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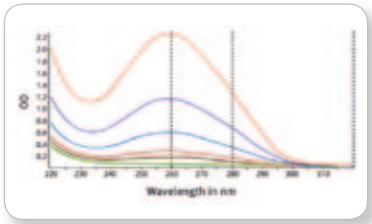

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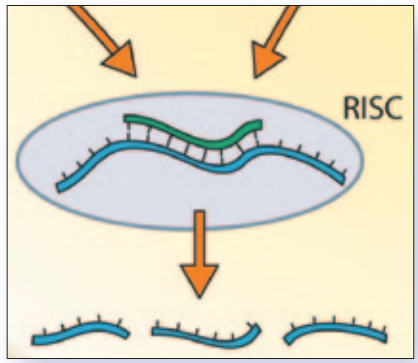

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ASBMB today

A monthly publication of
The American Society for
Biochemistry and Molecular Biology

ASBMB Today

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2008 APEX® AWARDS FOR PUBLICATION EXCELLENCE

letters to the editor

ASBMB accreditation

I write this in response to the article by Kennelly and Bell on accreditation in the February issue. I am very apprehensive about the American Society for Biochemistry and Molecular Biology getting involved in a program of accreditation based upon examinations. As noted in the article, the concept is logically simplistic.

One only has to look at the recent accelerated evolution of topic sections in the Journal of Biological Chemistry such that the journal covers virtually all areas of modern biology. I venture that a good number of senior authors of papers in the journal could not pass such an examination. Pity the poor undergraduate who has become very excited about a research project and spent a large part of his or her time and effort on a relatively narrow aspect of modern biology.

In sum, ASBMB and its flagship journal have evolved beyond the BMB, and it makes little sense at this point to accredit programs. In fact, I wonder how many biochemistry and molecular biology departments now exist. Most students pursuing these disciplines are in broader departments with broader names. Often, these might just as appropriately be accredited by the American Society for Microbiology, the American Society for Cell Biology or basically any Federation of American Societies for Experimental Biology member society. Indeed, let me suggest that perhaps accreditation might be more appropriate for FASEB.

Stuart Linn
Department of molecular and cell biology
University of California, Berkeley

Reply:

Dr. Linn is correct in asserting that a) accreditation should not be undertaken lightly and b) the development of an effective assessment instrument will be critical to our success or lack thereof.

However, I find myself in serious disagreement with his first point for a number of reasons. First, Ellis and I are not alone in believing that accreditation can serve as a constructive tool for raising the bar in undergraduate BMB education. We enjoy the privilege of serving as spokespeople for scores of ASBMB members who have devoted many, many hours to this issue. Moreover, we constantly are approached by people at meetings wanting to know when the accreditation program will be in place. While this anecdotal evidence hardly constitutes proof beyond a reasonable doubt, its consistency and pervasiveness suggests that the concept does possess merit. Second, I strongly believe that if we do not engage college students and their mentors, our society likely will fade away to a small publishing house precisely because young BMB professionals continue to be drawn to those professional societies that have established their brand with these professionals during their college years.

As for the use of an examination, while politics and history have led to the Byzantine proliferation of names for what is at heart BMB, I strongly suspect

continued on page 8

Budget challenges in biomedical sciences

BY SUZANNE PFEFFER

There has never been a more exciting time in biomedical research. Given all of the tools and information currently available, questions can be tackled in ways that simply were unthinkable in the not-too-distant past. Yet many researchers are more frustrated than ever and stymied in their ability to carry out exciting and important research. I receive e-mails on a regular basis from members who receive 10th percentile ratings on grant applications but are unable to obtain funding for their highly regarded and important research.

In the past, I have been somewhat reluctant to discuss this problem, because I didn't want to discourage our researchers-in-training. If faculty members at the top institutions are struggling to support their laboratories, how might students ever hope to compete? In the past, funding challenges were temporary, and therefore downplaying the challenge seemed justified. The current financial situation changes the equation; the fallout from the economic downturn has had major consequences for most scientists both in academia and in the pharmaceutical industry, and different countries (and companies) are responding in different ways.

> "We must do more with existing research dollars, and all of us must be willing to make sacrifices to help make this happen."

On Feb. 19, the U.S. House of Representatives voted in support of a Continuing Resolution (H.R. 1) to fund the federal government for the remainder of the 2011 fiscal year while cutting spending by more than $100 billion from the president's fiscal year 2011 request, thus making the largest single discretionary spending reduction in the history of Congress. This legislation includes a $1.6 billion cut (5.2 percent) in National Institutes of Health funding from the 2010 level, reducing its budget to the 2008 funding level, and a $359 million cut in funding for the National Science Foundation from the 2010 level. If enacted, the entire cut would have to be absorbed in the remaining months of fiscal year 2011, significantly intensifying the impact of the reduction. At the same time, the president outlined his budget for fiscal year 2012, which includes a 3.4 percent increase in funding at the NIH over 2010 enacted levels. The Senate rejected the massive cuts proposed by the House, forcing congress to pass several short-term continuing resolutions, thankfully steering clear of drastic cuts to NIH and NSF budgets.

Of important note is the fact that during the debate on H.R. 1, several congressional representatives proposed an amendment in support of the NIH. Although this amendment did not make it to the floor for a vote, Reps. Edward Markey, D-Mass.; Janice Schakowsky, D-Ill.; Joe Courtney, D-Conn.; Brian Higgins, D-N.Y.; Rush Holt, D-N.J., and Susan Davis, D-Calif., deserve our heartfelt thanks for introducing an amendment (213) to H.R. 1 to restore funding to the NIH. If you haven't done so already, **please contact your senators and representatives and help them understand the importance of research funding in your home state and district;** thank them for their continued support. Cures will require additional basic research, and research dollars bring jobs and economic benefits significantly beyond their actual cost.

In an excellent recent column in the New Yorker (1), James Surowiecki noted that while President Obama understood that the government needed to cut excessive expenditures (and thus called for a five-year freeze on domestic spending), he also called for sharp increases in investments in infrastructure, education and new technology, which will cost many billions of dollars.

Surowiecki wrote, "Instead of trying to stimulate short-term demand, the plan seeks to improve our

long-term growth rate by boosting supply: increasing the pace of innovation, and making workers more productive and commerce more efficient … Why do this when Washington is obsessed with tightening its belt? **Because spending on infrastructure, R. & D., and education has the potential to create more value than it costs.** The return on investment from the building of the Interstate Highway System in the nineteen-fifties and sixties has been estimated at thirty-five per cent annually. The economists Kevin Murphy and Robert Topel have suggested that the social benefits of medical research reach into the trillions of dollars. And investments in military technology during the original Sputnik moment gave us, among other things, satellites, the microchip, G.P.S., and the Internet, the cumulative benefits of which are incalculable … At the moment, we're spending too much on things that consume resources — like the military and earmarks — and not enough on things that create them." I could not agree more.

It is unlikely that we will see significant increases in overall funding in the near future, and we will need to fight hard just to maintain current support. If outstanding research projects are going unpaid, we must do more with existing research dollars, and all of us must be willing to make sacrifices to help make this happen. This is a time to call on the leadership of all funding organizations to make budget allocations as transparent as possible. What review processes are in place to ensure scientists (and taxpayers) that the dollars already allocated are yielding maximal value and benefit? Are we doing enough to ensure rigorous review of all current intra- and extramural NIH and NSF-supported programs?

Bruce Alberts has written recently about the dependency of many institutions on NIH indirect costs to support construction of ever-growing research enterprises (2). Such growth is not sustainable, and Alberts has proposed a phase-in solution whereby institutions will eventually need to cover half of all investigator salaries. Alternatively, the NIH could negotiate with individual institutions the number of soft money positions that can be accommodated. Alberts wrote, "Regardless of mechanism, here is my bottom line: A new NIH policy must make it unambiguously clear that expansion through laboratory building and construction requires a substantial, non-reimbursable, long term commitment of resources, including 'hard-money' faculty support, by any institution that wants to increase its facilities and research staff." To help current dollars go farther, others have proposed caps on indirect cost rates, either per grant awarded or per investigator, and caps on dollars awarded to a single investigator.

My personal hope is that action be taken soon that is preferably merit-based and as fair as possible to all investigators and institutions. We cannot wait much longer to take action, and all of us need to think hard about how to get the most bang for the currently available research bucks. As Alberts put it, "Although change will be painful, it is urgently needed to maintain a healthy biomedical research enterprise."

ASBMB President Suzanne Pfeffer (pfeffer@stanford.edu) is a biochemistry professor at the Stanford University School of Medicine.

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2. Alberts, B. (2010) Overbuilding research capacity. *Science* **329**, 1257.

Disaster insurance?

BY SUZANNE PFEFFER

I just learned of a new faculty member at Sendai University in Japan, whose family and home are both safe but whose very expensive microscopes were destroyed in the recent earthquake. My own lab sustained damage in the Loma Prieta earthquake of 1989 — luckily nothing too major. Double water-jacketed tissue culture incubators toppled over, but we worked with those very dented (but still functional) units for twenty years after. Centrifuges and -80°C freezers waltzed away from the walls – now they all are secured to the walls with wires; glassware cabinets now have strong hinges and chemical shelves all require lips. Who pays when expensive equipment is lost? Although some relief funding was made available, institutions often are shouldered with the responsibility to insure, and most of them "self-insure." For me, that meant that no new funds were available to replace damaged incubators. Now seems like an important time to re-evaluate how we protect our laboratories from natural disasters, as we watch the recovery just beginning in Japan.

ASBMB members meet with NIH leadership

PAAC suggests revisions to maintain the long-term health of scientific research

BY GEOFFREY HUNT

At the heart of the research funded by the National Institutes of Health lies the investigator-initiated grant. Designed to "support a discrete, specified, circumscribed project to be performed … in an area representing the investigator's specific interest and competencies, based on the mission of the National Institutes of Health," this funding mechanism has allowed basic researchers to lay the groundwork for advances in medical cures and treatments for more than 60 years.

Unfortunately, since 2003 (when the NIH budget doubling was completed), support for investigator-initiated research has declined markedly. Compared to 2003, 1,000 fewer grants were funded in 2010, while application success rates have dropped below 20 percent. Adding to the strain on resources is a stagnation of growth in the NIH budget. During its biannual meeting last month, the American Society for Biochemistry and Molecular Biology Public Affairs Advisory Committee met with officials at the NIH to offer proposals on how to reverse this trend and optimize the agency's resources. The PAAC suggested the following revisions to NIH policy:

1. **Rebalance the NIH budget portfolio back toward investigator-initiated research.** Approximately $20 billion of the NIH's $30 billion budget is allocated as research funds, of which 50 percent (approximately $10 billion) goes to investigator-initiated grants. Raising this amount to 55 percent of research spending would return the research portfolio balance to its 2003 proportions. Moreover, this rebalancing could easily be achieved by reducing or eliminating funding for inefficient, non-investigator-initiated programs.

2. **Adopt a competitively based sliding scale.** Various formulations could be used to institute this proposal: One would be 100 percent funding for the 1st through 5th percentiles, 90 percent funding for 5th through 10th percentiles, 80 percent for 10th through 15th percentiles, and 70 percent for 15th through 20th percentiles, assuming that, with all measures taken, funding would occur up to the 20th percentile. Under this policy, success rates would inevitably rise, allowing more investigator-initiated grants to receive at least partial funding.

3. **Restrict the amount of funding for any individual investigator.** To identify an acceptable cap, the research community would have to work with agency officials to strike a reasonable balance between impeding new research and making funding available for more grants, given current research initiatives. This proposal also requires recognition of the broad range of support that individual investigators receive and the vastly differing types of research performed. One model comes from the National Institute of General Medicine Sciences, which institutes an automatic review of grant applications from any investigator already receiving more than $750,000. The efficacy of such a proposal has been illustrated by a recent study conducted by NIGMS Director Jeremy Berg that indicated researchers with funding at or below $500,000 in direct costs were as productive or more productive than researchers receiving higher amounts.

The PAAC stressed that these proposals were not meant as permanent measures but rather as emergency actions during this perilous financial period to maintain the long-term health of scientific research in this country. Failure to retain our brightest minds in research today will lead to wide-ranging problems tomorrow and result in fewer innovations and decreased American competitiveness in the global arena. The recommendations made by the PAAC represent logical, pragmatic solutions that will allow a larger number of investigators to continue what they always have done: drive America forward.

Geoffrey Hunt (ghunt@asbmb.org) is the ASBMB science policy fellow.

Recent petition condemns NIH grant renewal policy

More than 2,000 scientists back petition

According to National Institutes of Health policy, "Beginning with original new applications (i.e., never submitted) and competing renewal applications submitted for the January 25, 2009 due dates and beyond, the NIH will accept only a single amendment to the original application. Failure to receive funding after two submissions (i.e., the original and the single amendment) will mean that the applicant should substantially re-design the project rather than simply change the application in response to previous reviews. It is expected that this policy will lead to funding high quality applications earlier, with fewer resubmissions."

At the present time, several NIH institutes are unable to fund applications unless they obtain scores of 7th or 8th percentile or better. Thus, even outstanding applications that obtain a 10th percentile ranking on second resubmission may not be funded. The following petition was circulated by Robert Benezra of Memorial Sloan-Kettering Cancer Center to raise awareness of this problem. Over 2,000 signatures were included on the petition below, which was sent to NIH director Francis Collins on Feb. 21, 2011.

• • •

Dear Drs. Collins and Scarpa,

I am writing on behalf of 2,356 U.S. scientists (listed below) committed to changing a new NIH policy that we believe will have an overwhelming negative impact on biomedical research in this country. The rule in question specifies that if a grant proposal is not funded on the first submission, only one revision can be filed with the same specific aims. If that revision is not funded, the proposal must be "substantially" changed. As we understand it, the rule was adopted to discourage "serial resubmitters" and was based on the observation that success rates of grants poorly scored in the first round did not benefit substantially from a second resubmission. In addition, it was designed to discourage the implicit "queuing" system, whereby poorer second revision applications (A2s) displaced A0s and A1s that were just "waiting in line" for funding. While such a policy could make sense in an era of reasonable pay lines, with the projected budgets rumored to be funding at the 7th percentile in some institutes, this could have a drastic and we would argue devastating effect on the biomedical research efforts in this country.

Consider the following:

The premise of our argument is based on the fact that all of us who have sat on study sections know that we cannot distinguish a 20th percentile grant (13 points from the hypothetical pay line) from a 5th percentile grant (which now is just in the fundable range). It is simply beyond the limit of resolution of the process. We are not after all just evaluating the impact or validity of a scientific finding or theory (as difficult as that can be), but the projected trajectory of some early findings, a process which is fraught with extraordinary uncertainties in fields as complex as ours.

Where then is the evidence that the majority of A1 applications that just missed the 7th percentile pay line (indistinguishable in quality from other A1s in that cycle that were funded) but were eventually funded as A2s, are not of great value and should be eliminated? So thoroughly flawed in fact that it is better to eliminate them entirely rather than displace (in their A2 submission round) some A0s and A1s into the next cycle? This argument is particularly worrisome if in fact the economic crisis ever abates even incrementally during a period when many potential meritorious A2s are being discarded from the pool.

