the chemical biology sessions are applicable to diverse systems. We anticipate that these sessions will stimulate lively discussions and even new collaborations. We are looking forward to the meeting and hope to see you there.

Chemical Biology Thematic Meeting

Organizers: Laura L. Kiessling, University of Wisconsin-Madison, and Anna K. Mapp, University of Michigan

Symposium: New Strategies for Imaging Protein Localization and Dynamics

- *Dynamic Visualization of Kinase Activity in Living Cells*, Jin Zhang
- *Latent Fluorophores for Biomolecular Imaging*, Ron Raines
- *Spatial Organization and the Mechanics of Cellular Signal Transduction*, Jay Groves

Symposium: Chemical Perspectives in Neurobiology

- *Using Conus Venom Peptides to Understand Nervous Systems and Discover Drugs*, Baldomero Olivera
- *Neuroreceptors of the Nicotinic Class: Structure to the Rescue?*, Dennis Dougherty
- *Optical Probing of Neuronal Membrane Proteins*, Ehud Isacoff

Symposium: Small Molecule Control of Protein Folding and Assembly

- *Cutting and Pasting Proteins in Vitro and in Vivo*, Tom Muir
- *Regulated Assembly of Transcriptional Complexes by Engineered Synthetic Ligands*, Aseem Ansari
- *Dissecting Protein Complexes with Small Molecules*, Anna Mapp

Symposium: Chemical Probes and Their Use in Identifying New Therapeutic Targets

- *Zebrafish Chemical Biology–Discovering Modifiers of Development and Disease*, Randall Peterson
- *Synthetic Ligands That Attenuate Bacterial Quorum Sensing and Outcomes*, Helen Blackwell
- *Small Molecule Probes of Mycobacterial Cell Wall Assembly*, Laura Kiessling.

Impact Factor Page Rank*led*

BY VINCENT C. HASCALL[‡†1], JOHAN BOLLEN[§], AND RICHARD W. HANSON[¶†1]

> **"Everything in life should be as simple as possible, but no simpler."**
>
> **Albert Einstein**

Prologue

Those of us who have used Google to search for items of interest cannot help but be amazed at its speed and accuracy. Somehow, it is able to list items of interest in an order ranging from the most important to the least important, and to do so for hundreds of thousands of entries! The brilliance of Google lies a good deal in its search algorithm, *PageRank*, named after one of its originators, Larry Page. PageRank is based on the Perron-Frobenius Theorem (Google lists 96,000 entries for this theorem), which is used extensively in algebraic graph theory, to establish the importance of a specific site on the Web, thus "bringing order to the Web." Since scholarly journals are now almost exclusively published on the Web, PageRank provides a potentially unique algorithm to evaluate both the relative importance of journals and the individual papers published in these journals. In this article, we review the recent use of PageRank to evaluate 5,709 scholarly journals that are currently published online and compare the results to those found using the currently popular method for ranking journals, Impact Factor. The *Journal of Biological Chemistry* (*JBC*) was ranked first by PageRank but 180th by Impact Factor. The possible reason for this dramatic difference in journal ranking, and its potential significance in ranking scholarly journals published on the Web, is the subject of this article.

Impact Factor *Versus* PageRank

Evaluating the relative impact of a paper published in the biomedical science literature has become more than a curiosity for authors interested in determining who is reading their work. In many institutions around the world, the perceived quality of the journals in which the research is published is being used as a key indicator of the scientific quality of the research itself. Promotion within an organization is often based not only on the number of an individual's publications but also on the impact that these publications have on research in their respective field of biomedical science. Different methods are used to establish impact, including letters and discussions with scientists in the field. One presumption in the review process is that the higher the impact of the journal in which the research is published, the better the research, and that a journal's impact may be evaluated objectively in relation to other journals. Thus it is of importance to evaluate the current methods by which the relative status of journals, and presumably the quality of the published research in these journals, is established.

The Impact Factor (IF), developed by Eugene Garfield of the Institute for Scientific Information (ISI), has been virtually the only method used to determine the relative impact of a scientific research publication. The IF is defined as the number of citations a journal receives over a two-year period divided by the number of research papers and reviews published in that journal. A number of articles and commentaries have noted inherent problems with the IF. These include: 1) the inclusion of review articles; 2) the inclusion of citations in commentaries, errata, and letters in the numerator, but not in the denominator of the equation used to calculate the IF; 3) the highly skewed, non-Gaussian distribution of citations for the articles; and 4) the lack of consideration of the size of the different fields of science represented in different journals. It is of interest that 7 of the top 10 journals with the highest IF publish only reviews and are often cited by authors to broadly cover an area of research on a specific subject (*Annual Reviews of Immunology* is number one on the list, and *Annual Reviews of Biochemistry* is number two) (Table I). While no single factor can address all of these issues fairly, the question remains whether there is a method to evaluate the status of a journal that provides a different, more

From the [‡]Department of Biomedical Engineering, the Cleveland Clinic, Cleveland, Ohio 44195, [§]Digital Library Research & Prototyping Team, Los Alamos National Laboratory, Los Alamos, New Mexico 87545, and the [¶]Department of Biochemistry, Case Western Reserve University School of Medicine, Cleveland, Ohio 44106-4935

[1]Associate editors of the *Journal of Biological Chemistry*.

TABLE I
The highest ranking journals according to the 2003 ISI IF, Weighted PageRank, and Y-factor, reproduced from Ref. 3

	ISI IF		PR_w 3 10^3		Y-factor 3 10^2	
rank	value	Journal	value	Journal	value	Journal
1	52.28	ANNU REV IMMUNOL	17.46	J BIOL CHEM	51.15	NATURE
2	37.65	ANNU REV BIOCHEM	16.51	NATURE	47.72	SCIENCE
3	36.83	PHYSIOL REV	16.02	SCIENCE	19.92	NEW ENGL J MED
4	35.04	NAT REV MOL CELL BIO	13.77	PNAS	14.36	CELL
5	34.83	NEW ENGL J MED	8.90	PHYS REV LETT	14.14	PNAS
6	33.95	NAT REV CANCER	5.93	PHYS REV B	11.32	J BIOL CHEM
7	33.06	CANCER J CLIN	5.72	NEW ENG J MED	8.73	JAMA
8	30.98	NATURE	5.40	ASTROPHYS J	7.83	LANCET
9	30.55	NAT MED	5.39	CELL	7.22	NAT GENET
10	30.17	ANNU REV NEUROSCI	4.90	J AM CHEM SOC	6.26	PHYS REV LETT

balanced approach for specifically assessing research contributions. In this regard, it is interesting that Eugene Garfield commented in a September 2005 speech in Chicago (1) that "In 1955, it did not occur to me that 'impact' would one day become so controversial. Like nuclear energy, the impact factor is a mixed blessing, I expected it to be used constructively while recognizing that in the wrong hands it might be abused."

The PageRank algorithm, which was developed by Brin and Page (2), forms the basis of the Google search engine now widely in use. A recent article by Johan Bollen and colleagues (3) describes the use of this algorithm to obtain a metric that reflects the *prestige* of a journal. They point out that IF is in reality an indicator of the *popularity* of a journal since it reflects the number of citations per article published over a two-year period, but it does not consider the relative *prestige* of the journals that cite the article. As noted by Bollen *et al.* (3), "Google's PageRank algorithm…computes the status of a web page based on a combination of the number of hyperlinks that point to the page and the status of the pages that the hyperlinks originate from. By taking into account both the popularity and the prestige factors of status, Google has been able to avoid assigning high ranks to popular but otherwise irrelevant web pages." The term "popular but otherwise irrelevant" as used in this context refers to publications that review, but do not themselves contain, the original scientific information being cited.

The Google PageRank algorithm is not limited to the Web; it can be applied to any network. If PageRank works so well for the Web hyperlink network, why not translate it to citation data and calculate journal PageRank (PR) values for the same journal citation network data now used to calculate the ISI IF?

Using PageRank to Rank Journals

What would happen if one were to rank all published scientific journals by their ISI IF and PR values calculated on the basis of the same citation data? Bollen *et al.* (3) have answered this question by comparing the Impact Factor and PageRank methods using the ISI 2003 citation database for 5,709 scientific journals (Fig, 1, Table I). Interestingly, the *Journal of Biological Chemistry* ranks first of all scientific journals in the PageRank method (Fig. 1, *horizontal green bar*); it is in a class with *Nature, Science*, and the *Proceedings of the National Academy of Sciences U.S.A.*, which publish articles in many different fields and serve other functions as well. In contrast to its high score in the PageRank assessment, the *Journal of Biological Chemistry* ranks ~180th overall among the 5,709 journals in its IF (Fig. 1, *vertical green bar*). For comparison, the *Annual Reviews of Biochemistry* ranks in second place on the IF scale but much lower than *JBC* on the PageRank scale (Fig. 1, *red bars*). In an interesting extension of the concept of prestige and popularity, Bollen *et al.* (3) proposed a new metric for the evaluation of scientific journals that takes into account *both* IF and PageRank, which they term the Y-factor. Thus, journals that score highly on the basis of their Y-factor will be highly ranked by either or both the IF and PageRank. As shown in Table I, the *Journal of Biological Chemistry* ranks number six among all journals in its Y-factor score.

