

ASBMB *today*

April 2012

VALID -OMICS DATA



ALSO INSIDE THIS ISSUE:

- ▶ Special events at the annual meeting
- ▶ Poetry contest winners

American Society for Biochemistry and Molecular Biology



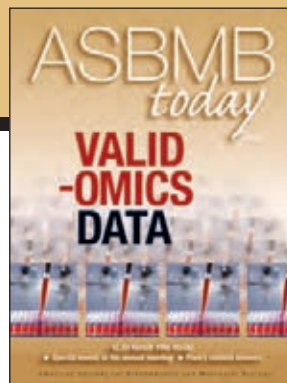
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online exclusives

We're pleased to announce that science writer Rajendrani Mukhopadhyay now has a blog.

Follow her quips and queries at www.asbmb.org/asbmbtoday.



ASBMB today

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Research Spotlight

Read two "Research Spotlight" interviews with Elizabeth Ntantie (left), a pharmacology graduate student at the Medical College of Wisconsin, and with Casonyta Matese Johnson (right), an associate professor of biology at Georgia State University, by ASBMB's education and professional development manager, Weiyi Zhao.



Discovery through writing

Want to know more about the scientists who won the ASBMB poetry contest being held in conjunction with Experimental Biology 2012? Make sure to visit our website to read their bios. You'll also find bios by the contest judges — some serious and some not so much.

ASBMB Today is now on Pinterest!

Join us at <http://pinterest.com/asbmbtoday/>. We've pinned all of our magazine covers from the past 10 years. If you let us know which ones are your favorites, it'll help us plan future covers.



April 2012

Evolution and molecular Lego

BY SUZANNE PFEFFER

Not far from the traffic and cacophony of downtown Bangalore is a quiet, secluded compound that houses India's National Centre for Biological Sciences of the Tata Institute of Fundamental Research. Now in its 20th year, this center of research excellence is powered by scientists studying biochemistry, biophysics and bioinformatics; cellular organization and signaling; ecology and evolution; genetics and development; neurobiology; and theory and simulation of biological systems. I had the pleasure of visiting the NCBS in February to attend an international workshop and research conference titled "The Evolutionary Origins of Compartmentalized Cells." India's International Centre for Theoretical Sciences provided funding for the meeting as part of its mission to nucleate new areas of research by bringing together scientists from diverse fields.

The conference was organized by Frances Brodsky from the University of California at San Francisco, together with Satyajit (Jitu) Mayor and Mukund Thattai from NCBS. Their goal was to bring together evolutionary biologists, cell biologists and immunologists to try to synthesize what these disciplines can teach us about the origins of the first eukaryotic cell and the origin of the human immune system. The conference taught me an important lesson: Evolution of a biochemical process can teach us a great deal about how it operates — it can help determine which features are fundamental and which represent cellular or organismal specializa-

tion. I often have neglected to consider evolution when trying to understand the molecular basis of a given cellular process. Evolution adds an important dimension.

"Bringing together molecular cell biologists, immunologists and evolutionary biologists who appeared ready to candidly discuss their favorite cellular processes and structures and debate the origins of cellular compartments and cellular immunity, in the context of new ideas about genes and their capacity for evolution, was a risky experiment for us as organizers of this conference," said Mayor. "The quality of discussion and the fount of new ideas generated suggest that this experiment was wildly successful. This augers well for a bright future for the exciting and emerging field of evolutionary cell biology."

Thattai echoed Mayor's sentiments, saying, "One of the great things about studying the evolution of cells is that no topic is off limits. Though ours was a diverse meeting by any standard, with topics ranging from organelle biology to phylogenetics to ancient viruses, I found fascinating and relevant ideas to take away from every talk."

Brodsky added, "Molecular cell biologists interested in the evolutionary origins of pathways we study can learn a lot from immunologists who have refined techniques to extract information from the co-evolution of host-pathogen interaction pathways, which are the most rapidly evolving in biology."

I was invited to the conference because I share a

common experience with one of the organizers, Brodsky. A manuscript referee once told each of us (independently) that the human proteins that we were describing couldn't be relevant because that gene product is not present in mice (even though it was present in all other vertebrates). Some take the even more extreme view that if we understand a process in yeast it is not



The conference was organized by Frances Brodsky of the University of California at San Francisco, Satyajit (Jitu) Mayor, center, and Mukund Thattai from India's National Centre for Biological Sciences.

worth studying in humans because we already understand the fundamentals.

This cannot be correct: We need to understand the regulation of human pathways that will differ in different cell types, tissues and/or developmental stages. Many diseases can be attributed to proteins that are found only in humans and for which the genes represent duplication and diversification to yield traits needed for our complex physiology. Thus, the study of human cells and tissues is important; the study of nonhuman organisms and pathogens is also important. When we see convergent evolution provide the same solution to a complex problem, we have a better understanding of its importance.