Also, we have been told that a measure of success of the new policy is a noticeable increase in the fraction of successful applications that are A0s. But this only makes sense if the majority of those funded A0s are derived from A2s that were forced to write "substantially new" and better applications. It is equally likely this results from the fact that there are fewer outstanding A2s in the pool that were eliminated essentially by chance. Trivially put, if no resubmissions were allowed then of course all funded applications would be A0s. Is that the goal of the new policy?

Therefore, we believe this new rule will have the consequence in the current funding climate of redirecting the efforts of many of our very best scientists on the basis of what will essentially be an arbitrary criterion.

The rule will have a disproportionately negative impact on young investigators with early stage and therefore less

diverse programs (particularly those at the stage of their first renewal), or more senior investigators who also have more narrowly focused programs. How can a young investigator, for example, who is just starting to build their program "substantially" change their aims when they have to focus their efforts on a very limited number of projects undertaken with limited funds and staff? These investigators are often hired by senior faculty on the strength of their first proposals in intensely competitive job searches. To be told they must change their focus on the basis of applications that fail despite being ranked better than 90 percent of grants submitted, seems at odds with all of our objectives. And worse, it is likely to be profoundly discouraging and destructive.

As a result of these considerations, we are urging you to return to the two-revision system at least for the subset of applications that cross a certain threshold in scoring as A1s. Certainly a metric can be found which would identify the threshold that would be the most beneficial using currently available statistics. Many of us would be willing to participate in that discussion.

We understand that even if these changes are implemented, many outstanding proposals will still not get funding solely because of budgetary constraints. And we as a group are contemplating ideas to help address that issue as well. We nevertheless believe the change in revision policy advocated here would allow for a much fairer assessment of the research proposals being generated by the best and the brightest investigators in our country.

In what we sincerely hope will be a transition period back to some semblance of the two revision system for grant submissions, investigators submitting "new" proposals now need more guidance on what constitutes a substantially revised application. We have read the CSR's "Evaluation of Unallowable Resubmission and Overlapping Applications" but find that Program Officers themselves are not sure what rule to follow in certain circumstances. If for example an unfunded A1 has two aims that are considered to be outstanding with a weaker third aim, are we to understand that one of the outstanding aims cannot be pursued unless substantially changed even if conceptually intertwined with the other? We have heard things from "51 percent different", "Change the tissue or cell type you are working on," "Any aim included in either the first application or revision cannot be included," and "If you are working on potassium channels, switch to calcium." It would be helpful to have clear, unequivocal and sensible guidance on this point very soon as "new" proposals are being prepared by a large number of investigators at this time whose careers depend on these applications.

We urge you to give this petition serious consideration and look forward to your response.

Yours sincerely,

Robert Benezra
(r-benezra@ski.mskcc.org)

Please note that any e-mail responses to this petition received from your offices will be forwarded to all of the signers below. Validation of each individual's willingness to sign will be provided upon request. Signatures were collected from 2/11/2011 to 2/17/2011 in response to a mailing of an earlier, incomplete draft to a list of 39 original recipients. XXX

Stretching NIH resources

A summary of a recent comment on the Sally Rockey Extramural Nexus blog

All of us must be prepared to make sacrifices to help National Institutes of Health dollars go farther, and we need to consider all options to decide how best to proceed. Recently, on Sally Rockey's Extramural Nexus blog, Daniel J. Noonan of the University of Kentucky College of Medicine commented on how to address current challenges in NIH funding. Some of his suggestions are excerpted here to encourage discussion.

Priority 1: Implementation of measures for increasing available dollars for funding investigator-initiated research awards.

1. Delay initiatives like the National Center for Advancing Translational Sciences; be wary of large projects for drug development and screening.
2. Limit NIH-funded independent research awards to three grants and $1,000,000 a year per investigator. Factor in

composite funding when deciding the merit of funding a grant application, especially in cases where the PI is an established investigator with huge non-NIH funding sources.

3. Use a diminishing formula for indirect costs on multiple grants (e.g., 100 percent for the first grant, 50 percent for the second, and 25 percent for the third).
4. Reduce maximum salary dollars available to 50 percent.
5. Limit, if not eliminate, the NIH-funded subsidization of research building projects.
6. End initiatives that either compete with or subsidize pharmaceutical company drug discovery efforts.
7. Trim waste and excess in NIH intramural funding.

Priority 2: Implementation of measures for increasing funding directed toward smaller research operations, especially those of unfunded established investigators.

1. Create vehicles that emphasize funding of smaller research operations. Although it is presumed that the initiatives in Priority 1 above will free money for R01 and R21 funding, it becomes irrelevant if you don't get the money into the hands of those needing it. Create a category of unfunded established investigators and fund this category in the 25 to 30 percent range.
2. Increase the funding of medically related basic research projects. These often are the focus of smaller laboratory operations; are the essential foundation of applied research; have led to most, if not all, of the major scientific breakthroughs for the past century; will lead to most, if not all, of the major scientific breakthroughs in this century; are an essential aspect of maintaining a leading international role in scientific discovery; and, perhaps most importantly, fund many of the projects that inspire and develop our next generation of medical researchers.

Priority 3: Implementation of measures for increasing the quality of reviews and reducing luck as the driving force of grant funding.

1. Require, as a stipulation of NIH funding, that funded investigators must serve on study sections for a minimum of one year for every three years of funding with no exceptions. This will assure that there are plenty of qualified reviewers and perhaps even moderate aspirations for a limitless number of NIH awards.
2. Do away with the two-strikes-and-you're-out rule and go back to the three-submission scenario.
3. Review, discuss and give priority scores to all grant submissions.
4. Allow and even encourage reviewers to provide constructive feedback in their reviews once again.

that all of us look for a remarkably similar set of fundamental knowledge and skills when we screen applications for graduate school or consider taking a new student into our laboratories: Do they understand the proper application of positive and negative controls, the difference between correlation and causality, or the dynamics of chemical equilibria? Can they perform the necessary calculations and manipulations to produce a buffered solution of defined composition? Do they understand what a catalyst is, why His tags bind to Ni^{2+} columns or why the distance a protein migrates on an SDS gel generally is related to its size? I agree that a multiple-choice BMB trivia game would likely prove challenging for our editors and found wanting as an assessment tool. But what we propose is quite different.

Informed by many years of distinguished service as a scientist and educator, Dr. Linn has offered a thoughtful challenge. In return, I would ask the question, "What should the society be doing to capture the attention of young biochemists, molecular biologists, cell biologists, etc.?" I do so because I believe that inaction is not a viable alternative.

Respectfully,
Peter J. Kennelly

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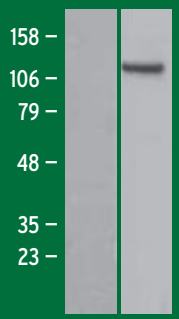

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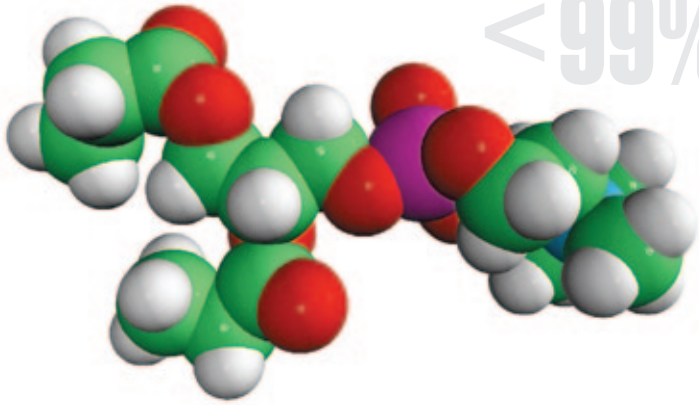

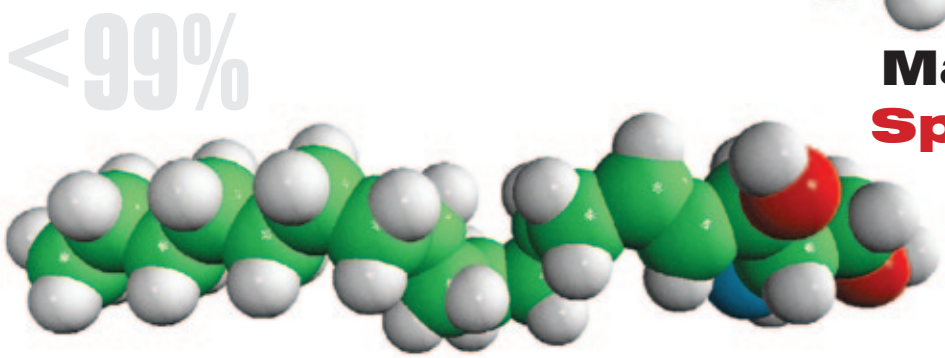

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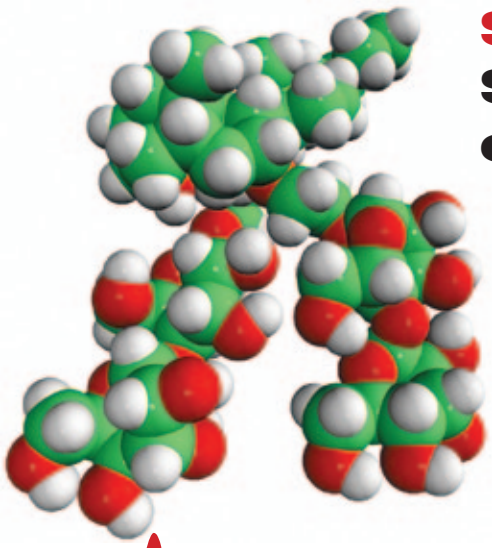

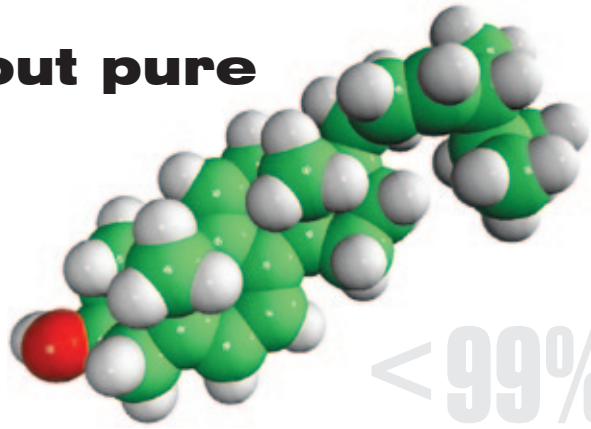

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History in the making

Journal announces new JBC/Herbert Tabor Young Investigator Awards

BY MARTY FEDOR

For many, the decision last year by the Journal of Biological Chemistry's longtime editor-in-chief Herbert Tabor to hand over the reins might have seemed like an end to an era. Forward-thinking as always, Tabor insists instead that it heralds the dawn of a new phase for the JBC, one that is full of opportunity, invention, innovation and discovery. I share Tabor's view and his enthusiasm for being part of this new phase.

I have always been inspired by the way Tabor views the JBC and how he has managed it. Invariably appreciative and respectful of JBC authors and reviewing editors, he certainly has never seen it as *his* journal. He constantly puts the quality of the journal and the needs of the scientific community front and center.

In view of Tabor's many contributions to the scientific community and the values of integrity and service that he represents, I am very pleased to announce the launch of a new award series: The Journal of Biological Chemistry/ Herbert Tabor Young Investigator Awards. These awards are meant to honor Tabor's invaluable contributions to the journal and to science as a whole. At the same time, the awards will recognize the innovators and achievers in new generations of researchers who exemplify his values of creativity and scientific excellence.

The associate editors, who know Tabor and the mission of the JBC best, will select promising young researchers at scientific symposia and meetings throughout the year that focus on the molecular and cellular basis of biological processes. So far, the JBC associate editors have identified a dozen meetings focused on areas long featured in the JBC and on emerging research areas in biological chemistry where great candidates are likely to convene.

Marty Fedor (mfedor@asbmb.org) is editor-in-chief of the Journal of Biological Chemistry.

How the award program works

The Journal of Biological Chemistry/ Herbert Tabor Young Investigator Awards will be presented by the journal's associate editors at meetings other than the annual meeting of the American Society for Biochemistry and Molecular Biology.

The awards will be issued each year to meeting participants who give outstanding oral or poster presentations. Students, postdoctoral researchers and faculty members who've not yet received tenure will be eligible.

The award includes a plaque and a $1,500 prize.

Meetings on the list

Gordon Research Conference: CAG Triplet Repeat Disorders
JUNE 5 TO 10 IN LUCCA, BARGA, ITALY

17th International Conference on Cytochrome P450
JUNE 26 TO 30 IN MANCHESTER, U.K.

Gordon Research Conference: Molecular and Cellular Biology of Lipids
JULY 17 TO 22 IN WATERVILLE VALLEY, N.H.

The 25th Annual Symposium of The Protein Society
JULY 23 TO 27 IN BOSTON, MASS.

ASBMB

Special Symposium: Recent Advances in Pathogenic Human Viruses
JULY 24 TO 26 IN GUANGZHOU, CHINA

Gordon Research Conference: Matrix Metalloproteinases
AUG. 6 TO 7 IN SMITHFIELD, R.I.

52nd International Conference on the Bioscience of Lipids
AUG. 30 TO SEPT. 3 IN WARSAW, POLAND

ASBMB

Special Symposium: 13th International ATPase Conference
SEPT. 27 TO OCT. 2 IN PACIFIC GROVE, CALIF.

9th Joint Meeting of the International Cytokine Society and the International Society Interferon and Cytokine Research
OCT. 9 TO 12 IN FLORENCE, ITALY

7th General Meeting of the International Proteolysis Society
OCT. 16 TO 20 IN SAN DIEGO, CALIF.

7th International Conference on Proteoglycans
OCT. 16 TO 20 IN SYDNEY, AUSTRALIA

The Cell Signaling Networks Conference
OCT. 22 TO 27 IN MERIDA, MEXICO

asbmb member update


BOND


CRAIK


ROBINSON


BASSLER


BENKOVIC


BERGER

Bond named FASEB president-elect

Judith S. Bond, professor and chairwoman of biochemistry and molecular biology at The Pennsylvania State University, has been named president-elect of the Federation of American Societies for Experimental Biology. She will begin her term on July 1, 2011, will serve as president-elect through June 30, 2012, and will take office as FASEB president on July 1, 2012.

Bond's research focuses on the structure, function and regulation of proteolytic enzymes called meprins. She was president of ASBMB from 2004 to 2006 and is currently an associate editor of the Journal of Biological Chemistry.

Craik garners Hirschmann Award in Peptide Chemistry

David Craik, a professor at the University of Queensland's Institute for Molecular Bioscience, has won the Ralph F. Hirschmann Award in Peptide Chemistry from the American Chemical Society.

Craik was recognized for his work with circular peptides, known as cyclotides. He described the first cyclotide and has been a major contributor to the field ever since. Recently, he engineered a new circular peptide to treat pain by combining a stable cyclotide with a conopeptide — a pain-blocking peptide found in the venom of marine cone snails. The engineered molecule has proven effective at treating pain in early trials.

The Ralph F. Hirschmann Award was established in 1988 to recognize and encourage outstanding achievements in the chemistry, biochemistry and biophysics of peptides. It is sponsored by Merck Research Laboratories.

Robinson wins women in science award

The European Molecular Biology Organization and the Federation of European Biochemical Societies recently announced that Carol V. Robinson, professor of chemistry at the University of Oxford, is the winner of the 2011 FEBS/EMBO Women in Science Award. Robinson was been recognized for her pioneering work in the development of mass spectrometry as a tool for investigating the structure and dynamics of protein complexes.