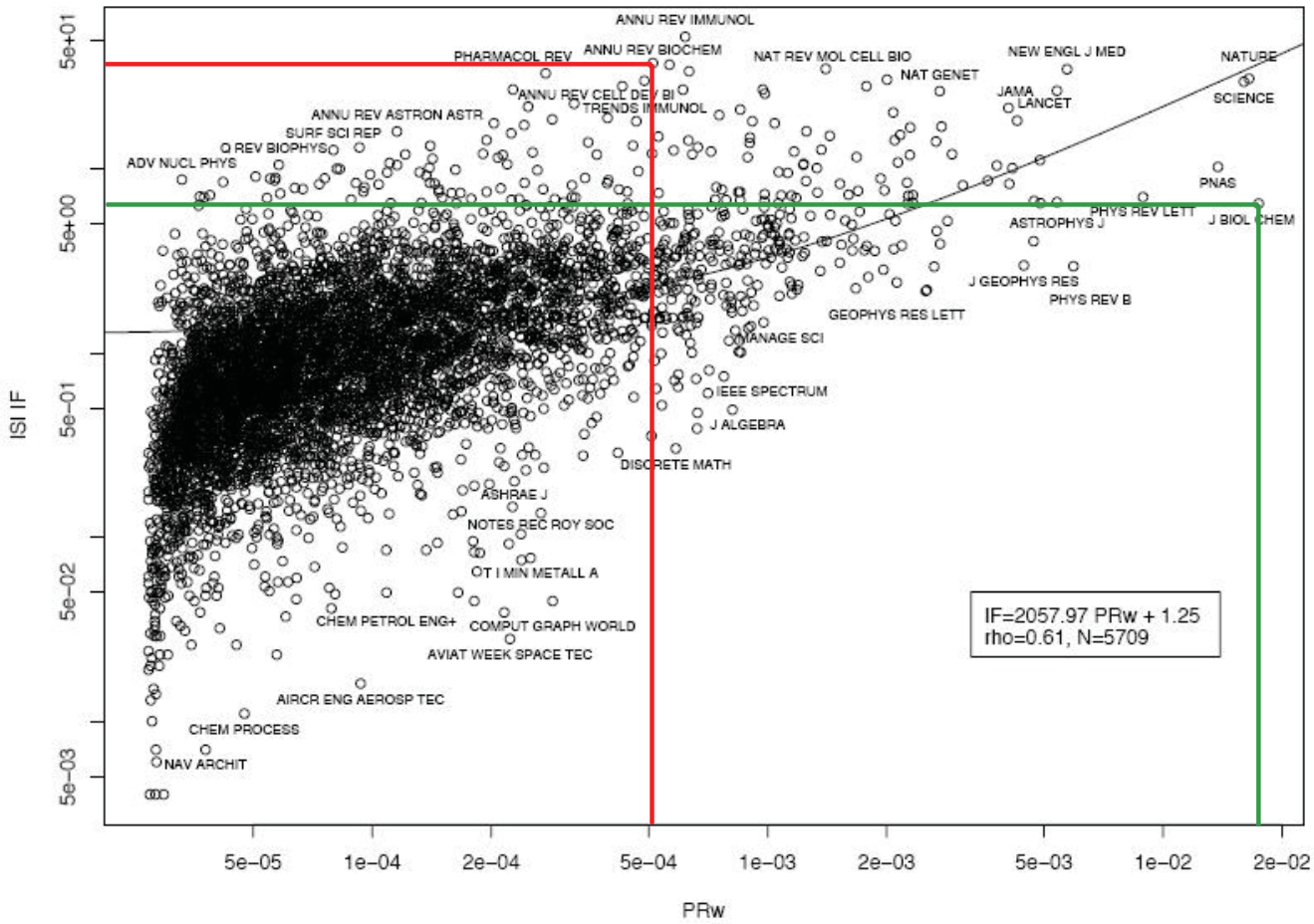


Fig. 1. **Scatter plot of 2003 ISI IF versus the Weighted PageRank (*PRw*).**

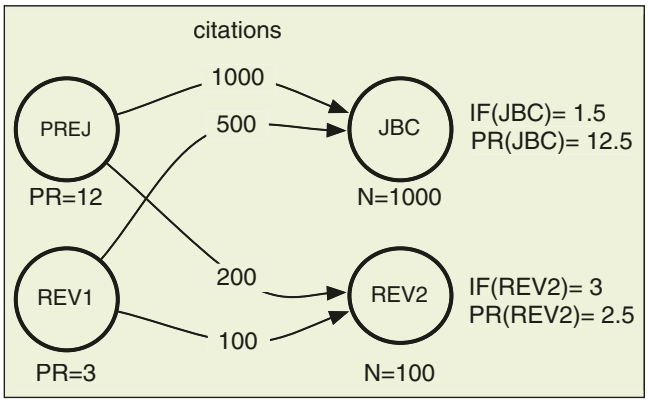


Fig. 2. **IF and PR lead to different rankings.**

How do the methods for ISI Impact Factor and the PageRank actually compare? Fig. 2 provides a model with four journals that demonstrates how IF and PR compare. In the model, two journals, PREJ and REV1, have cited two other journals, the *JBC* and REV2, during the test period. PREJ, a prestigious journal such as *Science*, cited the *JBC* 1,000 times and REV2 200 times, while REV1 cited the *JBC* 500 times and REV2 100 times. During the test period, the *JBC* published 1,000 papers, and REV2 published 100 papers. These ratios of citations of the *JBC* to a review journal (REV2) are reasonably realistic, as are the relative number of articles in the two journals. The IF divides the total citations for a journal by the number of articles published during the test period. This gives IF values of 1,500/1,000 = 1.5 for the *JBC* and 300/100 = 3 for REV2. Therefore the IF method in this model gives a higher number to the review journal.

The PageRank method gives each journal the same PR value at the beginning of the calculation and then follows the citations back and forth between pairs of all the journals in an iterative process in which the PR values are redistributed between journals as determined by the citations that point to each, compared with citations that point from each of the respective journals. The iteration is continued until the PR values converge to stable values as guaranteed by the Perron-Frobenius theorem. To illustrate this with the model in Fig. 2, assume that in this iteration the PR values of the two citing journals are 12 for PREJ

and 3 for REV1, which are also realistic relative values for a "prestige" journal such as *Science* and a "popular" review journal. The PR values of these two journals are then shared by the cited journals, *JBC* and REV2, on the basis of the PR of the respective citing journal multiplied by the proportions of citations in that journal for the recipient journal. Thus, PREJ gives values of 12(1,000/1,200) = 10 for the *JBC* and 12(200/1,200) = 2 for REV2, whereas REV1 gives values of 3(500/600) = 2.5 for the *JBC* and 3(100/600) = 0.5 for REV2. This results in a total PR value for the *JBC* of 12.5 and for REV2 of 2.5. The iteration would also distribute PR values back to PREJ and REV1 based upon how many citations *JBC* and REV2 cite for PREJ and REV1, and the process, which in reality involves the entire journal citation network, would continue until the PR values of all the journals stabilize. The values of the PageRank calculation for the ISI IF 2003 citation database are displayed on the *x-axis* of Fig. 1.

The notion of the convergence of propagated PR values is instrumental in understanding why review journals can have higher IF values than the *JBC* but lower PR values. In essence, REV2 is a more "popular" journal, *i.e.* its articles have a greater average citation rate and therefore a higher IF, whereas the *JBC* is a more "prestige" journal, *i.e.* its articles receive citations from more prestigious journals, and it is therefore ranked higher by Google's PageRank algorithm. In addition to this effect, the *JBC* further receives PR due to REV1's function as a portal that points to the articles in the *JBC* that contain the detailed information needed to understand the results outlined in the reviews.

It is difficult to explain PageRank in purely practical terms on the basis of small-example networks. The main problem is the concept of "convergence." Whereas the IF is calculated simply on the basis of static citation rates and publication numbers, PageRank is an iterative algorithm (4) that converges upon what is termed a "stationary probability distribution." As an example, consider a very large and dense cloud of little lemmings, jumping from one journal to the other using citation links (and randomly in a minority of cases) so that every journal has a chance of being visited. If one waited until the numbers of lemmings stabilized over all journals (*i.e.* the lemming cloud across journals takes a stable shape) and then counted the number of lemmings at each journal, one would arrive at an approximation of its PageRank. In informal terms, the importance or "prestige" of a journal is judged according to how the journal's citation graph directs simulated readers, *i.e.* our lemmings, to its publications. For more details see Refs. 3 and 5.

What would happen if one were to rank all published scientific journals by their ISI IF and PR values calculated on the basis of the same citation data?

Conclusions

It is important to note that the currently available methods for the evaluation of the quality of scientific papers and the status of the journals that publish these papers are themselves undergoing a period of profound re-evaluation. No metric of scholarly impact represents a final, perfect solution, and it is useful to think of scholarly impact as an abstract, multifaceted notion that can be measured in many different ways, some more appropriate and accurate in certain circumstances than others (6). The use of PageRank represents an improvement of the ISI IF when one is interested less in the general popularity of a journal and more in its expert appeal. Furthermore, as noted by Bollen *et al.* (3), "as an ever growing collection of scholarly materials becomes available on the web, and hence becomes searchable through Google and Google Scholar, our perception of article status (and hence of journal status) will change as a result of the PageRank-driven manner by which Google lists its search results. In the future, PageRank, not the ISI's IF, may very well start representing our perception of article and journal status." A compromise, of course, would be the use of Y-factor, which rates journals by using an equal measure of both IF and PageRank.