The award recognizes exceptional achievements by a female researcher in molecular biology during the previous five years. Winners of the award are role models who inspire future generations of women in science.

"Carol V. Robinson has pioneered, in an almost single-handed manner, the use of electrospray mass spectrometry for structural studies of large multimeric protein assemblies. She had the courage to do what experts regarded as not feasible and has succeeded in the face of strong skepticism," stated her collaborator Wolfgang Baumeister of the Max Planck Institute of Biochemistry in Martinsried, Germany, in his nomination of Robinson for the award.

Robinson's group was one of the first to use electrospray mass spectrometry to study large protein complexes. In collaboration with Micromass UK, she designed an instrument specifically adapted for the detection of high-mass complexes. This instrument has since gone into production in Canada and the UK and is in use in many laboratories around the world. More recently, Robinson's research has focused on combining mass spectrometry with cryoelectron microscopy.

National Academy honors four ASBMB members

Recently, the National Academy of Sciences honored four ASBMB members with awards recognizing their extraordinary achievements in science.

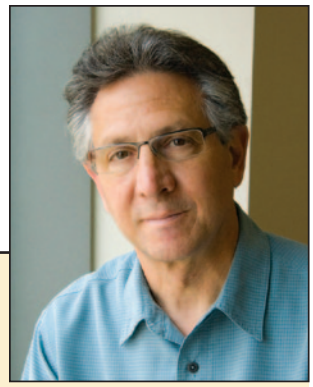
BONNIE L. BASSLER, a Howard Hughes Medical Institute Investigator and Squibb professor in the department of molecular biology at Princeton University, received the Richard Lounsbery Award for her pioneering discoveries of the universal use of chemical communication among bacteria and the elucidation of structural and regulatory mechanisms controlling bacterial assemblies.

STEPHEN J. BENKOVIC, Evan Pugh professor and Eberly chairman in chemistry at The Pennsylvania State University, was given the NAS Award in Chemical Sciences for his contributions to understanding catalysis and complex biological machines with his work on the purinosome and DNA polymerases.

JAMES M. BERGER, the Walter and Ruth Schubert Family chairman in biochemistry and molecular biology at the University of California, Berkeley, is the recipient of the NAS Award in Molecular Biology. He is being honored for elucidating the structures of topoisomerases and helicases and providing insights into the biochemical mechanisms that mediate the replication and transcription of DNA.

PHOTO: ROY KALTSCHMIDT, BERKELEY LAB PUBILC AFFAIRS.

CAROL A. GROSS, professor in the departments of microbiology and immunology and cell and tissue biology at the University of California, San Francisco, was given the Selman A. Waksman Award in Microbiology. She is being honored for her pioneering studies on mechanisms of gene transcription and its control and for defining the roles of sigma factors during homeostasis and under stress.



MARLETTA

Q&A with incoming Scripps president Michael A. Marletta

Renowned biochemist Michael A. Marletta recently was named the next president of The Scripps Research Institute (which also is home to Journal of Biological Chemistry editor Marty Fedor). Marletta will take the reins from Richard A. Lerner, who has led the nonprofit institution for 25 years, on January 1, 2012. We interviewed Marletta, who currently is the Aldo DeBenedictis distinguished professor of chemistry and professor of biochemistry in the department of molecular and cell biology at the University of California, Berkeley, about his new position.

ASBMB: For readers not familiar with your research, what do you do, in a nutshell?

Marletta: *My long-standing interest in enzymology and unusual enzyme-catalyzed reactions led us into nitric oxide synthesis and biological function. Over the years, that has led to more general questions, such as, How does biology tell the difference between molecules like nitric oxide and oxygen? The molecular basis for selective responses to gases such as these and the signaling pathways in eukaryotes and prokaryotes, including pathogens, is a current focus. The application of what we learn to the development of novel therapeutics remains an interest. We have also begun a program looking at Neurospora as a model organism for cellulose degradation.*

ASBMB: What do you see as the core strengths of the Scripps Research Institute?

Marletta: *Scripps is unique. Richard Lerner's vision over his 25 years of leading the institution was to recognize the importance of bringing molecular thinking to the first-rate biology that already existed at Scripps. He built a chemistry department from scratch, and when you couple that with a leading program in structural biology and then inextricably link the chemistry and structure to the biology, great things can happen and, in fact, have happened. This model has now spread across the country to Scripps Florida.*

ASBMB: What do you think your biggest challenge(s) will be as president of Scripps?

Marletta: *I want Scripps to continue to be at the forefront of discovery. To do this, we need to continue to build the science infrastructure and to bring the best of scientists, especially those at the beginning of their careers, to Scripps. To accomplish both of these essential goals, new sources of revenue must be found. I plan to spend my time taking the Scripps message forward to all who will listen and to convince them to support our efforts to make discoveries and cure disease.*

ASBMB: What's your vision of the future for Scripps?

Marletta: *This is a very exciting time for biomedical research. Never has the opportunity to interrogate and deeply understand biology been greater. I want Scripps to continue to lead and move into new and exciting areas of discovery. Scripps is one institution and two campuses — La Jolla and Jupiter. The La Jolla campus has a well-defined identity while that for Scripps Florida is quickly evolving. Together with faculty leaders from both campuses, we will chart a course to move forward.*

ASBMB: Scripps gets most of its money from the NIH, which has been experiencing ongoing pressure to cut its budget. How do you think this will affect Scripps' future research efforts?

Marletta: *This is a national issue. I don't deny the potential effect of reduced federal grant support on an institution like Scripps could be significant. The Scripps faculty members have proven themselves to be resilient. That resilience coupled with their drive and zeal for science will carry us a long way. We must diversify and broaden our support base and with success in this, Scripps' future research efforts will proceed unabated.*

ASBMB: During his time as president, Richard Lerner tripled the size of the institute and currently is able to pull in more than $330 million a year for research. Is it intimidating to fill such big shoes?

Marletta: *Actually, I was at Scripps last week, and I mentioned this question to Richard. He told me he wears a size 9.5. I wear a size 10, so it seems it's more his problem than mine. Seriously, the bulk of the value you mentioned includes outside grant support. As I mentioned above, securing Scripps' future via philanthropy is the goal. With those resources, the next generation of biomedical scholars will come and make the kinds of discoveries expected of Scripps.* XXX

PHOTO: MICHAEL BARNES, COLLEGE OF CHEMISTRY, UC BERKELEY.

The 2011 ASBMB Special Symposia Series

The American Society for Biochemistry and Molecular Biology's Special Symposia Program was developed with two primary goals: to bring scientists together in a unique environment that fosters interactive discussions on the latest cutting-edge research, and to provide students and young investigators the opportunity to highlight their research. In 2010, more than 450 scientists participated in the symposia series, including oral and poster presentations from 150 graduate and postdoctoral students.

This year, the symposia series will continue to offer a unique experience via six biochemistry themes being held July 20–Oct. 30 at a variety of locations, including Richmond, Va.; Pacific Grove, Calif.; Guangzhou, China; Snowbird, Utah and Tahoe City, Calif. Registration and abstract submission are now open for all meetings. Key deadlines for each symposium are included in the following articles and online at www.asbmb.org/special symposia. Also, don't forget to use the Tell a Friend link to invite colleagues to join you at a meeting.

Symposium: Cellular traffic of lipids and calcium at membrane contact sites

Joint meeting sponsored by ASBMB and Biochemical Society will be one of the first to focus exclusively on MCSs

BY TIM LEVINE AND WILLIAM PRINZ

Levine

Prinz

The exchange of information between intracellular compartments is vital for cells. There is growing evidence that this communication can occur at close contacts between organelles often called membrane contact sites. At these sites, the membranes of two organelles are closely apposed, often within about 10 nm of one another, close enough to be bridged by a single protein.

MCSs have been found in all cell types and often are between the endoplasmic reticulum and a second organelle. They also have been reported between the two membranes of gram-negative bacteria and between the internal membranes of mitochondria and chloroplasts. Small molecules, including lipids and calcium ions, are exchanged at MCSs. There also are a number of instances in which an enzyme on one of the organelles at an MCS acts on a substrate on the second organelle.

We are just beginning to understand how MCSs form and function, and many fundamental questions remain. A precise understanding of the roles of MCSs has been slowed by the relatively poor molecular understanding of how these highly conserved structures are formed and how they function in cells. Until recently, there was only a single MCS for which the structural components — the proteins that bridge the organelles — were known, making it hard to attribute cellular functions to MCSs.

Recently, the identities of a number of MCS components have been discovered as well as the make-up of several bridging components. This new, detailed knowledge promises to be the seed of a novel field of nonvesicular trafficking and signaling at MCSs, as there now is a sufficient base to propel the discovery of other active players and functions.

The "Cellular traffic of lipids and calcium at membrane contact sites" meeting, which is jointly sponsored by the American Society for Biochemistry and Molecular Biology and the Biochemical Society, will be one of the first to focus exclusively on MCSs. It will bring together scientists from diverse backgrounds with a common interest in nonvesicular trafficking and signaling at MCSs. In the past, people interested in signaling and molecular exchange at MCSs have tended to focus on either lipids or calcium. This meeting will allow researchers from all disciplines with a shared interest in MCSs to come together.

We have a diverse array of invited speakers, including Luca Scorrano of the University of Geneva and Benoit Kornmann of ETH Zurich, who will address the construction of bridges between organelles. Lipid transport, with an emphasis on lipid exchange mediated by lipid transfer proteins at MCSs, will be the subject of talks from several leaders in this field, including Vytas Bankaitis of the University of North Carolina School of Medicine, Shamshad Cockcroft of University College London, Dennis Voelker of National Jewish Health and Christoph Benning of Michigan State University. Tobias Meyer of Stanford University will talk about calcium signaling and calcium flows across MCSs, and Anamaris Colberg-Poley of the Children's National Medical Center will discuss her work on virus trafficking at organelle junctions. Several talks also will be chosen from submitted abstracts.

We are very pleased to have Richard Lewis of Stanford University Medical School give the meeting's keynote lecture. Lewis has been a pioneer in the study of calcium signaling at junctions between the endoplasmic reticulum and the plasma membrane, and he has done groundbreaking work on how calcium uptake across junctions is regulated. He also is a dynamic speaker who is sure to give an exciting talk.

The study of how organelle junctions form and function still is at an early stage, but rapid progress is occurring on many fronts. We hope to see you in Snowbird, Utah, to learn more about and participate in this exciting, emerging field.

Tim Levine (tim.levine@ucl.ac.uk) is a lecturer in cell biology at the University College London Institute of Ophthalmology. William Prinz (wp53m@nih.gov) is an investigator in the National Institute of Diabetes and Digestive and Kidney Diseases at the National Institutes of Health.

Cellular traffic of lipids and calcium at membrane contact sites

A joint meeting with the Biochemical Society

Oct. 6 – 9, 2011

Snowbird Ski and Summer Resort, Snowbird, Utah

Oral and poster abstract submission deadline: July 15, 2011

Early registration deadline: July 15, 2011

For more information, visit: www.asbmb.org/2011CellularTraffic

Symposium: Gene regulation by noncoding RNAs

Sessions will cover a variety of topics including the biogenesis of small noncoding RNAs and genetic, genomic and biochemical approaches to post-transcriptional silencing mediated by siRNAs

BY RICHARD CARTHEW AND JENNIFER DOUDNA

Carthew

Doudna

Traditionally, RNA has been thought of as a molecule that imparts information, structure or catalytic activities. However, it has become apparent that RNA also can directly regulate gene expression.

In eukaryotes, RNA mediates widespread defense against transposable elements and viruses, organizes the genome, and serves to regulate the expression of cellular protein-coding genes. Small RNAs that participate in this process are made up of 21 to 27 nucleotide fragments and are processed from double-stranded precursor molecules. Once formed, these siRNAs, piRNAs and miRNAs associate with cellular proteins and guide those proteins to complementary nucleic acids (chromosomal DNA or mRNA transcripts) and repress the target nucleic acids.

The impact of small noncoding RNAs has profoundly touched the fields of development and cell biology, functional genomics, human disease and drug therapy.

The "Gene regulation by noncoding RNAs" meeting will feature keynote speaker Phillip D. Zamore from the University of Massachusetts Medical School and the Howard Hughes Medical Institute. He is a world leader in the study of small RNAs, combining elegant genetics and biochemistry to understand the molecular mechanisms of RNA silencing.

The sessions will begin with talks describing the biogenesis of small noncoding RNAs featuring some of the latest advances in miRNA and piRNA mechanisms. With crystallographic and biochemical approaches, we have not only learned how small RNA processing occurs but also much more about how small RNA-Argonaute

complexes associate with target RNAs and catalyze their silencing. A structure-function session will feature Dinshaw Patel of the Memorial Sloan Kettering Institute, who is a pioneer in crystallographic studies of RNA-Argonaute complexes.

Sessions also will explore genetic, genomic and biochemical approaches to post-transcriptional silencing mediated by siRNAs and will feature Andrew Fire of Stanford University, who is a co-discoverer of RNAi and Nobel laureate.

Other sessions will focus on insights into how miRNAs repress mRNA transcript stability and translation. Given the lively and spirited debate about this topic in the miRNA field, the sessions promise to stimulate discussion both formally and informally. Two featured speakers recently have written thoughtful reviews on this subject and will discuss their discoveries, which are influencing the field.

Finally, small noncoding RNAs are not limited to regulating post-transcriptional gene expression. Steve Jacobsen of the University of California, Los Angeles and Xumei Chen of the University of California, Riverside will speak on transcriptional silencing in a session devoted to nuclear regulation. Fungal, plant and animal systems will be featured.

Session talks also will be chosen from submitted abstracts, providing a great avenue for graduate students, postdoctoral fellows and investigators with their own independent programs to present their work either orally or as posters.

Overall, the goal of this meeting is to promote sharing of ideas and discoveries between biochemists, molecular biologists, geneticists and systems biologists working in the field of small RNA biology.

Richard Carthew (r-carthew@northwestern.edu) is a professor at Northwestern University. Jennifer Doudna (doudna@berkeley.edu) is a professor at the University of California Berkeley and an investigator at the Howard Hughes Medical Institute.

Gene regulation by noncoding RNAs

Oct. 27 – 30, 2010

Tahoe City, Calif.

Oral and poster abstract submission deadline: Aug. 1, 2011

Early registration deadline: Aug. 1, 2011

For more information, please visit: www.asbmb.org/2011GeneRegulation

Symposium: Na,K-ATPase and related P-type ATPases: structure, biology and medicine

The four-day meeting will have sessions devoted to structure and mechanism, cell biology and trafficking, regulation, signaling, and mechanisms in physiology and medicine

BY KATHLEEN SWEADNER

Sweadner

The Na,K-ATPases, Ca^{2+}-ATPases and their relatives have extremely important physiological roles as transporters. They are much more than ion pumps, however, as they also play complex roles in cell biology that were unimagined 10 to 15 years ago. The interdisciplinary "Na,K-ATPase and related P-type ATPases: structure, biology and medicine" meeting will bring together biochemists, physiologists, doctors, geneticists and cell biologists with shared interests in this subject.