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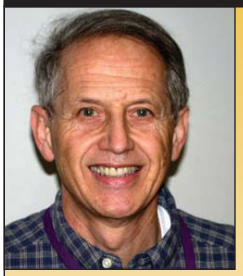


Baum Receives IADR Award

Bruce J. Baum, chief of the Gene Therapy and Therapeutics Branch of the National Institute of Dental and Craniofacial Research (National Institutes of Health), received the 2007 Oral Medicine & Pathology Research Award from the International Association for Dental Research (IADR).

According to the IADR, "Dr. Baum is an outstanding scientist, scholar, and mentor who has made highly visible and significant contributions to the field of oral medicine and oral pathology. He has conducted sustained cutting-edge research focused on the pathogenesis and management of salivary gland and related oral medical disorders."

The IADR Oral Medicine & Pathology Research Award is supported by Sunstar Americas, Inc., and consists of a cash prize and a plaque. It is one of the Distinguished Scientist Awards given annually by the IADR, representing the highest honor the IADR can bestow. Baum received his award in March during the opening ceremonies of the IADR's 85th General Session.

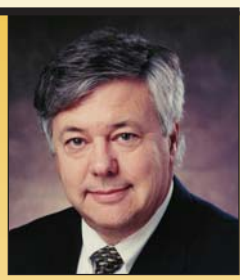
Bissell Recognized by AACR

Mina J. Bissell received the 2007 Pezcoller Foundation-American Association for Cancer Research (AACR) International Award for Cancer Research for her pioneering work on the relationship between cancer genetics and the three-dimensional structure of cells and tissues. Bissell is Distinguished Scientist in the Life Sciences Division at Lawrence Berkeley National Laboratory and a recognized leader in the study of the extracellular matrix and how it regulates genes in both normal organs and malignant tumors.

This year marks the 10th anniversary of the award, which recognizes an individual who has made a major scientific discovery in basic or translational cancer research. Bissell gave an award lecture at the AACR Annual Meeting in April 2007. In Bissell's honor, the Pezcoller Foundation held an award ceremony in early May in Trento, Italy, where she received a cash award of €75,000 and a medallion.

Bissell's studies have revealed that the critical unit of biological function is the integrated signaling circuit provided by the tissue (organ) architecture. She was honored for systematically looking beyond the single cell, showing that the interaction of cells with each other and with the extracellular matrix and the rest of the microenvironment influence cell proliferation, survival, morphogenesis, differentiation, and cell fate, all processes that go awry in cancer.

Joseph Goldstein



Michael Brown

Goldstein and Brown Receive National Award for Research

Joseph Goldstein and Michael Brown and received Research!America's inaugural Builders of Science Award for their achievements in developing the University of Texas (UT) Southwestern Medical Center into one of the world's premier research institutions.

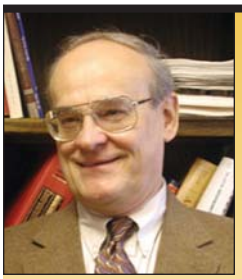
Goldstein and Brown, along with their mentor, Donald Seldin, were honored in March at the 11th annual Research!America Advocacy Awards gala in Washington, D.C.

Research!America is the nation's largest not-for-profit public education and advocacy alliance. Its mission is to make health research a higher national priority, and its awards are given to individuals and organizations that advance that mission.

Brown and Goldstein shared the 1985 Nobel Prize for their discovery of the underlying mechanisms of cholesterol metabolism. Their findings led to the development of statin drugs, the cholesterol lowering compounds that are now among the most important widely prescribed medications in the world.

Goldstein, a graduate of UT Southwestern Medical School, is chairman of molecular genetics at UT Southwestern and regental professor of the UT system. He also holds both the Julie and Louis A. Beecherl Jr. Distinguished Chair in Biomedical Science and the Paul J. Thomas Chair in Medicine.

Brown is regental professor of the UT system and at UT Southwestern directs the Erik Jonsson Center for Research in Molecular Genetics and Human Disease. He holds the W.A. (Monty) Moncrief Distinguished Chair in Cholesterol and Arteriosclerosis Research and the Paul J. Thomas Chair in Medicine.

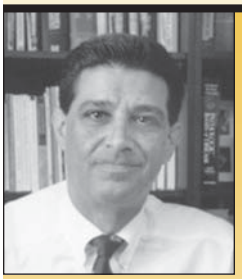


Mestecky Receives Honorary IADR Membership

Jiri F. Mestecky of the University of Alabama, Birmingham, was recently selected as an honorary member of the International Association for Dental Research (IADR). Each year, the three most recent living IADR past presidents select an honorary member who has made significant contributions to and/or supports dental research.

Mestecky is a mucosal immunologist who discovered the J chain, founded the international Society for Mucosal Immunology, and was the first to show in humans that the oral cavity was part of the mucosal immune system by demonstrating that ingestion of antigen led to antibodies in saliva.

The award recognizes not only Mestecky numerous scientific contributions to, but also his support of, oral and dental research, illustrated by his departmental leadership at the University of Alabama, which has led to the mentorship of numerous dental scientists who have, in their turn, produced high quality science that has made an enormous impact on dental research.

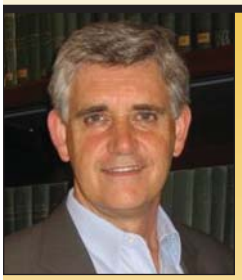


Serhan Honored by NYU

In March, Charles N. Serhan, Simon Gelman Professor at Harvard Medical School and director of the Center for Experimental Therapeutics and Reperfusion Injury at Brigham and Women's Hospital, received the New York University (NYU) Alumnus Achievement Award from the Biotechnology Study Center of the NYU School of Medicine.

The award recognizes the role of pure science in the development of pharmaceuticals and particularly honors those scientists whose work has led to major advances at the bedside. Serhan was honored for leading a worldwide effort to discover new chemical signals that control inflammation and its resolution.

Shortly after obtaining his Ph.D. from the NYU School of Medicine, Serhan identified novel lipid structures formed in the course of cell/cell interactions. Studying inflammation and its resolution, he identified, characterized, and worked out the modes of action of compounds he himself named lipoxins, aspirin-triggered epimers of lipoxins, resolvins, protectins, etc. The receptors for these agents turned out to recognize both endogenous ligands and novel derivatives that hold great pharmaceutical promise. Most recently he has found that some of these lipid intermediates function in the nervous system as regulators of neurogenesis. His laboratory leads a worldwide effort to discover new chemical signals that control inflammation and its resolution.



Stillman Receives Curtin Medal

Bruce Stillman, Cold Spring Harbor Laboratory (CSHL) president and Cancer Center director, received the 2006 Curtin Medal for Excellence in Medical Research from The John Curtin School of Medical Research (JCSMR) this past March.

"Professor Stillman's work brings us a step closer to understanding and developing tools to defeat the diseases of our time," said Professor Judith Whitworth, director of the John Curtin School of Medical Research at the Australian National University, who presented the Curtin Medal for Excellence in Medical Research.

Stillman's research on cell division has formed the building blocks for understanding illness, particularly cancer. His work focuses on DNA replication in cells, a process that ensures accurate inheritance of genetic material from one generation to the next.

His work has also contributed to knowledge of the mechanisms that control DNA replication of human viruses as well as the processes that ensure accurate replication of the human genome and its associated protein structures, or nucleosomes.

The Curtin Medal is an internationally recognized award given annually to a person who has made an outstanding contribution to medical science and is an Australian citizen, an Australian resident, or a person whose work has a significant Australian relevance. The award may be made for either a major discovery or for a lifetime achievement in medical research.

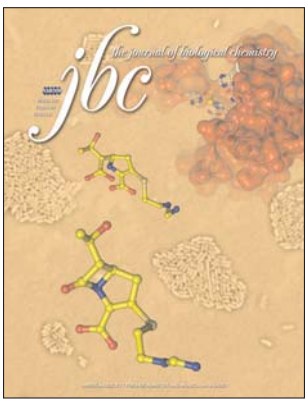
ASBMB Journal News

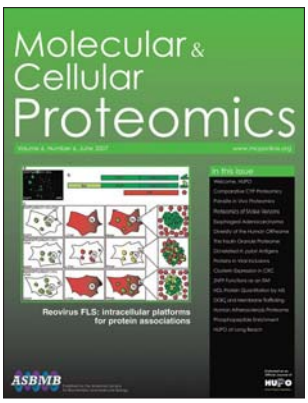
BY NICOLE KRESGE

JBC Gets New TOC

On June 22, subscribers to the *Journal of Biological Chemistry* (*JBC*) noticed something a little different about the journal's Table of Contents. To keep pace with biological chemistry's rapidly changing research landscape, the *JBC* underwent an overhaul of its Table of Contents, resulting in the addition of some new headings and the elimination of others.

At the *JBC,* a group of associate editors, known as the MAGIQ committee (**MA**naging **G**rowth-**I**mproving **Q**uality), is charged with making sure that the Journal continues to evolve as the field evolves. This committee was behind the recent changes in the Table of Contents headings.





As the committee explains, "The new headings are meant to better reflect the types of papers we currently publish and to encourage submission of manuscripts that report significant insights into mechanisms of biological processes in emerging areas."

For example, the former heading "Genes: Structure and Regulation" became "Transcription, Chromatin, and Epigenetics," and "DNA Replication, Repair and Recombination" was expanded to include "DNA Replication, Repair, Recombination and Chromosome Dynamics."