The P-type ATPases are membrane proteins that catalyze uphill transport via the hydrolysis of ATP. They are found in all domains of life. The group is named for the labile covalent phosphorylation of an aspartate residue as part of the reaction mechanism, and its members share essential structural features. Eleven human diseases caused by mutations in different P-ATPases have been found, and many more are thought to exist. Multiple crystal structures of the muscle Ca^{2+}-ATPase SERCA in different conformations have resulted in dynamic models of its mechanism.

Physiological regulation of transport occurs at multiple levels, which is consistent with the many indispensible biological roles of P-type ATPases. The enzymes are major pharmacological targets, notably for digitalin and omeprazole in humans, and they also are essential for many pathogens. While the subject of this meeting is focused narrowly enough to keep it cohesive, the scope of new discoveries and medical implications in the field is expanding rapidly.

The textbook concept of ATPases as ion pumps was turned upside down by the discovery that the Na,K-ATPase also is a signaling molecule integrated into the control of cell proliferation and hypertrophy with transport-independent roles in a number of diseases. It signals through interaction with either Src or the IP3 receptor.

More recently, a completely new and unrelated role has emerged for subunits of Na,K-ATPase in intercellular adhesion and cell junction structure and function and thus in tissue morphogenesis and cancer. Many of the really novel recent discoveries in P-type ATPases have encompassed such noncanonical roles.

Because P-ATPases are so diverse and widespread, no single national meeting attracts a critical mass of interdisciplinary experts in this field, who can range from crystallographers to clinicians. Few other meetings give the opportunity for cancer biologists interested in growth control or the modulation of cell adhesion to see where their interests intersect with those of cardiologists investigating contractility or endogenous ligands or neurobiologists investigating the basis of genetic defects, and then to relate these findings to atomic-level structures. This American Society for Biochemistry and Molecular Biology event continues a tradition of holding international meetings on P-ATPases that are attended by experts from all over the world every three years.

The meeting will be four days long with sessions devoted to structure and mechanism, cell biology and trafficking, regulation, signaling, and mechanisms in physiology and medicine. Invited speakers will discuss several kinds of calcium ATPases, Na,K-ATPases and H,K-ATPases, copper ATPases, proton ATPases and the exciting area of lipid flippases. The meeting scope will include the structures and the remarkable conformational dynamics of this class of molecules; mutations in mechanistic studies and in human disease; regulatory networks, trafficking and complexes associated with ATPases; the drugs and endogenous ligands that bind to ATPases; and the enzymes' unique regulatory proteins, such as phospholamban and FXYDs.

The meeting will have two keynote lectures. One, given by Poul Nissen, a professor at the University of Aarhus in Denmark and director of the Center for Membrane Pumps in Cells and Disease, will focus on recent P-ATPase structures and enzyme mechanisms. The other talk will cover equally exciting developments in the role of Na,K-ATPase as a signaling molecule with roles in cell survival and development in the brain and kidney. This talk will be given by Anita Aperia, a professor emerita at the Karolinska Institute in Stockholm, Sweden.

Kathleen Sweadner (sweadner@helix.mgh.harvard.edu) is an associate professor of cellular and molecular physiology at the Massachusetts General Hospital and Harvard Medical School. The meeting's co-organizers are Svetlana Lutsenko (Johns Hopkins University), Hiroshi Suzuki (Asahikawa Medical College), Zijian Xie (University of Toledo) and Jacob Sznajder (Northwestern University).

Na,K-ATPase and related P-type ATPases: structure, biology and medicine

Sept. 27 – Oct. 2, 2011

Talk and poster abstract deadline: July 1, 2011

Early registration deadline: July 1, 2011

Asilomar Conference Grounds, Pacific Grove, Calif.

For more information, please visit:
www.asbmb.org/2011ATPase

Symposium: Recent advances in pathogenic human viruses

ASBMB's first meeting in China will cover the molecular biology, pathogenesis and antiviral host defenses of a range of human viruses

BY KUAN-TEH JEANG AND DOUGLAS LOWY

Jeang

Lowy

Last year, for the first time ever, General Motors sold more cars in China than in the United States. Last year also was the first time that China's economy grew to a size larger than Japan's. This year will mark another first. The American Society of Biochemistry and Molecular Biology will be holding its first ever meeting in China. The meeting, "Recent advances in pathogenic human viruses," will be held July 24 to 26 in Guangzhou. It will be sharing the Baiyun Convention Center with a simultaneous larger molecular and cellular biology meeting, The Society of Chinese Bioscientists in America Thirteenth International Symposium (www.scbameeting2011.org). Guangzhou, the third-largest city in China, is beautifully situated on the Pearl River within 100 miles of Hong Kong. The city is easily accessible through its modern international airport as well as by train from Hong Kong.

The meeting will cover the molecular biology, pathogenesis and antiviral host defenses of a range of human viruses, including influenza virus, human immunodeficiency virus, herpesviruses, human papillomavirus, and hepatitis B and C viruses. We are excited by the prospect of having a good mix of speakers and attendees from North America,

Australia and Asia. If you are interested in virology, antiviral immunity or host defenses, this is a small, focused meeting that you will not want to miss. We welcome your submission of abstracts for consideration as short oral or poster presentations by the submission deadline of April 30, 2011. Space is limited, so act quickly to reserve your spot.

The meeting's keynote speaker will be Michael M. C. Lai, who currently is a distinguished investigator at Academia Sinica in Taiwan. For many years, Lai was a Howard Hughes Medical Institute investigator at the University of Southern California as well as a long-standing editor of Virology. Lai will present his latest findings on the molecular pathogenesis of hepatitis C virus. Several other outstanding plenary speakers also have committed to attend this meeting, including Elliott Kieff of Harvard University, Dong-Yan Jin of the University of Hong Kong, Bernard Moss of the National Institute of Allergy and Infectious Diseases, Bryan Williams of Monash University in Australia, and Diane Hayward of the Johns Hopkins University.

As part of a new initiative by the Journal of Biological Chemistry, invited speaker and JBC Associate Editor Charles Samuel of the University of California, Santa Barbara will present The Journal of Biological Chemistry/Herbert Tabor Young Investigator Award to one outstanding participant presenting research at the meeting. This prestigious award will include a $1,500 prize and a plaque.

If you never have visited China, this is an opportunity for you to attend a top-notch small virology conference, discuss cutting-edge science with enthusiastic colleagues from around the world and experience first-hand a rapidly modernizing Chinese culture. And if you have been to China, we know you will want to go back again for this event.

Ni hao! We look forward to seeing you in July in Guangzhou. XXX

Kuan-Teh Jeang (kjeang@niaid.nih.gov) is chief of the molecular virology section at National Institute of Allergy and Infectious Diseases, National Institutes of Health. Douglas Lowy (drl@helix.nih.gov) is chief of the laboratory of cellular oncology at the National Cancer Institute, NIH.

Recent advances in pathogenic human viruses

July 24 – 26, 2011
Guangzhou, China
Talk and poster abstract deadline: April 30, 2011
Early registration deadline: April 30, 2011
For more information, visit:
www.asbmb.org/2011HumanViruses

Symposium: Student-centered education in the molecular life sciences II

Follow-up meeting will emphasize student-centered approaches in the classroom and laboratory

BY J. ELLIS BELL

Bell

"Student-centered education in the molecular life sciences II" is the follow-up to the highly successful "Student-centered education in the molecular life sciences I" meeting that was held at Colorado College in 2009. Following up on the release of the report "Vision and change in undergraduate biology education" by the American Association for the Advancement of Science and the National Science Foundation last year, this year's meeting also could be titled "Putting the change into vision and change," given its strong emphasis on refocusing what students need to know and how to use more student-centered approaches in the classroom and lab. The meeting also builds on the American Society for Biochemistry and Molecular Biology's RCN-UBE grant titled "Promoting concept-driven teaching strategies in biochemistry and molecular biology through concept assessments" as well as recent initiatives supported by various Howard Hughes Medical Institute grants to undergraduate institutions focusing on interdisciplinary science integration into the curriculum.

The meeting will be held at the University of Richmond starting on Wednesday, July 20, with a midday check-in and lunch followed by an opening plenary session starting at 1:00 p.m. that will include several speakers associated with the NSF education report. After the plenary, there will be parallel afternoon sessions on active learning strategies, organized by Harold White of the University of Delaware, and outreach activities, organized by Lisa N. Gentile of the University of Richmond and Neena Grover of Colorado College. Throughout the meeting, the parallel sessions will be followed by a best-practices session that will summarize the earlier sessions and allow everyone to hear the outcome of each session and contribute to the discussion. On the first day, this session will be chaired by Brenda Kelly of Gustavus Adolphus College and Teaster Baird of San Francisco State University. The afternoon will conclude with an opening reception and dinner sponsored by Springer Publishing Company.

The second day will begin with a plenary talk featuring

Mike Klymkowsky from the University of Colorado, who will introduce the issues involved in promoting concept-driven teaching strategies in biochemistry and molecular biology through concept assessments. The remainder of the morning will be devoted to three grant-writing workshops organized by program officers and former program officers from the NSF and focusing on grants for research, education and instrumentation. A key feature of these workshops is that they will connect faculty members interested in grant writing with both the funding agency and successful grant applicants from other institutions, who will function as potential mentors. The afternoon will have three parallel sessions: "Sharing laboratory ideas and assessments," moderated by Ben Caldwell of Missouri Western State University; "Process-oriented guided-inquiry learning (POGIL)," facilitated by Vicky Minderhout and Jennifer Loertscher of Seattle University; and "What skills do students need for graduate school and industry?" moderated by Peter Kennelly of Virginia Polytechnic Institute and State University, Ann Stock of the UMDNJ-RW Johnson Medical School, Greg Bertenshaw of Correlogic Systems Inc. and Weiping Jiang of R&D Systems Inc.

These sessions will be followed by a best-practices wrap-up chaired by Takita Sumter of Winthrop University and Henry Jakubowski of College of St. Benedict and St. John's University. Dinner on the second day will be followed by a poster session and networking event. Posters on any topic relevant to the meeting may be presented.

The focus of the sessions on the third day is "research across the curriculum," and the morning plenary will be given by Cheryl Kerfeld of the US Department of Energy Joint Genome Institute, who is the recipient of the 2011 ASBMB education award. Follow-up sessions titled "Starting and sustaining undergraduate research" and "From proposal to publication: writing and critical thinking skills" will be organized by Carla Mattos of North Carolina State University and Joseph Provost of Minnesota State University Moorhead. The best-practices wrap-up session will be moderated by Cynthia Peterson of the University of Tennessee-Knoxville and Christopher Rohlman of Albion College. The afternoon will focus on integrated science curricula and the society's RCN-UBE grant, with sessions chaired by 2010 ASBMB Education Award winner Lisa Gentile and J. Ellis Bell, both of the University of Richmond. After the sessions, there will be a dinner and poster session, which will focus on a variety of integrated science curricula topics and include examples of undergraduate research.

The final morning of the meeting will feature a plenary talk by David Asai of HHMI and Harvey Mudd College and a wrap-up session titled "Best practices and action plans for the future," which will revisit the themes of the vision and change report and include an open discussion of ways to implement the ideas that emerge both from that document and the meeting itself.

J. Ellis Bell (jbell2@richmond.edu) is a professor of chemistry at the University of Richmond.

Student-centered education in the molecular life sciences II

July 20 – 23, 2011
University of Richmond, Richmond, Va.
Poster abstract submission deadline: May 20, 2011
Early registration deadline: May 20, 2011
For more information, visit:
www.asbmb.org/2011Education

Symposium: Chemical, synthetic and systems biology: new directions of biochemistry in the 21st century

Second special symposium on systems biology will explore the connections between the three areas of modern biochemistry

BY ARCADY MUSHEGIAN AND ALED EDWARDS


Mushegian


Edwards

In October 2009, about 60 scientists attended an American Society for Biochemistry and Molecular Biology special symposium titled "Systems biology for biochemists" at Granlibakken resort in Lake Tahoe, Calif. The news article in the April 2009 issue of ASBMB Today read:

"[What biochemists and molecular biologists] wanted to know, and were not hearing from even hard-line systems biologists, were the important facts, or at least claims, about the molecular level of living systems that would emerge from the systems-level analysis.

"…some [complex] networks exist in a real sense: a signal can be sent from an Internet address to other addresses, and perhaps from some cells in metazoan neural system to some other cells. But is there any physi-

cal sense in, say, protein-protein interaction network? For example, can anything be sent or propagated across it? Another question has to do with the quality of the evidence: after the first round of claims that certain biological networks are 'scale-free,' or 'small-world' or 'highly robust,' we are now at the stage of much more careful analysis when many of these earlier conclusions are being refined and sometimes even refuted. Finally, there is 'so what?' factor. Much attention has been given to the global properties of biological networks, such as their node-degree distribution. However, even when we finally describe such properties with some accuracy, will they end up being important for understanding of life?"

By many accounts, that meeting was a success in that it combined the breadth of scope represented in the talks with a compact format and gave plenty of opportunity for participants to interact with each other. Yet the scientific questions explored during the first meeting still are not close to being solved. Moreover, other interrelated disciplines are now coming of age, such as chemical biology and synthetic biology. It is of great interest to biochemists to know what truly is new about these new areas of biology and also to understand the connections between these new areas and the wealth of scientific knowledge obtained in the past hundred years. Much like genomics can be viewed as a logical extension of genetics that allows us to utilize high-throughput technologies to see the gene ensembles as a system, we think these new biologies are the logical extensions of classical biochemistry and molecular biology for our era.

The advances in the three biologies and their scientific roots in mechanistic biochemistry will be explored in the ASBMB special symposium titled "Chemical, synthetic and systems biology: new directions for biochemistry in the 21st century." The meeting will take place Oct. 12 to Oct. 16 at Snowbird Resort in the heart of the Wasatch-Cache National Forest, only 30 minutes from Salt Lake City International Airport.

The plenary session on the first evening will open with a talk by Luís A. Nunes Amaral from Northwestern University. Amaral is a Howard Hughes Medical Institute Early Career Scientist and one of the most influential researchers working in complex systems today. Thematic morning sessions in the following three days will include presenta-

continued on page 23

RNAi therapeutics run interference

RNA interference is getting the axe at major pharmaceutical companies. Is it too soon?

BY CHRISTEN BROWNLEE

In February of 2008, the future looked bright for Arthur Krieg and a little technology known as RNA interference. Krieg had just joined Pfizer after the pharmaceutical giant acquired Coley Pharmaceutical Group, a company he had cofounded in 1997 and where he had served as the chief scientific officer and executive vice president of research and development. Based on his extensive experience in developing oligodeoxynucleotides, Pfizer asked Krieg to head up a new division devoted solely to RNAi.

This biological phenomenon, which knocks down or dramatically lowers the protein output of selected genes by inserting a piece of double-stranded RNA into cells, was making leaps and bounds in the lab. Pfizer and many other big pharma companies saw this new technology as the wave of the future — a new way to target practically any gene that has a known sequence. The possibilities at the time seemed practically endless for target validation or developing therapeutics for conditions with no current treatments.

But this February — precisely three years to the day after he started his new position — Krieg stood in front of the 100-member group that Pfizer had hired to run its RNAi program to make a terrible announcement.

"I had to tell the group that we were being shut down. Both of the sites focused on our RNAi program were being closed, and all positions were being eliminated," he says.

What happened in those three intervening years? Whatever it was had also happened to other big pharma companies who invested in RNAi. Roche, Novartis, and Abbott Labs recently terminated their RNAi programs and severed their ties with biotech partners who were helping to develop the technology, sending shock waves through the field.