Changes were also made to accommodate the new roles for RNA in biology and mechanistic studies of RNA-mediated processes. The former "RNA: Structure, Metabolism and Catalysis" was divided into two new headings: "RNA Processing and Catalysis" and "RNA-mediated Regulation and Noncoding RNAs."

Another new Table of Contents heading, "Biomolecular Networks," was added to cover papers dealing with integration of information from genomics, proteomics, and metabolomics studies from the perspective of biological mechanisms.

Corresponding changes have also been made to the *JBC* Editorial Guidelines to broaden their scope and to ensure that published studies of all macromolecules have the mechanistic slant appropriate for the *JBC*.

For more information on these changes, see the editorial "JBC Calls for Papers in RNA Biochemistry and Systems Biology" and the "Guidelines for Editorial Decisions" on the *JBC* Web site (www.jbc.org).

MCP Endorsed as HUPO Journal

Recently, *Molecular & Cellular Proteomics* (*MCP*) became the first publication to be endorsed as an official journal of the Human Proteome Organization (HUPO). As part of the agreement between the journal and the organization, *MCP* will contain a special section devoted to HUPO news. This section, which is marked by the HUPO logo, premiered in the June issue of the journal with an overview of the HUPO 2006 World Congress.

In an editorial in the June issue, *MCP* Co-editors Ralph A. Bradshaw and Alma L. Burlingame remarked, "We feel that this is a real addition to *MCP* and are pleased to be able to offer it to our readership. We encourage all individuals interested in proteomics to regularly peruse this section because it will undoubtedly contain important and interesting information and announcements."

HUPO is an international scientific organization representing and promoting proteomics through international cooperation and collaborations by fostering the development of new technologies, techniques, and training. The organization was launched in February 2001.

The relationship between *MCP* and HUPO dates back to 2002 when the journal published the abstracts for the first HUPO World Congress in Versailles. *MCP* has continued to publish the abstracts for every HUPO congress since then.

HUPO members will also receive 50% off the annual ASBMB Regular membership rate.

ANDREW D. ROBERTSON: *Creating a Vision*

A few years ago, while I was still a biochemistry professor at the University of Iowa, my wife and I were having one of our "kitchen table" chats, and we sketched out the perfect job for me, life science broker: I would track the latest advances in life science, identify potential but heretofore unrecognized overlapping interests in different fields, and then help scientists working on complementary problems to connect and collaborate with one another. At that time, neither of us could point to a real job with these qualities, but having the ideal job description in mind subsequently proved to be very handy.

I have now held three jobs over the last 3 years or so: I was on the faculty at the University of Iowa for over 13 years, but in 2004 I started a very stimulating year as a medical writer at Merck Research Laboratories (MRL), and in 2005 I became chief scientific officer (CSO) at Keystone Symposia, a nonprofit organization that coordinates over 50 life science research meetings each year.

I oversee the process of selecting meeting topics and organizers; review meeting proposals and shepherd these proposals through additional peer review by our Scientific Advisory Board; and help raise funds from government agencies like the National Institutes of Health (NIH). The mission at Keystone Symposia is "connecting the scientific community," so I truly feel like I found the ideal job. And although I could not have anticipated it, I would probably not be CSO at Keystone Symposia if I had not made the jump from professor to medical writer in 2004.

The transition in 2004 from a tenured full professor in an academic research-intensive position to one where clinical research and writing ruled the work day was pretty dramatic. As a medical writer, I coauthored manuscripts summarizing the results of clinical trials involving vaccines. I was even able to offer input into trial design—although I am not sure that my suggestions ever ended up in any trial protocols. Up to that point in my career, biochemical research had dominated my professional life for over 20 years. Graduate school and postdoctoral training were fun, and as far as careers go, I had only ever imagined that I would be a faculty member at a university.

As I moved through the ranks in my department at the University of Iowa, I received good support from colleagues, enjoyed teaching and interacting with students, and relished research. The decision to change my career stemmed from dissatisfaction with what evolved into a less enjoyable position coupled with the allure of something new. After a few years, I felt like I was treading water scientifically: with a relatively small research budget and a small lab, pursuing new research directions was difficult. On the other hand, I continued to enjoy writing.

I was fortunate to have some serious writing teachers dating back to my "surfer" high school in southern California. (One of our often exasperated English teachers, originally from the East Coast, remarked that she felt like she was doing missionary work.) Also, the curriculum at my undergraduate institution, the University of California, San Diego, heavily emphasized writing. I did not recognize then that I was acquiring one of my most important—and very transportable—professional skills.

Once I settled on medical writing as my new career goal, I took steps in that direction. I considered myself a good writer but nevertheless took writing classes to work on the craft. I joined

Andrew D. Robertson

Andy Robertson received a B.A. in Biochemistry and Cell Biology from the University of California, San Diego, and a Ph.D. in Biochemistry from the University of Wisconsin-Madison. He was a Damon Runyon-Walter Winchell Cancer Research Fund postdoctoral fellow in Biochemistry at Stanford University before joining the biochemistry faculty at the University of Iowa College of Medicine in 1991. In 2004, he joined Merck Research Laboratories as an associate director in the Medical Communications Department and then assumed his current position as chief scientific officer at Keystone Symposia in 2005.

professional organizations such as the American Medical Writers Association and the Council of Science Editors, and I started attending their meetings. These organizations offered opportunities for training and for learning about medical and scientific writing. My membership also showed a commitment to the profession.

As I pursued a career in writing, I heard the following rule over and over again: to get a job in writing, nothing is better than experience. In my case, I had many scientific papers resulting from my 20-plus years in research. I also sought additional writing opportunities: I wrote a personality profile of another researcher for the medical alumni magazine and had another article published in a regional magazine.

In applying for writing jobs, I tailored my resume to reflect the positions: depending on the position, I emphasized some parts of my training and experience over others. Attending professional meetings turned out to be key to getting the job at MRL. At one such meeting, I met my eventual boss, and the following week, I was invited for an interview. I learned later that I was hired because of my research and writing experience, oral communication skills, eagerness to learn new material, ability to work in a team, and a commitment to writing.

I was very happy at MRL. My co-workers were bright and highly motivated, the work was interesting, and MRL offered many opportunities for professional development on both the scientific and management sides. This was also my first exposure to real interdisciplinary teamwork, and I enjoyed that. In fact, I would happily still be at MRL if I had not spotted the ideal job description, for CSO at Keystone Symposia, in a scientific journal.

Because my wife and I had already outlined the perfect job for me, no special preparation was needed to apply for the CSO position. My broad interest in biology, a background in both basic and clinical research, and good communication skills helped me move to the top of the list of applicants.

Looking back, I had no plan that would take me to my ideal job. I did have the nerve to change my career when I wanted to do something new, and I think that I succeeded by taking advantage of valuable—and highly transportable—technical, problem-solving, and communication skills that I acquired in studying for a Ph.D., doing basic research, and teaching.

Hendrix and Bradshaw Assume New Posts

ASBMB President Heidi Hamm has announced that Mary J. C. Hendrix will replace William R. Brinkley as chair of the ASBMB Public Affairs Advisory Committee and that Ralph A. Bradshaw will assume the post of Society historian.

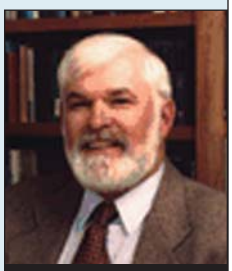
Mary J. C. Hendrix

William R. Brinkley

Hendrix, who is president and scientific director of the Children's Memorial Research Center at Northwestern University, has been an ASBMB member since 1981. She has served on the ASBMB Public Affairs Advisory Committee since 2001 and was president of FASEB from 2001 to 2002.

Brinkley is currently senior vice president for Graduate Sciences and dean of the Graduate School of Biomedical Sciences at Baylor College of Medicine, Houston. He is a Distinguished Service Professor in the Department of Molecular and Cellular Biology and serves as co-director of the W. M. Keck Center for Computational Biology. In addition to chairing the Public Affairs Advisory Committee from 2000 to 2007, Brinkley served as president of FASEB from 1998 to 1999.

Bradshaw is professor in the Department of Pharmaceutical Chemistry and deputy director of the Mass Spectrometry Facility at the University of California, San Francisco. He has been involved in writing the Society's centennial history book and has also contributed articles on ASBMB history to *ASBMB Today*. Bradshaw has been an ASBMB member since 1971, was president of FASEB from 1996 to 1997, and is currently deputy chair of the Public Affairs Advisory Committee and co-editor of *Molecular & Cellular Proteomics*.



Ralph A. Bradshaw

Preparing Graduate Students and Postdocs: *A Model Program*

BY CHERIÉ BUTTS AND JAYNE REUBEN

Making a successful transition from graduate student to postdoctoral fellowship to an independent career was the focus of a national workshop at the recent Experimental Biology (EB) 2007 meeting. The National Postdoctoral Association (NPA) and the Federation of American Societies for Experimental Biology (FASEB) Career Resources/Minority Access to Research Careers (MARC) Program jointly sponsored the first-ever Postdoctoral Preparation Institute (Institute) at this gathering of scientific societies and international researchers. The Institute is an emerging model that assists early-career scientists in navigating through these critical transition points in their training and professional growth. The event took place in Washington, D.C., and included sessions on April 27 and 28 as a pre-conference event.