But while RNAi is getting the axe at big pharma, the technology has continued to march quietly forward at smaller biotech companies and academic labs. Animal studies recently have shown that RNAi could hold incredible promise for treating HIV, and human studies for cancers and other diseases are moving ahead into Phase 1 and 2 clinical trials. Could big pharma have pulled the plug before RNAi hit the big time?

Pulling back

RNAi still is an incredibly nascent technology. It only was discovered in the late 1990s, detailed for the first time in a seminal 1998 Nature paper by Andrew Fire and Craig Mello. There, the two scientists wrote about a strange phenomenon whereby double-stranded RNA injected into C. elegans had the power to potently silence genes. Since then, researchers have discovered that this concept also works for all living things — plants, insects and, eventually, humans.

The ability to silence any gene in the body would prove to be an incredible boon to research. No longer would scientists patiently have to wait a year or longer to make knockout mice to study gene function — with RNAi, the knockout could happen instantly. Additionally, trying to decipher the functions of genes essential to life wouldn't necessarily have to happen at the embryonic stage, before organisms bit the dust early on. Rather, researchers could knock these down later in life and see what happens.

After Fire and Mello's influential paper, basic researchers flocked to RNAi. It was enough to win the two researchers the 2006 Nobel Prize in Physiology or Medicine, an unheard of turnaround in a novel field.

But years before Fire and Mello accepted their prize in Stockholm, RNAi also had caught the notice of pharmaceutical companies. The ability to silence specific genes, thereby ridding the body of pesky disease-causing proteins, also could provide unprecedented gains for therapies. Though about two-thirds of pharmaceutical targets currently are considered undruggable — with no small molecule currently identified or no way to specifically hit a target without causing other unspecific and undesirable effects — RNAi could provide a way to home in on a desired target through its gene sequence, making more targets druggable.

The problem, Krieg says, is that delivering double-stranded RNA has proven incredibly tricky. RNAs that are too long can provoke an interferon response that muddies any effect of the RNAs themselves — a holdover from the earlier days of evolution when double-stranded RNA automatically equaled a viral attack. RNAs that are too short might not be enough to prompt sufficient interference. Naked RNAs

are vulnerable to degrading RNAses circulating in blood and tissues. Finding a way to coat RNAs of the right size and sequence now has become a field in itself.

"People thought, 'Here we have this platform in which we're going to identify genes for breast cancer or chronic obstructive pulmonary disease or Alzheimer's, and then we'll have these RNAi compounds that we can give to patients, and they'll go where we want them to go and the patients will get better,'" Krieg says. "With more experience working with this, they realized that it's not going to work that way."

Delivery seems to have proven tricky for other big pharma companies as well, even those that are sticking with the technology. Over e-mail, Alan Sachs, the global head of exploratory and translational science at Merck, noted that the company had explored more than 300 different delivery technologies for a range of disease targets. But although Merck acquired RNAi biotech Sirna Therapeutics in 2006 for the astronomical sum of $1.15 billion, the company has yet to have any RNAi therapeutic candidates in clinical trials.

"Merck recognized from the outset that developing RNAi therapeutics would be a long-term investment and not a quick path to blockbuster drugs," he says, adding that the company "is taking a careful and steady approach to RNAi."

But the length of that investment— the time it would take to understand the best targets and develop the most effective delivery strategies— may have been more than the companies that dropped RNAi could bear. Though Krieg and his colleagues at Pfizer hoped to get an RNAi compound into the pipeline by this year and were making progress with their top candidate, a treatment for liver cancer, the team still had some distance to go by the time their program folded.

Krieg suspects that the story at Pfizer is the same elsewhere. As the company started to realize how much of an outlay RNAi would take to get to the clinic, it realized it probably wouldn't be able to recoup its investment. "The lifetime of patents by the time you get a drug approved is really insufficient to return the investment on a drug most of the time," he explains. "If you look at the pipeline, it's inadequate to support their infrastructure."

Going strong

Roche, which also has invested heavily in RNAi therapeutics during the past few years, pouring hundreds of millions into its collaborations with biotech partners, issued a cagey statement about its own decision to leave RNAi behind. "The primary goal is to enable this important scientific work to continue outside of Roche and offer the best chance of success in providing benefits to patients," it said, adding that "Roche would consider the possibility of re-entering the field through external collaboration as clinical stage compounds emerge."

That re-entry might be just around the corner, says Barry Greene of Alnylam Pharmaceuticals, an RNAi therapeutics company that partnered with Roche until the company severed its agreement with Alnylam late last year.

Greene points out that Alnylam and other companies are rapidly moving ahead with their own RNAi therapeutics. At his company alone, several RNAi-based drugs already are moving through clinical trials. Alnylam even started its own initiative earlier this year named "Alnylam 5 x 15"—an effort to get five products in advanced clinical development by the year 2015. The most advanced therapeutic candidate in this program is a drug for transthyretin amyloidosis, an autosomal inherited disease

How RNAi Drugs Work

RNAi therapeutics start acting when a short piece of double-stranded RNA (somewhere between 20 and 25 or so nucleotides) enters a cell. In the cytoplasm, the RNA bumps into an enzyme called dicer, which acts like a samurai sword-wielding ninja, chopping the dsRNA into smaller pieces known as small interfering RNAs. These siRNA unzip into two strands. One of the strands gets picked up by a group of different proteins known as the RNA-induced silencing complex. The entire package hunts down strands of messenger RNA inside a cell that compliment the contained siRNA. Once that complementary strand is found, a group of enzymes chop up the matching mRNA. Without that mRNA, the corresponding protein can't get made. Since most diseases are the result of problematic proteins — either faulty construction of a necessary protein or too much of a good thing — ridding cells of certain proteins might lessen their consequences or, in the case of some infectious diseases, cure certain conditions altogether.

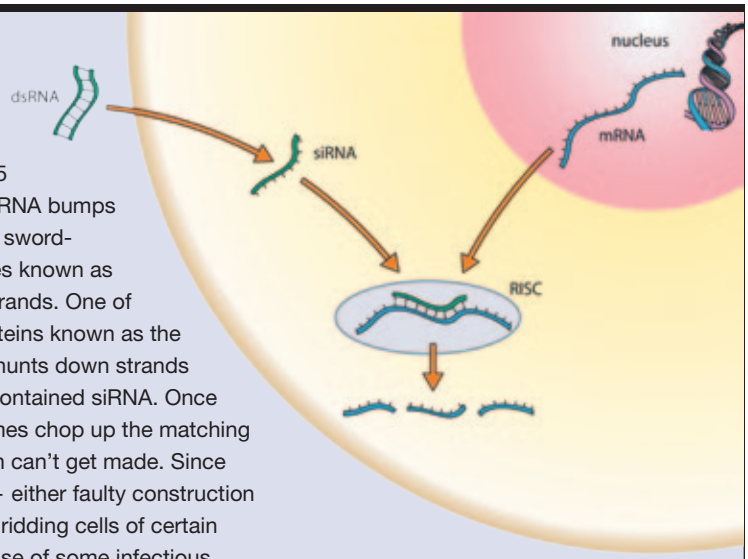


Figure from Robinson, R. (2004) *PLoS Biology* **2**, e28.

that affects about 50,000 people worldwide and universally kills patients within five to 15 years of diagnosis. The drug currently is in Phase 1 clinical trials.

This disease, which attacks the liver, is an attractive target since the organ has a natural propensity to take up the nano-lipid delivery vehicles created by Alnylam partner Tekmira that encapsulate the desired RNAi snippets.

Greene notes that Alnylam also has other RNAi-based drugs in clinical trials with the aid of pharmaceutical partners, including one for respiratory syncytial virus in Phase 2 and one for liver cancer in Phase 1. He hints that Roche and other companies soon will rue the day they decided to back out of RNAi research.

"I used to run the Boston Marathon every year, and this is like someone signing up and then quitting about 12 to 13 miles into the race," he says. Those companies that gave up too early, he adds, "aren't prepared to feel the thrill of the finish line."

Promising RNAi therapeutics research also is advancing in academic labs. In January of this year, John Rossi at the Beckman Research Institute of City of Hope published a paper in Science Translational Medicine showing that attaching an aptamer to a small piece of double-stranded RNA (known as a small interfering RNA or siRNA) could provide a dual way of attacking HIV. The aptamer itself showed the ability to neutralize free-floating HIV in infected mice, and when attached to the siRNA, it ferried the siRNA into HIV-infected cells. Results showed a significantly reduced viral load in the animals treated with the combination. Rossi says the team currently is experimenting with using different siRNAs to attack multiple HIV genes at once.

He adds that Dicerna Pharmaceuticals, the RNAi therapeutics company he co-founded in 2007 based on his findings that slightly longer siRNAs than those commonly used have a more potent knock-down effect, actually got a boost while other pharma companies were pulling back. Around the time Roche announced its own RNAi program termination, Japanese pharma company Kyowa Hakko Kirin forged a new agreement with Dicerna that could total up to $1.4 billion.

"We're really doing well at this point," says Rossi, who still serves as chair of the company's scientific advisory board.

In March of last year, chemical engineer Mark Davis of the California Institute of Technology published the results of a small Phase 1 trial of an RNAi drug targeting solid tumors aided by a nanoparticle delivery system. These encapsulated siRNAs were the right size, about 70 nanometers, to escape the leaky blood vessels that surround tumors, and they were tagged with transferrin, a protein for which many cancer cells carry receptors on their surfaces. This combo allowed the siRNAs to specifically bombard tumors.

The trial showed that the therapy was safe, and biopsies from some of the volunteers' tumors showed the RNAi was doing its job— the targeted mRNA was cleaved at just the spot where the researchers would expect. Calando Pharmaceuticals, a company that Davis cofounded but is no longer involved with, currently is continuing the trial, proof that they're not giving up anytime soon on RNAi.

"Despite what pharma says about RNAi, I think it's a really exciting area," he says. "I like to tell my students to work on something of high significance. It will be difficult, of course, but I'd rather work on something with high significance than something people don't really care about."

Christen Brownlee (christenbrownlee@gmail.com) is a freelance science writer based in Baltimore, Md.

special*symposia* continued from page 20

tions from established as well as young investigators. The presentations will be supplemented by shorter evening talks selected from the submitted abstracts and poster presentations. Women and underrepresented minorities, as well as graduate and undergraduate students, are strongly encouraged to submit abstracts.

Arcady Mushegian (arm@stowers.org) is director of bioinformatics research at the Stowers Institute for Medical Research and professor of microbiology at Kansas University Medical Center. Aled Edwards (aled.edwards@utoronto.ca) is Banbury Professor at the Banting and Best department of medical research at the University of Toronto.

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Student/postdoc Hill Day: a Capitol success

BY ANGELA HVITVED

Graduate students and postdoctoral fellows descended on Capitol Hill in March for the third student/postdoc Hill Day, an initiative of the American Society for Biochemistry and Molecular Biology's Public Affairs Advisory Committee. The tremendously successful event, now an annual fixture in the ASBMB public affairs schedule, had more participants than ever and included twice as many office visits as last year's Hill Day.

On March 15, 16 young scientists joined forces with members of ASBMB's PAAC and public affairs staff to make a whopping 58 visits to House and Senate offices in addition to meeting with the Senate Committee on Health, Education, Labor and Pensions and the House appropriations committees. "They certainly had a full schedule," said Ben Corb, ASBMB's director of public affairs.

Students were paired with PAAC members from their home states and primarily met with their own congressional delegations. "We want to remind members of Congress that scientists are also their constituents," Corb said. "It's great for them to meet some of the young scientists they represent and to hear the enthusiasm and dedication that these students bring to their research."

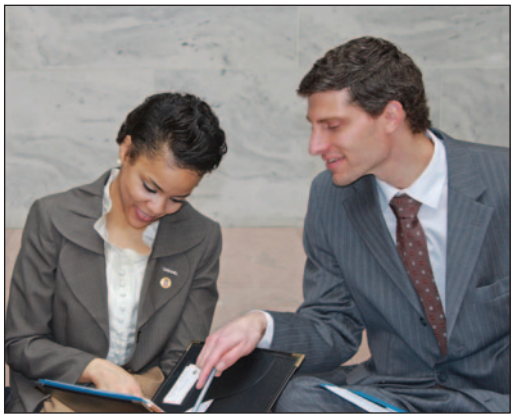
ASBMB's public affairs office prepared customized materials for each office visit showing the amount of National Institutes of Health funding directed to the state or district and an overview of its economic impact. The teams used this information to underscore the importance of NIH funding and the critical role the federal government plays in supporting biomedical innovation.

In addition to providing district-specific information, each group made the case for ASBMB's federal funding targets in the fiscal 2012 budget. These targets include an allocation for the NIH of $35 billion to retain the gains made during the American Recovery and Reinvestment Act and a fiscal 2012 budget of $7.8 billion for the National Science Foundation.

Despite Congress's historically strong support for biomedical research, the participants acknowledged the challenges presented by the current economic climate. "In a time of severe fiscal challenges at every level in our country, I think it's important that those in power don't forget that American science played a big part in putting the United States in a position of power in the world and still shoulders much of the responsibility for keeping us there," commented Drew Pruett, a postdoctoral researcher at the University of Mississippi Medical Center.

As important as the budget numbers are, the fundamental message of the day was one all ASBMB members could identify with: Biomedical research saves lives and stimulates the economy through innovation.

Staunch NIH supporter and LHHS appropriations subcommittee member Rep. Rosa L. DeLauro, D-Conn., takes time out of her busy schedule to meet with Eric Patridge of Yale University.



ASBMB science policy fellow Geoffrey Hunt rests for a moment with Angel Byrd of Brown University to discuss strategy in advance of their next meeting in the Hart Senate Office Building.

Erika Geihe, Stanford University, and Yun Xin Lim, Oregon Health Sciences University, get ready to meet with Sen. Dianne Feinstein, D-Calif., for one of the almost 60 meetings ASBMB members had on Capitol Hill.

Although many of the student participants were new to advocacy, this year's group included two returning participants, Lauren Amable, a postdoctoral researcher from the University of South Alabama Mitchell Cancer Institute, and Angel Byrd, an M.D./Ph.D. student from Brown University. Byrd, who intends to study childhood obesity as a pediatric endocrinologist, hoped her visits helped convince lawmakers of the "power of research and the long-term investment in its goals and vision."

PAAC members, many of whom have logged long hours in the halls of Congress, thoroughly enjoyed the opportunity to accompany the students. "Interacting with the congressional offices is a vital way to connect about the importance of research to our country's well being, and it's clear the representatives and their staffers paid particular interest to the young people and their stories," observed Susan L. Forsburg, PAAC member and professor at the University of Southern California.

Overall, it was a terrific experience for the student participants, many of whom commented on how much they had learned. "It's been really beneficial for me, and it's been a great way to learn about science policy and how the budgeting process works," said Kristen Kelps, a doctoral candidate from the University of Kentucky. Rob Watkins, a doctoral student at Montana State University, added, "It's opened my eyes to a lot of new things ... As a biomedical researcher and end-user of government-allocated funds, I underestimated the complexities of the decision making behind federal spending."

By the end of the day, several students had remarked on the importance of standing up for science and said they would encourage their peers to do the same. Eric Patridge, a postdoctoral associate at the Yale University School of Medicine, concurred. "Events like today's are absolutely essential to the future of the NIH and our research as scientists."

Hopefully, other student and postdoctoral members of ASBMB feel the same way and will consider helping make next year's Hill Day an even bigger success.

Angela Hvitved (ahvitved@asbmb.org) is managing editor of Molecular and Cellular Proteomics.

The senators and representatives visited for Hill Day

Rep. Rodney Alexander, R-La.
Rep. Karen Bass, D-Calif.
Sen. Max Baucus, D-Mont.
Speaker John Boehner, R-Ohio
Rep. Jo Bonner, R-Ala.
Sen. Barbara Boxer, D-Calif.
Sen. Scott Brown, R-Mass.
Sen. Sherrod Brown, D-Ohio
Sen. Richard Burr, R-N.C.
Rep. Ken Calvert, R-Calif.
Sen. Benjamin L. Cardin, D-Md.
Sen. Robert P. Casey, D-Pa.
Rep. Michael E. Capuano, D-Mass.
Sen. Saxby Chambliss, R-Ga.
Rep. Ben Chandler, D-Ky.
Rep. David Cicilline, D-R.I.
Sen. Thad Cochran, R-Miss.
Sen. John Cornyn, R-Texas
Rep. Elijah Cummings, D-Md.
Rep. Danny K. Davis, D-Ill.
Rep. Rosa L. DeLauro, D-Conn.
Sen. Richard J. Durbin, D-Ill.
Rep. Anna G. Eshoo, D-Calif.
Rep. Chaka Fattah, D-Pa.
Sen. Dianne Feinstein, D-Calif.
Rep. Marcia L. Fudge, D-Ohio
Sen. Kay Hagan, D-N.C.
Sen. Orrin Hatch, R-Utah
Sen. Kay Bailey Hutchison, R-Texas
Sen. Johnny Isakson, R-Ga.
Sen. John Kerry, D-Mass.
Sen. Mark Kirk, R-Ill.
Sen. Mary Landrieu, D-La.
Sen. Mike Lee, R-Utah
Rep. John Lewis, D-Ga.
Sen. Joseph Lieberman, I-Conn.
Rep. Edward Markey, D-Mass.
Rep. Jim Matheson, D-Utah
Sen. Mitch McConnell, R-Ky.
Sen. Jeff Merkley, D-Ore.
Sen. Barbara Mikulski, D-Md.
Sen. Rand Paul, R-Ky.
Sen. Rob Portman, R-Ohio
Rep. Charles Rangel, D-N.Y.
Sen. Jack Reed, D-R.I.
Rep. Denny Rehberg, R-Mont.
Rep. John Sarbanes, D-Md.
Rep. Jan Schakowsky, D-Ill.
Sen. Charles E. Schumer, D-N.Y.
Sen. Jeff Sessions, R-Ala.
Sen. Jon Tester, D-Mont.
Rep. Bennie Thompson, D-Miss.
Rep. Paul Tonko, D-N.Y.
Sen. Pat Toomey, R-Pa.
Sen. David Vitter, R-La.
Rep. Mel Watt, D-N.C.
Sen. Sheldon Whitehouse, D-R.I.
Sen. Roger Wicker, R-Miss.
Sen. Ron Wyden, D-Ore.

Meet the Hill Day attendees

BY NICOLE KRESGE

The 16 students who attended the 2011 American Society for Biochemistry and Molecular Biology Hill Day ranged from an undergraduate student from Miami University who studies the stability of tannins under gastrointestinal conditions to a mathematician at the University of Mississippi Medical Center who is interested in integrated physiological modeling.

Lauren Amable
Postdoctoral fellow
University of South Alabama
Mitchell Cancer Institute

Amable studies chemotherapeutic-drug resistance in cancer cells with the goal of identifying the molecular mechanisms involved in drug resistance to develop alternative cancer treatments.

Jessica Bockhorn
Graduate student
University of Chicago

Bockhorn's research focuses on understanding the mechanisms of breast cancer progression by examining interactions of co-activators with the estrogen receptor and looking at the role of miRNAs in metastasis.

The 2011 ASBMB Hill Day attendees pose on the steps of the Capitol building.

Kevin Bonham
Graduate student
Harvard University

Bonham studies the signaling cascade downstream of Toll-like receptors.

Angel Byrd
Graduate student
Brown University

Byrd is using a phosphoproteomic analysis of primary human neutrophils to look at the modulation of neutrophil function and behavior by integrins.

Erika Geihe
Graduate student
Stanford University

Geihe studies drug delivery with a special emphasis on the delivery of oligonucleotides for therapeutic applications.

Vineet Gupta
Graduate student
University of Louisiana-Monroe

Gupta focuses on the role of glucosylceramide synthase in the formation and maintenance of breast cancer stem cells.

Christa Heyward
Graduate student
University of Pennsylvania

Heyward's research looks at the mechanism by which tumors evade detection by the immune system.

Kristen Kelps
Graduate student
University of Kentucky

Kelps focuses on understanding the neuroprotective mechanisms of propeptides derived from the glial cell line-derived neurotrophic factor, forming a platform for developing new therapeutics for the treatment of neurodegenerative diseases.

Laura Koontz
Graduate student
The Johns Hopkins School of Medicine

Koontz is exploring the genetic and biochemical characterization of a novel repressor of the Yki-Sd transcriptional complex in Drosophila.

Melanie Krook
Undergraduate student
Miami University

Krook currently studies the stability of tannins (polyphenols) under gastrointestinal conditions.

Yun Xin Lim
Graduate student
Oregon Health Sciences University

Lim is investigating the effects of formaldehyde on mutant frequency and the mutational fingerprint of formaldehyde.

Eric Patridge
Postdoctoral fellow
Yale University

Patridge's principal focus is developing prodrugs that are selectively activated in hypoxic tumor cells to be used as anticancer therapies.

Drew Pruett
Postdoctoral fellow
University of Mississippi Medical Center

Pruett is a mathematician interested in integrated physiological modeling, especially transitioning from molecular level models to systems level models.

Kevin Roelofs
Graduate student
University of Maryland

Roelofs studies the bacterial second-messenger cyclic-di-GMP that controls the switch between a motile and sessile lifestyle with the goal of identifying and characterizing receptors that will serve as potential targets for pharmaceutical intervention.

Kelly Ruggles
Graduate student
Columbia University

Ruggles currently focuses on the mechanisms of lipid droplet formation and lipotoxicity in yeast and mammalian models and the role of lipotoxic processes in the progression of Type 2 diabetes in humans.

Rob Watkins
Graduate student
Montana State University

Watkins investigates pathogen-derived mediators of host inflammation and defines their influences on morbidity and mortality with special attention paid to innate immune function.

Nicole Kresge (nkresge@asbmb.org) is the editor of ASBMB Today.

Reactions

We asked our Hill Day attendees about their experiences on the Hill, and here's what they had to say:

"Today has been a great experience. We've talked a lot about ASBMB and how NIH funding is absolutely necessary to keep our research going … I think events like today's and lobbying for science funding and STEM funding are absolutely essential to the future of the NIH and research in general."

Eric Patridge

"My experience has been very educational. It's great to hear what our representatives and senators think of our research and about funding our research. It's been a very interesting learning experience … I think it's very important that scientists get involved in advocacy, because what we found today is that a lot of [representatives and senators] didn't fully understand how important NIH research is."

Jessica Bockhorn

"It's been really great to watch people who do this on a regular basis and [learn] how it's actually done – I had no idea."

Kelly Ruggles

"[The experience] has opened my eyes to a lot of new things, especially budgeting and how the process proceeds."

Rob Watkins

To learn more about the attendees and to see videos of them at Hill Day, go to http://bit.ly/ATodayHillDay2011.

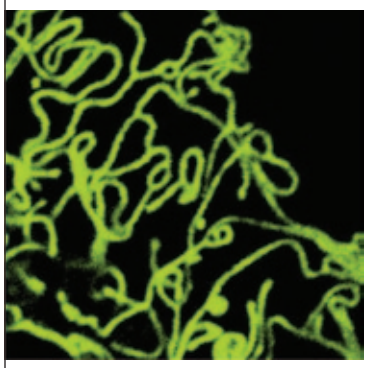
Annual meeting scientific workshops

The American Society for Biochemistry and Molecular Biology is pleased to offer two research-based workshops at the 2011 annual meeting. More information can be found at www.asbmb.org/meetings.

I think it's mitochondrial dysfunction, but how do I measure it?

We commonly use the term "mitochondrial dysfunction" to describe abnormal mitochondrial function that impacts cellular viability or function. But how can it be measured? The ASBMB workshop "Measuring Mitochondrial Function and Dysfunction" on Sunday, April 10 will give an overview of the basic principles of studying a variety of mitochondrial parameters and will explore the current methodologies available. It also will address the rationale behind choosing certain bioenergetic tests and will explain the interpretation of the results. We have lined up three great speakers for this event.

David Nicholls of the Buck Institute for Research on Aging will describe the principles of measuring changes in mitochondrial $\Delta\Psi$ and comparing mitochondrial $\Delta\Psi$ of different cell samples. He also will explain the considerations that should be taken into account when choosing a fluorescent probe. Membrane potential commonly is studied by microscopic imaging, and Nicholls will discuss the interpretation of the data obtained from imaging using membrane potential dyes. Nicholls also will demonstrate an EXCEL-based simulation that he developed to allow researchers to run dry experiments in silico, a practice that can help in the design of an experiment.



A prize will be awarded to the scientist at the mitochondria workshop who can correctly determine the number of mitochondria in this image.

David Ferrick of Seahorse Bioscience will describe the principles of studying mitochondrial oxygen consumption. He will explain the choice of using intact cells versus isolated mitochondria and also give an overview of the bioenergetic parameters collected during an oxygen consumption study and their biological significance. Finally, he will outline the design of an experiment used for the initial assessment of bioenergetic dysfunction and the interpretation of its results.

And finally Orian Shirihai of Boston University will describe common changes in mitochondrial architecture and their interpretation. He will outline the morphological changes that point toward alterations in mitochondrial fusion activity and describe the more sophisticated tests for quantification of fusion as well as the approaches to the study of mitochondrial motility and autophagy.

Lipids, lipids everywhere

Lipid research is a broad and interdisciplinary field encompassing work at the organism, cellular and molecular levels. To provide an introduction to and discussion about the current state of lipid research, ASBMB is holding a roundtable workshop on Monday, April 11 titled "Lipid basics: phosphoinositides and sphingolipids in health and disease." The workshop is being organized by Robert Stahelin of Indiana University School of Medicine-South Bend and the University of Notre Dame, and presenters will include lipid experts Julie Saba of the Children's Hospital Oakland Research Institute, Charles Chalfant of Virginia Commonwealth University and Edgar Kooijman of Kent State University.

The workshop will highlight the roles of phosphoinositides and sphingolipids in cellular homeostasis as well as the tools available to analyze them. There also will be a discussion on the basics of working with phosphoinositides and sphingolipids in vitro and in cellular and animal models of diseases. Our aim is to bring together scientists from around the globe to summarize concisely the basics of the lipid research field. The format will include brief presentation and discussion sessions to illustrate where the field is headed and how the gaps may be filled in with new technologies.

Our hope is to provide attendees with a basic understanding of phosphoinositide and sphingolipid signaling while teaching them appropriate handling methods and available technologies for experimental analysis. Avanti Polar Lipids has agreed to sponsor the session and will hold a drawing for a free lipid extruder at the event.

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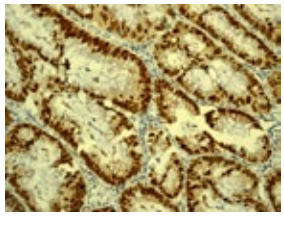
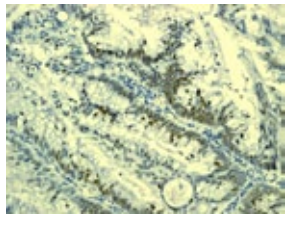
IHC		

Paraffin-embedded human colonic carcinoma tissue stained with Epitomics' CDX2 RabMAb (Cat.# 2475-1) and Vendor A's CDX2 Mouse Monoclonal under optimal conditions

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Overcoming obesity

Annual meeting symposium will look at treatment, prevention and complications of obesity

BY JOSE R. FERNANDEZ

Overcoming the obesity epidemic continues to be a concern for scientists, epidemiologists, health professionals, policy makers and millions of overweight men and women. According to the World Health Organization, more than 200 million men and nearly 300 million women worldwide are obese (1). In the United States, where the abundance of food and the reliance on labor-saving technology have increased in the past 50 years, the incidence of obesity, defined as body mass index greater than 30 (BMI = kg/m^2), continues to rise. An obesity prevalence of 30 percent or greater has been reported in almost 20 percent of the states in the continental U.S. (2).

There is little argument that the consequences of obesity are detrimental. It has been documented that obesity is a risk factor for other chronic diseases, such as diabetes, hypertension, cardiovascular disease and cancer. Obesity reduces life expectancy (3), and it costs us billions of dollars in health care. Research demonstrates that the accumulation of fat that characterizes obesity impacts physiological processes through biochemical mechanisms such as inflammation, mitochondrial dysfunction, oxidative stress, increased apoptosis and lipotoxicity. However, it also is well established that the consequences of obesity both as a disease risk and as a precursor to abnormal biochemical processes do not carry an equal burden in all individuals.

To address this issue, the American Society for Biochemistry and Molecular Biology Minority Affairs Committee is presenting a symposium titled "Treatment, prevention and complications of obesity" at the annual meeting in Washington, D.C. When comparing the prevalence of obesity in racial/ethnic groups across the U.S., data show a greater prevalence in African Americans and in Hispanic Americans than in European Americans. These are striking statistics that present scientists with intriguing questions. From the perspective of complications, it is known that most of the comorbidities associated with obesity differ among groups. However, the extent that molecular and biochemical mechanisms resulting from obesity also differ within and among racial/ethnic groups and the mechanisms underlying these differences remain unknown. From the perspective of prevention, the statistics challenge us to explore the multifactorial etiology of obesity in innovative ways that account for the uniqueness of different groups in developing preventive strategies. From the perspective of treatment, we need to understand whether pharmacological agents and other treatments will deliver comparable results among individuals of diverse backgrounds. Certainly, we do not want to repeat previous mistakes of using medications targeted to specific racial/ethnic groups without a clear idea of an appropriate biological racial/ethnic marker.

Eliminating the racial/ethnic barriers underlying complications, treatment and prevention of obesity will require the awareness that a one-size-fits-all approach might not be the most effective model in the fight against obesity. However, as we collectively work to overcome obesity as an epidemic in the population, it is necessary to keep an appropriate perspective. The development of obesity as a disease starts with the basic and essential need for food. Therefore, moving toward an individualized approach to fight obesity will require understanding which foods and what quantities are necessary for a healthy weight range based on biological, cultural, physiological and behavioral characteristics and practices. Individualized approaches must be complemented by education — every morning, people should ask themselves two questions: how well did they monitor their energy intake and expenditure the previous day, and how well will they monitor it today? Perhaps the most relevant question right now is, have you started to ask these questions yourself?