The primary goal of the Institute was to encourage participants to consider their next professional steps and to provide helpful information and resources to make the transition smoother. The Institute was created as FASEB leadership recognized the increasing need for enhanced professional development of today's early-career scientists at the graduate student, postdoctoral, and junior faculty levels. Both FASEB Career Resources/MARC Program and the NPA have a history of sharing with early-career scientists valuable information essential for the development of a thriving scientific career. In addition, for the past 3 years the NPA and its Diversity Committee have put together similar types of programs in collaboration with the National Science Foundation-funded Alliance for Graduate Education in the Professoriate (AGEP) programs at Howard University and University of Texas at El Paso. Ultimately, the organizers hope that providing this information will help participants avoid some of the more common mistakes of many early-career scientists, including unfocused research goals, unrealistic career aspirations, and lack of preparation for various career paths.

The program was divided into two days, with workshops that address the needs of early-career scientists as well as a session for heads of laboratories. The April 27 program included plenary talks, brown-bag lunch discussion tables, and breakout sessions for graduate students and postdocs. The April 28 program included talks focused on mentoring and managing postdoctoral fellows within the laboratory setting. There were approximately 125 participants each day. Leaders in scientific policy, experts in professional development, and several outstanding researchers, educators, and administrators from a variety of organizations provided exhilarating discussions on a wide range of session topics, including:

- Thinking about next steps
- Different career paths available to scientists
- Considerations for funding opportunities
- The keys to successful networking
- The importance of respecting cultural differences
- Best practices for increasing laboratory productivity
- Structured mentoring
- Reducing conflict within the laboratory
- Results of the Sigma Xi Postdoc Survey

The following individuals served on the Organizing Committee for the event: Jayne S. Reuben (Baylor College of Dentistry/Texas A&M Health Science Center), Cherié L. Butts (National Institute of Mental Health/NIH), Phillip Clifford (Medical College of Wisconsin), David Burgess (Boston College), L'Aurelle Johnson (University of Minnesota), Joan Lakoski (University of Pittsburgh), Alyson Reed (National Postdoctoral Association), and Jacqueline Roberts (FASEB Career Resources Program).

The NPA is a professional association that provides a unique, national voice for postdoctoral scholars and seeks to enhance the quality of the postdoctoral experience. The NPA hopes that other scientific societies will host similar events and that other institutions will host local events so that this information will enable as many early-career scientists as possible to have successful careers. Additional information about the NPA can be found at www.nationalpostdoc.org. For more details about this event, please visit www.eb2007.org/pages/page7i.htm.

Assessing What Students Learn

BY J. ELLIS BELL

Assessment is an issue that is not going to go away. As educators we all should be thinking creatively about assessment of teaching, of programs, and of individual students. I believe that courses should work together to augment student learning and that while individual faculty may decide the majority of course content, the department or program should interpret guidelines from professional societies and ensure that courses provide adequate learning opportunities for the students. The graduating student is the product of the program, and because assessment is focused on student learning outcomes it reflects the collective success or failure of the program and not of any individual course or experience.

So what type of assessment can be used to provide more dynamic information that can truly help in education? It must be course- or program-embedded, and needs to reflect both the retention of knowledge and the acquisition of skills. Too often you see in an "assessment" plan that assesses knowledge in a course-embedded manner. This usually means that the instructor keeps a record of how well students perform in class and on exams. Such information is clearly expedient. Presumably the program wishes to teach facts and information that the student can carry on to later courses in the curriculum. If that is the case then student retention, understanding, and use of the knowledge should be assessed in those later courses. This brings up the issue of making courses work together to benefit both the student and the program. As a department or program, the faculty should decide on what knowledge and skills the student should acquire and when they should acquire them.

Most programs have a sequence of introductory courses that must be completed before upper level courses. If there is a defined order of courses, then each course should build on the skills and knowledge taught in the previous courses. Each instructor could, for example, list the knowledge and skills needed to take the course as well as those required for successful completion of the course. Such an exercise in itself will assist faculty in understanding the overall goals of the program and how the curriculum works to foster the final outcomes. By examining and discussing this information as a department, all faculty will understand how the courses contribute to the program's goals, and it will encourage interactions between the courses.

I know from my own experience that too often I have assumed that students have mastered certain skills or facts in an earlier course only to find they haven't. Necessary information could be categorized as "fully covered" or "introduced but in need of reinforcement," allowing faculty to plan appropriate repetition in the curriculum. This information base also provides a starting point for dynamic assessment tools for use in the classroom. Each instructor devises several questions on each point of essential background knowledge or value-added knowledge during the course. Early in the course the appropriate questions can be used in a take-home problem set or in-class quiz. Instead of collecting and grading the answers, the instructor can go through the answer rubric in class, indicating where students should "grade" themselves. At the end of the class the student-graded quiz/problem set is handed in and analyzed by the instructor to assess the students' state of knowledge. In this way, the background material from previous courses is reviewed in a way that allows learning points to be assessed without students being threatened and in a context enabling them to see how the instructor analyzes and answers a question.

This approach can also increase the dialog between instructors: questions I think a student should be able to answer coming into a course can be compared with questions the instructor of the prior course feels the students should be able to answer after taking that course. Any disconnects can be ironed to optimize the way the curriculum works for student learning. Some think this approach breaks down academic freedom and that instructors should be able to teach whatever they want. Unfortunately such comments miss the point: with academic freedom comes academic responsibility. When a course is a required part of a sequence and later courses depend on its content, then academic responsibility says that the content must be there. Professional responsibility says that it must be there at an anticipated level and coverage. Academic freedom says feel free to teach content in any way that you like provided you can demonstrate the effectiveness of the style, which of course brings us back to assessment.

Alexandra Newton: Understanding the Inner Workings of Cells

BY PAT PAGES

Alexandra Newton, professor of pharmacology at the University of California in San Diego, has always been fascinated by how molecules work and how they interact with each other. During her 20-year career, Newton's curiosity and enthusiasm led her to explore how proteins and lipids interact in cell membranes, how protein kinases are activated within cells, and recently how proteins she nicknamed PHLPP are part of signaling pathways involved in cancer, diabetes, and heart disease.

Newton's interest in science started as a child. One of her most vivid memories was reading *The Double Helix: A Personal Account of the Discovery of the Structure of DNA*, by renowned biologist James D. Watson. "The book—which I read when I was 12—was a fascinating account of the scientific race between Watson, working with Francis Crick, and Linus Pauling to discover the structure of DNA," Newton says. "Reading it fueled my desire to become a scientist."

During her childhood, Newton also spent many summers in Greece, where she was captivated by the sea life of the Mediterranean. "I loved spending time near the water, snorkeling, or catching octopuses with bare hands," she says. "This made me want to become a marine biologist."

During her academic years at Simon Fraser University in Vancouver, Canada, Newton developed a passion for chemistry, so instead of majoring in marine biology, she decided to major in biochemistry.

Newton's first chance to investigate the inner workings of proteins started in 1981 while working on her Ph.D. in chemistry at Stanford University. The topic of her research was how membrane proteins interact with lipids, sparking an interest in membrane biochemistry that has influenced her throughout her career.

After finishing her Ph.D., Newton went to the University of California, Berkeley, to work with Daniel Koshland, Jr., known for his "induced fit" theory of enzyme interaction, which states that enzymes change shape as they react with other molecules. Newton studied how lipids control the activity of protein kinase C (PKC), an enzyme that attaches a phosphate group to specific proteins and is involved in pathways that control various physiological functions such as learning and memory, the working of the immune system, and cell proliferation.

In Koshland's laboratory, Newton discovered for the first time that PKC attaches phosphates onto itself by an intramolecular mechanism, akin to a snake biting its own tail. This showed that PKC did not need to be tagged by other proteins to modify its function, which is now a common theme in cell signaling.

In 1988, after setting up her laboratory at Indiana University in Bloomington, Newton decided to study how PKC is activated in cells. Scientists knew that PKC was activated by calcium ions and diacylglycerol—a product of the breakdown of membrane lipids—but the activation mechanisms were not completely understood. One thing scientists had hypothesized was that the PKC active site was blocked by a segment called a pseudosubstrate that needed to be freed to activate PKC.

Newton investigated how calcium ions, diacylglycerol, and PKC worked together and revealed a process that would generate much attention from other biochemists working on this protein. She showed that when calcium ions are released in the cell—by the endoplasmic reticulum—they bind to PKC and allow it to tether to the cell membrane. The membrane-bound PKC then moves on the membrane and, when it gets close to a diacylglycerol molecule, binds to it as well (see Fig. 1). This induces a change in the PKC internal conformation that releases the pseudosubstrate, freeing the active site and allowing PKC to attach phosphates on other proteins.