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Undergraduate education in the responsible conduct of research

Although teaching RCR to undergraduates is not a new activity, we should seize the opportunities created by granting agency mandates

BY FRANCIS L. MACRINA

The first federal mandate requiring education in the responsible conduct of research (RCR) was implemented in 1990 by the National Institutes of Health. The scope of that requirement was limited to trainees receiving support from specific types of NIH grants. Initially, the policy created anxiety and raised questions. Who, what, how and when would we teach RCR? Another course for the already overloaded curriculum? Don't mentors do this already? Who's going to pay for this? The angst from 20 years ago may rear its head from time to time, but it largely has given way to a variety of newly created teaching models, self-study packages, textbooks and a variety of resource materials.

The evolution of the graduate and postgraduate RCR curriculum has tracked with the implementation of other related research policies. Most notable are policies that prescribe sharing data or require a description of mentoring activities planned for grant-supported postdocs. The newest policy is found in the America COMPETES Act of 2007. It requires that National Science Foundation proposals "provide appropriate training and oversight in the responsible and ethical conduct of research to undergraduate students, graduate students, and postdoctoral researchers participating in the proposed research project."

The opportunity

The 1990 NIH RCR educational mandate required RCR instruction for Institutional National Research Service Award research training grants. This included awards under the Minority Access to Research Careers Program, which provides undergraduate training in academic research. Thus, mandated formal undergraduate instruction in RCR is not new. And with the NSF mandate in place for the past year, there has been increased thinking about and participation in undergraduate RCR teaching. Of course, there's an army of faculty members who have been designing, refining and teaching RCR to pre- and postdoctoral trainees for more than 20 years. The collective experiences and the resources coming from this teaching have created a framework that is useful in informing how we should educate undergraduates.

Many scientists hold that it is our obligation to teach trainees about the responsible conduct of research. The early government mandates provided the catalyst for formalizing RCR education. They heightened awareness of the need for such instruction, and they accelerated the development of resource material. But the members of the scientific community are the stewards of the RCR educational movement. Although teaching RCR to undergraduates is not a new activity, we should seize the opportunity created by the NSF mandate. Beginning to instill the norms and culture of responsible research in undergraduates makes enormous sense. For those destined to devote their lives to science, the earlier they grasp the concept of responsible research, the better. And for those who don't pursue careers as scientists, an RCR course may well afford a view of how science works. This is a good first step in facilitating a much-needed public understanding of science.

Engaging undergraduates in thinking and learning about RCR

Below are some thoughts to consider in developing or refining undergraduate RCR instructional curricula and platforms.

Rationale, goals and objectives

Set the stage for learning by providing a rationale for the course. For example, you might note that science as a profession has specific laws (e.g., research subject use), policies (e.g., authorship) and best practices (e.g., record keeping) that apply to the conduct of research. There are codes and guidelines to be aware of and to abide by. The volume and complexity of these has grown dramatically

in recent times, and learning cannot be effectively accomplished by trial and error, on-the-job training or observation of others' behavior. Formal education that centers on such information provides the basis for acting responsibly and ethically in research. Create learning objectives that realistically reflect the content of your teaching. What new knowledge do you want to impart to build a foundation upon which responsible research conduct is based?

Content

The NSF mandate did not recommend topics for inclusion in RCR teaching. However, the NIH instructional guidance recommends specific topics, including conflicts of interest, human and animal use, safe lab practices, mentoring, collaboration (including with industry), peer review, data acquisition, management, sharing and ownership, research misconduct and policies for handling it, authorship and publication, and the scientist as a responsible member of society. Critical thought should be given to the scope and depth of undergraduate RCR instruction. Undergraduates are not likely to have had much, if any, research experience. Thus, undergraduate RCR courses should be thought of as introductory in nature and designed accordingly.

Instructional format

Establish a course or program that is recognized by your institution. At the very least, students should receive an official document indicating completion of their RCR training. Presenting RCR education in the form of an official course that results in a grade is ideal. Ad hoc approaches, such as one-time workshops, occasional lectures and the like send a message that RCR training is incidental. Courses should be interactive. Online resources can augment the teaching of RCR but are not recommended as the sole means of instruction. Topics in RCR courses lend themselves to active learning. Small group, face-to-face discussions of cases, videos or current event coverage can be used with success. Role-playing scenarios that present ethical dilemmas are effective as well. Books, short stories, films and plays also can be used to engage students. Typically, RCR courses are taught by teams. Course directors should recruit researchers and content experts to help them deliver instruction. When an active researcher participates in the teaching, whether it is in the classroom or in a small group discussion, a powerful message is sent about the importance of RCR education.

Measure success

Use methods that enable assessment of student learning. Writing assignments that allow you to gauge mastery of the material are a good idea. Another strategy is to have students write cases for discussion in class or write solutions to previously written cases. Simple writing assignments include things like having students come to class with responses to relevant questions. For example, when covering the topic of conflicts of interest, have students briefly articulate an example of a conflict that might apply to them in the research training environment. Oral presentations offer other opportunities for instructors to confirm learning. Having students lead discussion of some relevant current event, news story, video clip or fictional vignette merits consideration. The evaluation of student learning should be tied to your course objectives. Keeping these objectives in mind will help guide you in selecting your method of evaluation. End-of-semester evaluations can provide information that may help you improve future course iterations. Such course evaluations are an accepted good practice and should be part of RCR education. But they do not provide information that allows you to verify that the students have learned the material and have met course objectives.

Concluding thoughts

Preparing scientists to conduct their work with integrity is crucial to the research enterprise. It ensures excellence in the process of knowledge creation. This, in turn, affords a better understanding of the world around us and provides the best opportunities to translate discoveries into beneficial applications. Teaching and practicing responsible research conduct is necessary to earn and maintain the trust of our colleagues and the trust of the public. It's a big agenda, but it's one that falls squarely on the shoulders of the scientific community. Our objective should be training that ensures the next generation of scientists will conduct their research responsibly and ethically.

Francis L. Macrina (macrina@vcu.edu) is the Edward Myers professor of dentistry and vice president for research at Virginia Commonwealth University.

For more information

Go to the online version of this article at http://bit.ly/ATodayRCR for a list of responsible conduct of research education resources.

jbc THE JOURNAL OF BIOLOGICAL CHEMISTRY

Short reviews, long-term impacts: nuclear receptors and molecular heart beats

BY ANGELA HOPP

The Journal of Biological Chemistry's thematic minireview series aim to round up the best of cutting-edge research and present it in an approachable format, establishing guideposts for scientists in near and far fields.

In 2010, the journal published nine thematic minireview series. Just a few short months into 2011, the JBC associate editors already have an equal number of series in the publication pipeline.

The year was kicked off with a series coordinated by Jerry B Lingrel called "Nuclear receptors in biology and disease," and last month marked the online launch of Jim Stull's series, which is titled "Signaling in cardiac sarcomeres in health and disease."

Lingrel's nuclear receptor series so far contains five minireviews covering the steroid receptor coactivator family, estrogen signaling via estrogen receptor β, small molecule inhibitors as probes for estrogen and androgen receptor action, cellular processing of the glucocorticoid receptor gene and protein, and the exploration of endogenous ligands for nuclear receptors. Lingrel says in his prologue, co-written with Sohaib Khan, that today, more than 50 years after the discovery of the estrogen receptor, "the scientific community owes … founding members of the nuclear receptor family much gratitude, for they have taken us through a remarkable expedition filled with eureka moments to understand how hormones and other ligands function!"

The mission of Stull's series, he says in a prologue co-written with R. John Solaro, is to help "identify new diagnostic and therapeutic strategies guided by our understanding of the role of sarcomeric proteins in cardiac disorders." The minireviews included cover the cardiac Z-disc signaling network, the giant protein titin, proteolysis in the cardiac sarcomere, signaling and myosin binding protein C, signaling pathways of myosin regulatory light chain, protein phosphorylation and signal transduction in cardiac thin filaments, and redox signaling and cardiac sarcomeres. Seeing as how Stull's series reports on matters of the heart, it seems fitting that his wife and collaborator, Kristine E. Kamm, is a co-author of one of the minireviews.

Several other series already are rounding the bend to completion, including "Computational systems biology," which is being organized by Joan Conaway and guest editor Arcady Mushegian, and another series tentatively titled "Biochemistry in medicine: asthma" that was conceived by the late Dale Benos and is now being shepherded by Luke O'Neill.

For more information about the JBC's stand-alone and thematic minireviews, visit www.jbc.org/content/by/section/Minireviews. If you have an idea for a future JBC minireview or series, contact Angela Hopp.

Angela Hopp (ahopp@asbmb.org) is managing editor for special projects of the Journal of Biological Chemistry.

JLR THE JOURNAL OF LIPID RESEARCH

Getting the skinny on DGAT

BY MARY L. CHANG

Diglyceride acyltransferase, known to lipidologists as DGAT, gets a lot of attention in the April issue of the Journal of Lipid Research, where it's the focus of an article by researchers at Columbia University and AstraZeneca and a related commentary. What makes DGAT such a hot topic? It's an important enzyme in the formation of triglycerides, high levels of which have been linked to atherosclerosis, heart disease and stroke. Inhibitors of DGAT have the potential to help fight obesity, and Phase 2 clinical trials currently are testing the efficacy of these agents in promoting weight loss and increasing insulin sensitivity.

Li Liu of Columbia University and colleagues studied mice with the DGAT1 gene knocked out to assess the impact of short- versus long-term loss of DGAT1 activity. The knockout mice were known to be resistant to obesity and insulin resistance, but it was unclear how the absence of DGAT1 led to these effects.

Lui and colleagues found that mice without DGAT1 had lower levels of messenger RNA for the peroxisome proliferator-activated receptor (PPAR) family of nuclear receptor proteins, which act as gatekeepers to regulate traffic between the nucleus and the cytoplasm. The mice also had lower mRNA levels of downstream target genes that are directly involved with lipid uptake and degradation. Expression of the glucose transporters GLUT1 and GLUT2 was found to be elevated as well. Thus, these findings show that loss of DGAT1 activity decreases mRNA levels of some genes involved in lipid uptake and oxidation.

Rinke Stienstra and Sander Kersten of Wageningen University in the Netherlands have written a commentary on Liu's findings, suggesting that the next big questions in this area of study are how each of the different PPARs contributes to the resistance to obesity and increased insulin sensitivity

observed in DGAT-deficient individuals or those who have impaired DGAT function, and what role the decreased activity of the PPARs has in preventing the cellular, tissue or organ damage usually caused by abnormally large amounts of lipids in the body. Another consideration they note is that the hearts of DGAT1-deficient mice have several characteristics similar to those of mice experiencing inflammatory processes like sepsis or infection with endotoxins, so it has been proposed that perhaps the lack of DGAT1 causes a similar inflammatory reaction. Further study is warranted to clarify the various ways DGAT1 affects the body as a whole so that one day this research can be applied to help the growing obesity epidemic.

Mary L. Chang (mchang@asbmb.org) is the managing editor of the Journal of Lipid Research.

MCP **MOLECULAR AND CELLULAR PROTEOMICS**

The beauty of proteomics

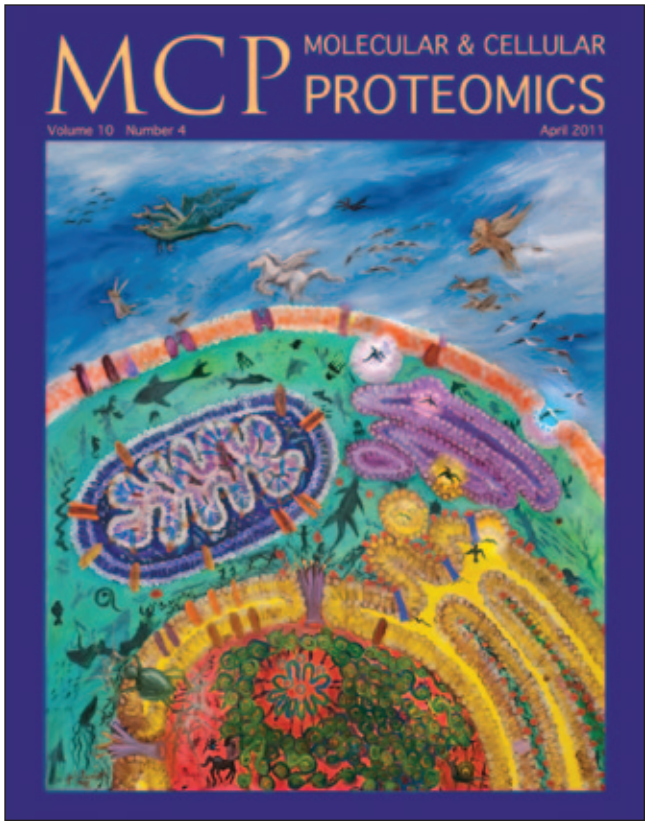
BY ANGELA HVITVED

It may be beautiful, but the April cover of Molecular and Cellular Proteomics is not just another pretty picture. The cover artwork, commissioned by MCP, is an oil painting by artist Julie Newdoll titled "The Worlds of Proteomics." The painting is the first of a series in which the artist explores proteomics and stems from a collaboration with MCP co-editors Al Burlingame and Ralph Bradshaw. Newdoll worked with Burlingame and Bradshaw to learn about the many aspects of proteomics research and to understand the broad scope of science that MCP publishes. Their goal in initiating the series is to promote a deeper, richer appreciation for the field by those directly and indirectly involved with proteomics research.

Newdoll has a master's degree in medical illustration and previously worked as a visualization specialist at the University of California, San Francisco. She found that fusing the powerful and beautiful concepts of science with cultural references both ancient and contemporary provided a new lens for creating her own view of the fascinating world of science. Other commissioned paintings by Newdoll can be found at her website, www.brushwithscience.com.

The painting on the cover is accompanied by the artist's description, which explains Newdoll's inspiration for the piece:

"When proteins are made in the cell in response to some stimuli or event, they are targeted via an address system for a specific location or locations. In this painting, the various areas in a cell are represented by various worlds — there is the world of the sea in the cytosol, that of the air outside the cell and land or earth inside the nucleus. Inside the mitochondria and the endoplasmic reticulum, little islands have their own color scheme. A protein meant to be secreted to the outside of the cell follows an elaborate path of production,



first forming inside the endoplasmic reticulum, later packaged into a membrane bubble, which melds with the Golgi, and finally repackaged and released to the outside of the cell.

"From the artist's perspective, a protein meant for the outside of the cell is rendered as a flying creature in this painting. It never ends up in the deep sea environment of the cytosol, or it would 'drown.' Likewise, proteins destined for the deep sea of the cytosol could not breathe outside the cell in the open air. And then there are the amphibians…"

"The Worlds of Proteomics" represents the broadest perspective of proteomics research, and Newdoll intends to use it as the foundation of the series. "The first in the series displays all realms of proteomics, while future paintings will zoom in on the various worlds and microcosms mapped out here," she explains. The co-editors intend to feature future pieces on the journal's cover to highlight specific areas of research.

To celebrate the debut of the new cover artwork, MCP, normally an online-only publication, has printed 500 copies of the April issue as well as a poster of the painting for distribution at the American Society for Biochemisty and Molecular Biology annual meeting on April 9–13 and to members of its editorial board.

Angela Hvitved (ahvitved@asbmb.org) is managing editor of Molecular and Cellular Proteomics.

Helping scientists stay in science

An interview with BenchFly.com founder Alan Marnett

In 2009, chemist Alan Marnett decided he'd seen too many of his friends struggle in the lab and eventually leave science. Desperate to help reverse this trend, he left his postdoctoral fellowship at the Massachusetts Institute of Technology to start BenchFly.com, a resource dedicated to providing researchers with protocols to support their lives both in and out of the lab.