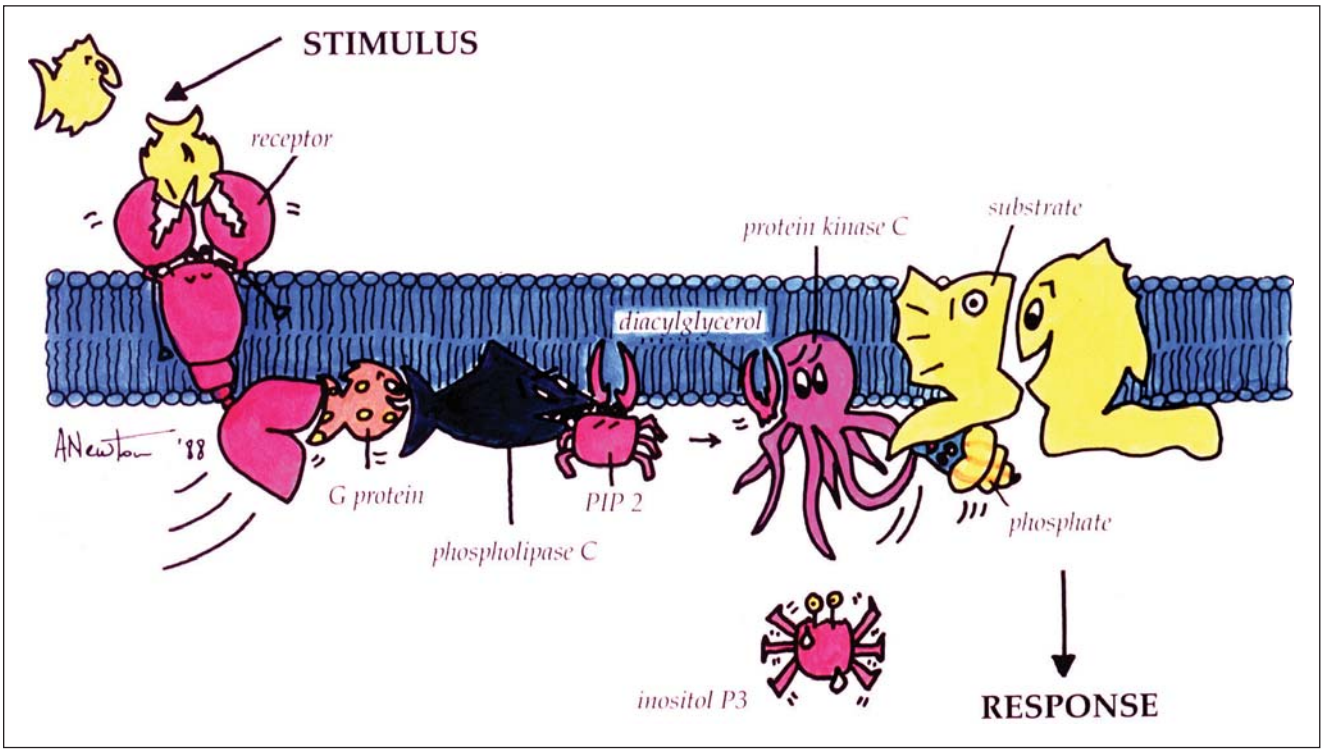


Fig. 1. **Schematic representation showing that diacylglycerol tethers protein kinase C (*octopus*) to the membrane, allowing the kinase to attach a phosphate molecule (*sea shell*) to a substrate (*yellow fish with gaping mouth*).**

"The chances that PKC finds diacylglycerol on the membrane by simply bouncing on and off the membrane are relatively low, so nature has chosen a clever mechanism to increase the efficiency of this happening," Newton says. "Binding of calcium ions to PKC essentially pretargets it to the membrane, where it can start a much more effective search for diacylglycerol."

In 1994, Newton and her colleagues made another discovery. They showed that before PKC even binds to the cell membrane, it needs to be phosphorylated. Newton's team, along with Koshland's team, identified three sites on which PKC needs to be phosphorylated: a segment near the entrance to the active site called the activation loop and two positions in the carboxyl terminus that Newton named the turn motif and the hydrophobic motif. This was important because these sites are conserved in many other kinases, showing that these sites could be regulatory switches in other kinases as well.

Newton's lab showed that PKC phosphorylation occurs in an orderly way. A protein called phosphoinositide-dependent protein kinase 1 (PDK1) first phosphorylates the activation loop, which then triggers PKC to phosphorylate itself at the turn and hydrophobic motifs.

After moving to the University of California in San Diego in 1995, Newton's laboratory used imaging technologies to visualize the dynamics of PKC in cells through a collaboration with Roger Tsien, a professor of pharmacology who has pioneered the use of live cell imaging technologies. This work showed when, where, and for how long PKC is active in the cell and revealed for the first time where PKC activity was sustained and where it was rapidly turned off.

In 2000, Newton also turned her attention to another protein kinase related to PKC called protein kinase B or Akt. The Akt signaling pathway is critical in regulating cell growth and death and is linked to many common human cancers.

Instead of determining which proteins phosphorylate Akt—as she had done with PKC—Newton wondered whether a protein that removes phosphates, or phosphatase, may be involved in the Akt signaling pathway as well.

"By then, it was well known that Akt, like PKC, needs to be phosphorylated to become active, but the mechanisms terminating Akt activity were not well studied," Newton says. "Removing the phosphates would mean stopping the Akt pathway, which also means knowing how to control pathways leading to important diseases such as cancer, diabetes, and heart disease."

Newton and her colleagues noticed that many known proteins in the Akt pathway have a common domain called pleckstrin homology (PH). So

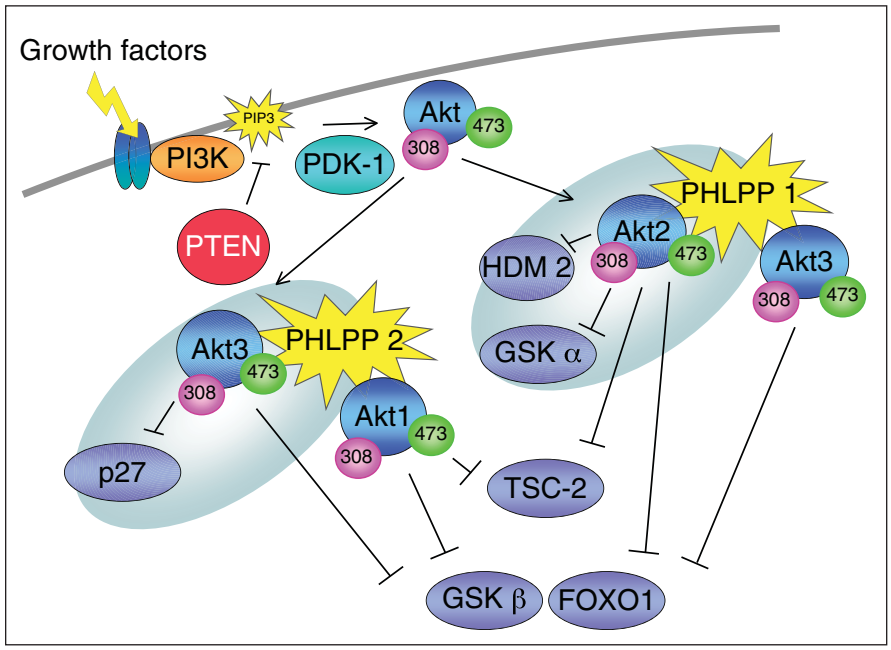


Fig. 2. **Schematic representation showing how the signaling pathways for Akt1, Akt2, and Akt3 are inactivated by PHLPP1 and PHLPP2 through specific complexes (*blue-shaded ovals*) of the PHLPP and Akt molecules.**

the scientists decided to scour GenBank™ for a phosphatase with a PH motif. They found only one protein, which they called PH domain leucine-rich repeat protein phosphatase (PHLPP, pronounced "flip"). The researchers then showed that PHLPP was indeed involved in the Akt pathway.

The researchers next showed that PHLPP levels are markedly reduced in colon and brain cancer cells that had elevated Akt phosphorylation. By introducing PHLPP in these cells, they showed that tumor growth was dramatically suppressed.

In March 2007, Newton's team published their discovery of a second type of PHLPP protein, which they dubbed PHLPP2. The scientists showed that PHLPP—now called PHLPP1—and PHLPP2 terminate different Akt signaling pathways, which involve three different Akt proteins called Akt1, Akt2, and Akt3.

Although both types of PHLPP proteins prevent tumors from growing, the researchers found that they are also involved in pathways that promote diabetes, heart disease, and neurological conditions. In particular, PHLPP1 terminates the Akt2 pathway, which is involved in maintaining a constant level of glucose in the bloodstream, whereas PHLPP2 inactivates the Akt1 pathway, which promotes cell survival (see Fig. 2).

These results show that varying the levels of the PHLPP proteins can have two opposing effects, which can be used to treat various conditions. Increasing the role of PHLPP proteins would help suppress tumors in cancer patients, but inhibiting the proteins would help treat patients with diabetes, heart disease, and neurological disorders.

"We first discovered that PHLPP controls Akt, which is the driver on the pathway to tumor growth," Newton says. "PHLPP is like a brake that, when 'on,' slows the driver but when 'off' allows the driver to move. In cancer, we want the driver to brake, to prevent cell proliferation leading to tumor growth. But in diabetes, heart, or neurological disease, where we want to promote cell growth and survival, we don't want to slow the driver down."

Newton is very excited about these new results. Throughout her career, not only has she revealed how known proteins interact with each other in key cellular pathways, but she also has discovered formerly unknown proteins that now offer potentially new ways of curing major diseases.

"PKC has led our lab on an amazing journey, with new discoveries at every turn," says Newton. "But perhaps what has been most rewarding is how it led us to discover the phosphatase that terminates signaling by PKC and its close cousin Akt. This phosphatase is poised as a major therapeutic target, and I hope our results may one day lead to new cures against cancer, diabetes, and heart disease."

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Jack Griffith: Seeing What No One Has Seen Before

BY PAT PAGES

Jack Griffith, a professor of microbiology and immunology at the University of North Carolina in Chapel Hill, likes to see—literally—DNA and proteins. During his 38-year career, he has been perfecting electron microscopes to do just that, revealing how DNA and proteins interact with each other to carry out replication or recombination reactions and uncovering the structure of chromosome ends.

These discoveries and many others have made Griffith's laboratory famous around the world. Biologists seeking to understand how their molecules work often ask him to visualize their molecules in action. "Most biochemists use indirect ways to study complex molecular mechanisms," Griffith says. "But combining biochemical assays with electron microscopy makes the job much easier."

What prepared Griffith to become an international expert in electron microscopy was his love for photography and things manual at an early age. Raised in Alaska, he hunted caribou and moose with his father for winter food, built the family homestead, and assembled outboard boats. He also loved taking things apart and spent countless hours breaking down pieces of wrecked aircraft in a military dump near the family house.

Early on, Griffith developed a keen interest for science, especially physics. He read with interest scientific reprints of papers published by the U.S. Department of Energy about nuclear reactors and, while in high school, won the Alaska science fair by building a miniature nuclear reactor complete with a neutron source.

"I always enjoyed understanding how machines or pieces of equipment work and then trying to see how to improve them," he says. "Physics helped me do that, not so much from the formulas that you are taught in school but from understanding how and why things affect each other."

In 1960, Griffith went to Occidental College in Los Angeles with the goal of becoming a nuclear physicist. In 1963, his interests changed when he was offered a summer internship at Oak Ridge National Laboratory in Tennessee to study how radiation affects DNA with Dick Setlow, a renowned physicist turned biophysicist. The internship was such a positive experience that, after returning to Occidental College for his junior year, Griffith decided to major in biophysics.

"At that point, I became aware that experimental physics was an area dominated by large groups of people working on big projects," he says. "I was more interested in setting up small—but original—experiments for which you can get answers to your questions pretty quickly."

Griffith explains that he has always been drawn to scientific questions that he can address by setting up "simple and elegant" experiments. "Sometimes, you don't need to build complicated set-ups," he says. "You just have to find an elegant way to address your problem without creating other problems that would interfere with what you are looking for. It's not easy, but when you succeed in doing it, it's very rewarding."

Using electron microscopes provided many such opportunities to Griffith. His first chance was in 1965 when he was a Ph.D. student at the California Institute of Technology. One of the questions scientists had tried to address was how DNA is assembled in chromosomes. The resolution of the micrographs was too crude to show the finer details of DNA, so Griffith found a way to improve it.

Until then, visualizing DNA with an electron microscope required coating the molecule with a thick layer of protein and then a metal layer to make DNA appear thicker and more visible. But the finer details of the DNA were lost. So Griffith found ways to reveal these details by limiting the amount of coating materials and by attaching the DNA to better supports.

To prepare the metal coating, gold or platinum was heated until it evaporated, and then it was sprayed over the sample so that the outline of the metal coating could be "seen" by the microscope. To view DNA, such metals would crudely cover it, so Griffith tested other metals and discovered that tungsten, which melts at higher temperatures than gold and platinum, produced a finer spray and a more detailed image.

One of Griffith's initial results using his new methods was the first image of DNA bound to DNA polymerase—the enzyme responsible for DNA replication (see Fig. 1). The work was performed in 1969 at Caltech with Arthur Kornberg, who won the Nobel Prize for identifying DNA polymerase. The results showed that electron microscopy could do more

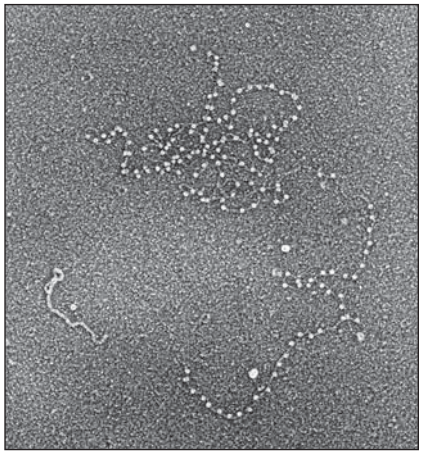

Fig. 1. **The first electron microscope image of DNA polymerase bound to DNA.**

than take pictures—it could also be used to analyze how DNA interacts with proteins.

In 1978, Griffith set up his laboratory at the University of North Carolina with the goal of using electron microscopy to understand how proteins bind, fold, and loop DNA. One of the laboratory's most interesting results in the early 1980s was to uncover the inner workings of recA, a protein used by bacteria to recombine its DNA. These results later paved the way for studies of DNA recombination proteins in humans.

In the early 1990s, Griffith and his colleagues looked at unusual continuous three-base repeats in DNA known to cause diseases such as Fragile X syndrome, a leading cause of mental retardation, and myotonic dystrophy, a motor neuron disease. In the case of Fragile X syndrome, Griffith's team showed that the repeats caused a segment of the chromosome to be very unorganized and unprotected, making it more susceptible to breaking than other parts of the chromosome and turning off a critical gene.

In 1995, the team started what would become a landmark contribution: the study of the structure of telomeres, which are structures at the ends of chromosomes. When cells divide, the new cells have shorter telomeres than the original one. As cell divisions proceed during a lifetime, the telomeres eventually become so small that the cells cannot divide anymore and die. So telomeres act as an aging clock, limiting the life span of cells, and help to stop cancer cells from dividing continuously.

Until 1999, it was widely assumed that telomeres looked like the ends of shoelaces. But in 1999, Griffith suggested that—based on his previous recA studies—telomeres might instead form a large loop. So Griffith's team worked out ways of isolating human telomeres and examining them directly in an electron microscope. What the scientists saw confirmed Griffith's hypothesis: long, lasso-like loops (Fig. 2). He was so happy that he personalized the license plate of one of the cars he collects—an old Ferrari—with the word "Telomere."

These results and those of other researchers may be used one day to slow down the shortening of telomeres, making people stay young longer, or to develop anti-cancer drugs that make telomeres shorter in tumors. But more studies are needed to understand the structure and properties of telomeres. Griffith's team is now using electron microscopy to understand how telomeric DNA is folded by a set of a half-dozen proteins that the scientists had previously isolated.

To make the most of the images collected with the electron microscope, Griffith and his team also use other biochemical techniques, including gel electrophoresis, chemical probing, and the generation of mutant proteins. Combining both approaches helps the researchers understand the properties of the molecules under study and verify what they see in the microscope.

In the future, Griffith would like to combine electron microscopy with an emerging technique called single-molecule microscopy, which uses a light microscope and cameras to follow the movement of molecules live in solution. Although this new technique does not allow one to "see" DNA or proteins, their movement can nevertheless be followed through fluorescent tags.

Fig. 2. **Electron microscope image showing that DNA at the end of a chromosome—or telomere—forms a loop.**

When Griffith talks about his research, he seems to be as excited as he probably was the first time he used an electron microscope. "What I find most exciting about this technique is that it allows me to see things never before seen by the human eye," he says. "It's like when I used to hunt or hike with my father in the backwoods of Alaska. It was always thrilling to go over a new valley or a new mountain and see what no other human being had ever seen before."

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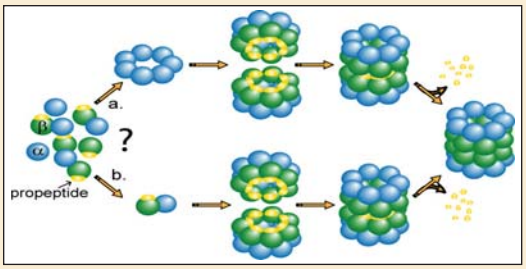
J. Biol. Chem. 2007 282: 18448-18457

Mass Spectrometry Reveals the Missing Links in the Assembly Pathway of the Bacterial 20 S Proteasome

Michal Sharon, Susanne Witt, Elke Glasmacher, Wolfgang Baumeister, and Carol V. Robinson

The 20 S proteasome is composed of 28 subunits (14 α-type and 14 β-type) arranged in a cylindrical architecture consisting of two outer α-type subunit rings embracing two central β-type subunits rings. The formation of the 20 S proteasome is a complex process that involves a cascade of folding, assembly, and processing events. In this *JBC* paper, the authors use a real-time mass spectrometry approach to capture transient species along the assembly pathway of the 20 S proteasome from *Rhodococcus erythropolis*. By recording mass spectra throughout the reaction time course they were able to monitor the formation of an early α/β-heterodimer as well as an unprocessed half-proteasome particle. Formation of the mature holoproteasomes occurred in concert with the disappearance of half-proteasomes. They were also able to determine in great detail the cleavage sites within the β-subunit propeptides during the different assembly states.



Two possible assembly scenarios for the *Rhodococcus* 20 S proteasome.