ASBMB: How did you get involved with science and eventually decide to become a scientist?

MARNETT: For as long as I can remember, I've been a math and science guy. They just always made more sense to me in school. I think my research started in the kitchen with baking soda and vinegar. Not surprisingly, those experiments never yielded anything more than a huge mess.

There was also probably a serious genetic component to my interest in science — both my father and grandfather are chemists. So I grew up around the lab, and it was a powerful influence on how my career unfolded.

In college, I decided it was time to explore what else was out there. I took philosophy, religion, economics, you name it. If it didn't have a lab, I took it. Two years later, I realized that maybe it was time to get back to the lab. I joined an organic chemistry group and was incredibly fortunate to work with a terrific postdoc who showed me what real research looked like, and I was hooked.

ASBMB: It seems that you traveled the typical path of training and preparation to become an academic scientist up through your postdoc. At what point did you realize or what experience(s) did you have that made you realize that you didn't want to do bench science anymore?

MARNETT: From the first day of graduate school, I thought I wanted to be a professor and one day have a lab of my own. So I trained and prepared accordingly both as a grad student and a postdoc. About two years into my postdoc, I felt I owed it to myself to at least consider other career options before deciding to marry the lab.

I had also developed an idea for a resource I thought could benefit scientists, and I realized that time was running out if I ever wanted to try to move it from my head to reality. In exploring other career options, I found that entrepreneurship offered many of the aspects I loved about academics while also allowing me to pursue my dream.

ASBMB: Was it difficult to commit to the decision to leave bench science?

MARNETT: It was very difficult. I had been in the lab for nearly 15 years, and I loved doing experiments. Research had really become part of my identity, so leaving that behind was tough. Part of me worried that all of the training at the bench wasn't worth it since I ended up leaving anyway.

Because I had always envisioned becoming a professor, I think there was also a feeling of failure in leaving the academic path. There was a sense that somehow leaving the bench was not fulfilling the trajectory that grad students and postdocs should follow. Much of that may have been a result of pressure I put on myself.

I also think it was tough because you never [want to] feel like you're disappointing people. Throughout my career at the bench, there were many friends, family members and colleagues who helped me pursue the academic path. So I worried that changing course would let them down. Fortunately, that worry was really in my head, as everyone has been very supportive of my transition away from the bench.

ASBMB: After you decided that you didn't want to follow the more traditional path, what road less traveled did you take?

MARNETT: I think starting a lab is much like starting a small [business] venture, so as I looked around for other careers, I gravitated toward entrepreneurial opportunities. I had been kicking an idea around for a web-based resource for scientists called BenchFly for several years, and the time seemed right to take a chance on it.

The seeds were planted for BenchFly during my undergraduate research experience, though I didn't realize it at the time. I worked with a fantastic postdoc, Chad Peterson, who had a passion for teaching and

who also had golden hands — every reaction he set up seemed to work. Chad taught me all of the tips and tricks he'd learned over the years, and it was those techniques that gave me the skills and confidence to continue in research.

As I entered graduate school, it became clear to me that not everyone was like Chad. I realized that whether a student gets properly trained or not is unfortunately pretty random — it depends on the project, the lab, the PI. I saw many colleagues end up in bad situations that eventually soured them on research and drove them to leave science altogether. It seemed to me we could do better.

So, although I didn't have the details quite worked out, I knew that I wanted to try to develop a resource that supported scientists and made them feel that they have a mentor and partner committed to their success both in and out of the lab — like a virtual Chad.

ASBMB: Could you give our readers an idea of what your current job involves?

MARNETT: Much like research, the job requires creative problem solving. However, instead of thinking about proteins, cells and gels, I focus on site functionalities, content development, marketing, Facebook, Twitter, etc. — no two days are the same. While it's always challenging, it's been fun and rewarding to see BenchFly become a reality after years of existing only in my head.

Our mission is to provide researchers with the community and tools they need to develop both professionally and personally in order to make research a better career today and for future generations of scientists. We're [also] trying to knock down some of the stereotypes that learning science has to be serious and boring — showing the world that science can be fun, irreverent and exciting. There's a video on the site showing a grad student trying to eliminate static from a scale. Nontraditional science to say the least… but very valuable information.

In addition to videos, our blog topics range from professional (What Makes a Great Graduate Student?) to personal (Lessons from a Recovering Postdoc) to recipes (Poverty Nutrition: A Fugue in Egg Minor) to, well, Chuck Norris (Chuck Norris, Scientist?).

For more information

To read more from the interview with Alan Marnett, go http://bit.ly/ATodayMarnett.

Sphingolipids: always providing new scientific puzzles to solve

2011 ASBMB Avanti Young Investigator Award recipient Charles Chalfant talks research and mentoring

Products of arachidonic acid, eicosanoids, are well-established mediators of inflammatory responses with major roles in the pathogenesis of these disease states. The production of AA by phospholipases is the initial rate-limiting step in eicosanoid biosynthesis, and the major phospholipase that regulates eicosanoid synthesis in response to inflammatory agonists is group IVA cytosolic phospholipase A2 (cPLA$_2\alpha$).

The Chalfant laboratory at the Virginia Commonwealth University School of Medicine was the first to discover that ceramide-1-phosphate generated by ceramide kinase is a novel and specific activator (both in vitro and in cells) of group cPLA$_2\alpha$. Specifically, the Chalfant laboratory demonstrated that C1P can directly bind to cPLA$_2\alpha$ in a Ca^{2+}-dependant manner via the CaLB/C2 domain and that C1P also increased the enzymatic activity of cPLA2α in vitro. Recent findings demonstrated that the specific interaction site for C1P is localized to the calcium binding loop II of the C2 domain of cPLA$_2\alpha$, specifically the cationic β-groove, making the laboratory group the first to fully characterize a specific interaction site for a bioactive sphingolipid.

Finally, the Chalfant laboratory came full circle and demonstrated that mutagenesis of amino acids critical for C1P interaction within this site inhibited the ability of cPLA$_2\alpha$ to translocate to intracellular membranes in response to numerous inflammatory agonists. These findings, published in the Journal of Biological Chemistry (1), suggested that the C1P/cPLA$_2\alpha$ interaction is a target for a new generation of therapies to combat inflammatory disorders, and a main thrust of the laboratory now is to determine whether modulation of this interaction in preclinical animal models affects inflammatory phenotypes.

A second major research focus for the Chalfant laboratory is the alternative splicing of caspase 9 and Bcl-x, major regulators of apoptosis and chemotherapy sensitivity. In previous studies by the laboratory, the generation of de novo ceramide and the activation of protein phosphatase-1 were defined as major components of the signal transduction pathway regulating both the 5' splice site selection of Bcl-x exon 2 and the inclusion of the exon 3,4,5,6 cassette of caspase 9 in a pro-apoptotic fashion. Recent endeavors of the laboratory in this area have been focused on the survival/oncogenic pathways that antagonize the ceramide pathway in regulating the alternative splicing in an anti-

Chalfant: committed to mentoring

BY LAURA CHALFANT

Charles Chalfant does not like to take the credit for his scientific findings or any success that his research program has obtained. Instead, he gives most of the credit to his staff and his numerous mentors over the years. "One has to have dedicated graduate students and postdoctoral trainees to undertake this research. Furthermore, the mentoring provided by Denise (Cooper), Yusuf (Hannun), Lina (Obeid) and Sarah (Spiegel) has been invaluable," says Chalfant.

As a result, Chalfant's trainees have accumulated an impressive list of fellowships and awards under his tutelage. These include predoctoral and postdoctoral fellowships from the American Heart Association; T32 fellowships from the National Institutes of Health in wound healing, cancer signaling and lipidomics; and a career development award from the Veterans Administration, which will lead one of his senior postdoctoral fellows to an independent research career. Recently, Chalfant also was awarded the 2010 Outstanding Teaching Award in Biochemistry and Molecular Biology from the Virginia Commonwealth University School of Medicine.

Chalfant is committed to mentoring and credits his staff for pushing the research forward. "Honestly, I don't know how my staff, or my wife for that matter, puts up with me!" says Chalfant. His mantra is, "Science can't wait." But if science can't wait, it is apparent that Chalfant can't wait for science either. His constant requests for data from the many graduate students and postdoctoral fellows that have walked through the Chalfant laboratory doors will not cease as long as science is on the move.

Laura, his wife, is just happy that she gets to see him home safe for dinner. XXXX

Laura Chalfant is an accomplished poet and writer of short stories.

apoptotic fashion. Specifically, two recent reports by the Chalfant laboratory have linked the alternative splicing of caspase 9 to the AKT pathway, an antagonistic pathway to ceramide signaling (2, 3). These findings showed a pathway controlled by ceramide signaling that was dysregulated in NSCLC tumors favoring caspase-9b expression, which is the anti-apoptotic form of caspase-9 that promotes tumor formation, growth and maintenance. Further investigation discovered that the phosphorylation of both SRp30a and hnRNP L, RNA trans-factors, promoted the expression of caspase-9b.

"We're dealing with an unexplored area of RNA trans-factors in relation to cancer and lipid signaling," says Chalfant. "Before these studies, there had been very little evidence of an RNA splicing event modulated by a lipid signaling or an oncogenic pathway, let alone regulating a tumor biology significant to cancer development. This study points to caspase-9b being a very important target in the development of a durable therapy for nonsmall cell lung cancer, and our future research will focus on how ceramide signaling is blocking caspase 9b expression. In essence, we will now marry our early findings on de novo ceramide signaling with these findings on oncogenic/survival signaling and determine the merge point that acts as a biostat for programmed cell death and the sensitivity of cancer cells to chemotherapies like erlotinib/Tarceva." ⟡

Charles Chalfant (cechalfant@vcu.edu & charles.chalfant@va.gov) currently is a tenured associate professor of biochemistry and molecular biology at Virginia Commonwealth University School of Medicine.

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Beyond the bench: social media in science

Social media is more than just reconnecting with old friends on Facebook

BY LESLIE W. CHINN

The job-seeker's mantra always has been "network, network, network," and the internet has made networking a far more efficient process than it used to be. Where to start? You could use Facebook, but there's always the possibility of your future boss happening upon embarrassing photos from some long-past summer break. A widely used alternative is LinkedIn, which bills itself as the world's largest professional network on the Internet and maintains a membership of more than 90 million people worldwide.

Career counselors at scientific institutions often encourage membership in LinkedIn. At the National Institutes of Health, the Office of Intramural Training and Education has transitioned from forwarding job postings via e-mail to sending them to members of its LinkedIn group, providing an incentive for members of the NIH community to join LinkedIn.

It's easy to think of one's self as the beneficiary of all of those connections — a node at the edge of the network — but for scientific organizations, the real power of social media comes from being at the center of it all. "I think the conversation has changed to a large extent for all of us endeavoring to further scientists' careers," says Melanie Sinche, formerly a career counselor at the NIH and the new director of the Office for Postdoctoral Affairs at Harvard University. "We are no longer simply sending information in one direction, to be consumed by a passive population — we are now actively engaged in conversation," Sinche explains.

While social media can help broadcast an organization's message more clearly or advertise a scientific seminar more efficiently, maintaining the conversation takes time and effort: updating blog posts often enough to keep people coming back, for example. "Incorporating social media into any organization's mission takes thoughtful planning and strategic thinking," Sinche notes. To that end, Sinche held a workshop at the National Postdoctoral Association's annual meeting in which she examined case studies of how scientific organizations have used social media successfully to engage postdocs and assist them in career development. For those interested in using social media, Sinche recommends an initial review of current best practices — she likes the U.S. Army's Social Media Handbook. But don't be intimidated by all of the guidelines, says Sinche: "Try blogging or tweeting on a topic of interest — you might find you really enjoy it!"

Whether you're an outlying node in the social network or in the thick of it, there is actual science to be had. If you miss the excitement of benchwork, try citizen science, in which you can participate in a project, often with a network of volunteers, to conduct research. One of the longest-running citizen science projects is the Audubon Society's Christmas Bird Count, conducted by volunteers every November since 1900. A century later, NASA introduced its ClickWorkers project, which enlists volunteers to count craters on the surface of Mars. There's also DIYbio, an organization "dedicated to making biology an accessible pursuit for citizen scientists." Local DIYbio groups use social media sites like Meetup.com and Google Groups to coordinate events from Chicago to Copenhagen, tackling projects both simple (extracting DNA from cheek swabs in New York City) and complex (developing an inexpensive way to synthesize Taq polymerase in Baltimore).

Scientists are making use of social media in their day jobs too. This past April, researchers from Stanford University published a paper describing an algorithm they developed to predict the spread of infectious disease and inform vaccine administration using social networking data collected from Facebook. And in October, astronaut Douglas Wheelock checked in to the location-based social media site Foursquare from space, then tweeted about it moments later to nearly 100,000 Earth-bound followers.

From job searches to vicarious space travel, social media surely is every scientist's friend. XOXO

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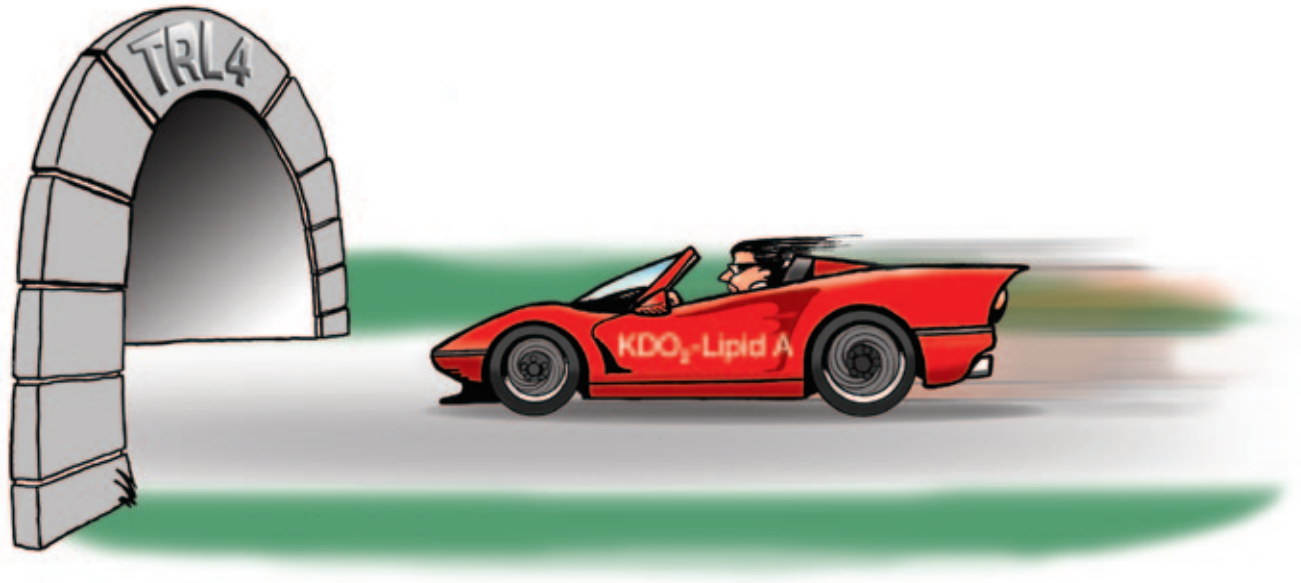

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