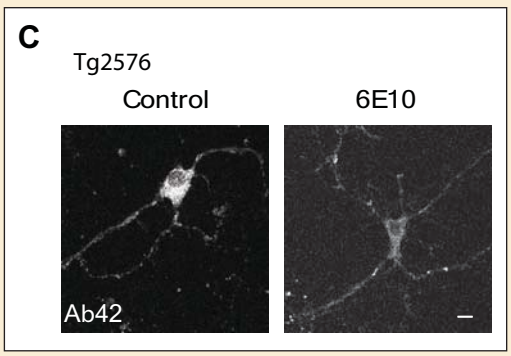
jbc

J. Biol. Chem. 2007 282: 18895-18906

Internalized Antibodies to the Aβ Domain of APP Reduce Neuronal Aβ and Protect against Synaptic Alterations

Davide Tampellini, Jordi Magrane, Reisuke H. Takahashi, Feng Li, Michael T. Lin, Claudia G. Almeida, and Gunnar K. Gouras

Immunotherapy against β-amyloid peptide (Aβ) is a leading therapeutic direction for Alzheimer disease. Experimental studies in transgenic mouse models of the disease have demonstrated that Aβ immunization reduces Aβ plaque pathology and improves cognitive function. However, the biological mechanisms by which Aβ antibodies reduce amyloid accumulation in the brain remain unclear. The authors of this paper show that Aβ antibodies decrease levels of intracellular Aβ in Alzheimer disease mouse mutant neurons in culture. This reduction in cellular Aβ appears to require that the antibody bind to the extracellular Aβ domain of the amyloid precursor protein (APP) and be internalized. The authors also found that treatment with Aβ antibodies protects against synaptic alterations that occur in APP mutant neurons.



Treatment with Aβ antibody 6E10 reduces Aβ42 immunofluorescence.

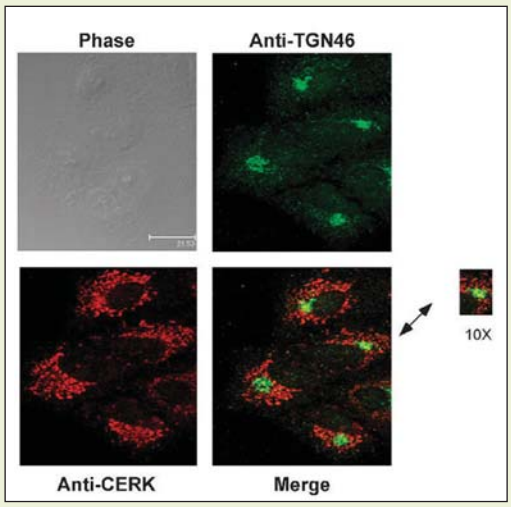
jbc

J. Lipid Res. 2007 48: 1293-1304

Ceramide Kinase Uses Ceramide Provided by Ceramide Transport Protein: Localization to Organelles of Eicosanoid Synthesis

Nadia F. Lamour, Robert V. Stahelin, Dayanjan S. Wijesinghe, Michael Maceyka, Elaine Wang, Jeremy C. Allegood, Alfred H. Merrill, Jr., Wonhwa Cho, and Charles E. Chalfant

In mammalian cells, ceramide kinase (CERK) phosphorylates ceramide to produce ceramide-1-phosphate (C1P). In this study, the authors determined that the main forms of C1P in cells are $C_{16:0}$ C1P and $C_{18:0}$ C1P, suggesting that CERK uses ceramide transported to the *trans*-Golgi apparatus by ceramide transport protein (CERT). To confirm this, they downregulated CERT by RNA interference and showed that it dramatically reduced the levels of newly synthesized C1P as well as the total mass levels of C1P in cells. The authors then localized CERK to the *trans*-Golgi network, placing the generation of C1P in the proper intracellular location for the recruitment of cytosolic phospholipase $A_2\alpha$. These results demonstrate that CERK localizes to areas of eicosanoid synthesis and uses a ceramide "pool" transported in an active manner via CERT.



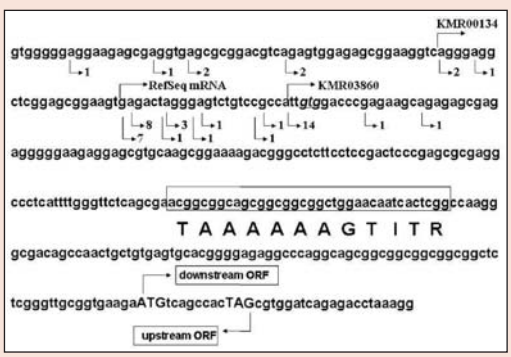
CERK localizes to the *trans*-Golgi apparatus.

Mol. Cell. Proteomics 2007 6:1000-1006

Diversity of Translation Start Sites May Define Increased Complexity of the Human Short ORFeome

Masaaki Oyama, Hiroko Kozuka-Hata, Yutaka Suzuki, Kentaro Semba, Tadashi Yamamoto, and Sumio Sugano

Open reading frames (ORFs) are portions of DNA that contain bases that encode proteins. They are located between a start-code sequence (ATG codon) and a stop-code sequence. Surprisingly, some sequence analyses have indicated that several cDNAs have at least one ATG codon upstream of the presumed coding sequence, indicating the presence of potential coding regions in the genes' 5'-untranslated regions (UTRs). In this study, the authors used an automated two-dimensional nano-LC system coupled with a high resolution hybrid tandem mass spectrometer to confirm the presence of several upstream ORFs in the presumed 5'-untranslated regions of mRNAs. They also found evidence of novel short coding regions that were likely to be translated from the upstream non-AUG start site or from the new short transcript variants generated by utilization of downstream alternative promoters. These findings reveal a novel post-transcriptional system that can augment the human proteome via the alternative use of diverse translation start sites coupled with transcriptional regulation through alternative promoters or splicing.



Structure of the 5'-UTRs of the human *YTHDF3* transcripts.

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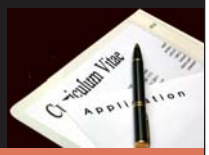

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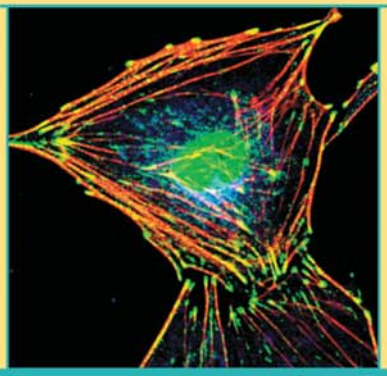
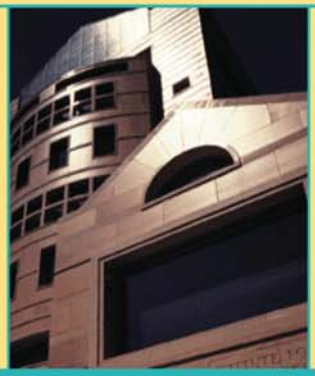
SEPTEMBER 2007

48th International Conference on the Bioscience of Lipids
SEPTEMBER 4–8, 2007
TURKU, FINLAND
www.icbl2007.abo.fi

British Mass Spectrometry Society Meeting
SEPTEMBER 9–12, 2007
EDINBURGH, SCOTLAND
www.bmss.org.uk/meetings.htm
E-mail: bmssadmin@btinternet.com
Tel.: 44-(0)-1480-880-669

Mass Spectrometry in Clinical Chemistry and Molecular Diagnostics
SEPTEMBER 14–18, 2007
PACIFIC GROVE, CA
www.asms.org
E-mail: office@asms.org
Tel.: 505-989-4517

OCTOBER 12th-14th, 2007
PORTLAND, OREGON

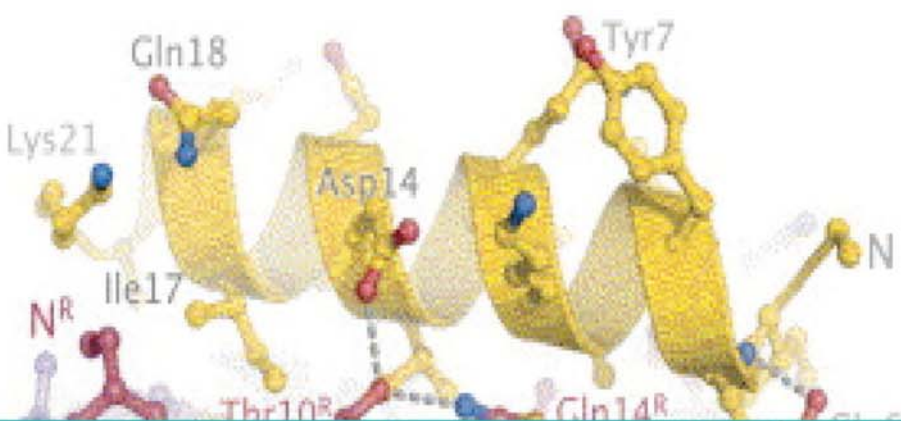




Second International Conference on ANCHORED cAMP SIGNALING MECHANISMS

Special Plenary Session
Friday October 12th, 2:00-4:30:
Tony Hunter - Tony Pawson - Brian Druker

This bi-annual conference plans to bring together a multidisciplinary group of investigators who work on various aspects of anchored cAMP signaling pathways to discuss their latest research.

For More Information: visit www.akap2007.com or contact Lorene Langeberg, langeber@ohsu.edu



Featured Speakers

- Joe Beavo
- Meredith Bond
- William Catterall
- Marco Conti
- Dermot Cooper
- Mark Dell'Acqua
- Carmen Dessauer
- Kimberly Dodge
- Mary Hunzicker-Dunn
- Brian Druker
- Antonio Feliciello
- Rodolphe Fischmeister
- Jim Goldenring
- Johannes Hell
- Miles Houslay
- Tony Hunter
- Jeffery Karpen
- Robert Kass
- Enno Klußmann
- Craig Malbon
- G. Stanley McKnight
- Alexandra Newton
- Tony Pawson
- Scott Soderling
- Kjetil Tasken
- Susan Taylor
- Manuela Zaccolo

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