Molecular Lego

As we obtain more and more protein structures, we see that certain folds are used to achieve distantly related but likely functionally similar processes. Sometimes structure conservation is achieved by gene duplication, but other times convergent evolution appears to come to a common solution. Structural biologists surely know more of this than the rest of us (and I implore them here to please write a review or send one to me); all of us should learn more about this. When we find proteins of unknown function, structurally related proteins may provide us with important clues to how that protein works. A wonderful example is the structure of certain nuclear pore complex proteins that resemble elements of clathrin transport vesicle coats: They are made up of an alpha solenoid connected to a beta propeller to form a flexible, macromolecular assembly. Transport vesicle tethering factors share this feature; perhaps this is trying to tell us that transport vesicle coats once performed a tethering role.

The conference was flanked by tutorial lectures by many of the speakers to provide the background information needed for students (and faculty members) from diverse areas to be able to appreciate the topic. This made it possible to include a truly interdisciplinary set of speakers and topics. In times of tight research funding, it may be more important than ever before to encourage scientists to organize and attend such combination workshop/conferences. A great way to initiate valuable collaborations is to bring people together and provide them with lots of time to interact with one another and to learn what each other is thinking about. Collaboration will continue to be more important when funds are tight, and the best collaborations team scientists from different disciplines who can bring to the table distinct approaches and tools. Meetings can

energize us, stimulate new ideas and catalyze the discovery of novel connections between diverse proteins, pathways or systems.

This month, ASBMB holds its annual meeting in San Diego, and we are also sponsoring a number of member-initiated, smaller meetings on a variety of topics. We encourage you to help identify cutting-edge, interdisciplinary topics for consideration for ASBMB-sponsored special symposia and/or annual meeting themes for next year and beyond. In the meantime, I look forward to seeing you in San Diego! XXXX



ASBMB President Suzanne Pfeffer (pfeffer@stanford.edu) is the Emma Pfeiffer Merner professor of medical sciences and a biochemistry professor at the Stanford University School of Medicine.

2012 ASBMB SPECIAL SYMPOSIA

NEW THIS YEAR:

Minority travel awards are available for each symposium. See the website for deadlines and details about this and other opportunities.

www.asbmb.org/specialsymposia

Trypsin-Like Proteases: Structure, Function and Regulation

June 7 – 10, Tahoe City, Calif.

Mitochondria: Energy, Signals and Homeostasis

June 27 – June 29, East Lansing, Mich.

Frontiers in Lipid Biology

Sept. 4 – 9, Banff, Alberta, Canada

Transcriptional Regulation: Chromatin and RNA Polymerase II

Oct. 4 – 8, Snowbird, Utah

Post-Translational Modifications: Detection and Physiological Role

Oct. 11 – 14, Tahoe City, Calif.





Hill Day 2012

BY JULIE MCCLURE

On March 27, 19 students and post-docs joined the American Society for Biochemistry and Molecular Biology Public Affairs Advisory Committee in Washington, D.C., to meet with more than 60 congressional offices and advocate for basic research funding and biomedical-related legislation. This year represents the fourth annual ASBMB Student/Postdoc Hill Day, and every year we refine our message to Congress. Here are some of the issues the Hill Day participants addressed this year.

Strong, sustained funding for the National Institutes of Health

Since 2008, the National Institutes of Health's funding levels have increased — but at a rate lower than that of inflation. As a result, the purchasing power of the NIH has dropped steadily. Feast-or-famine funding at the NIH is highly disruptive to training, careers and long-range research projects. Sustained funding for the NIH is critical if researchers hope to continue their work. This year, the Hill Day participants brought a message to Congress that addressed this. ASBMB is calling for \$32 billion in funding for the NIH for FY13 with a move to reach \$35 billion by FY15. This plan will provide the NIH and biomedical researchers with predictable NIH funding to maximize our nation's long-term return on its investment in research.

The positive economic impact of an investment in biomedical research

All you have to do is turn on the news today and you'll quickly see that the economy is on everyone's mind. Unemployment remains high, and the country is wondering how we will turn this economic downturn around. During Hill Day, ASBMB members showed their elected officials how investing in biomedical research not only is an investment in the overall health of our nation but also an investment that results in millions of jobs. It's easy to show that areas such as Boston, San Francisco and North Carolina's Research Triangle are reaping the benefits of research funding, but many members of Congress are surprised to see the significant economic impact research has throughout the country. Take Kansas, for instance. The state received \$136.4 million from the NIH

in 2011 (1). This funding has an economic effect that reaches far beyond the individual labs it goes to, creating more than 15,000 new jobs and producing \$182 million in new business activity in Kansas (2). The positive economic effect of the research enterprise is a message that carries significant weight on both sides of the aisle.

Support for legislation that benefits biomedical researchers

While NIH funding is always the main topic of discussion on Hill Day, there are several pieces of legislation that have been put forward in the 112th Congress that would have positive effects on the biomedical research community. In both the U.S. House and Senate, there are several bills that propose tax credits for costs associated with biomedical or life-science research. The Stem Cell Research Advancement Act would allow the use of federal funding on research using human embryonic stem cells. The Stopping American-Trained Ph.D.s from Leaving Our Economy Act, otherwise known as the STAPLE Act, proposes immigration reforms that would allow students who earn science, technology, engineering or math Ph.D.s to continue to work in America. The Hill Day participants highlighted bills such as these in their meetings to try to garner further support for them.

The visits to the Hill are part of an ongoing education strategy directed by ASBMB's PAAC. Visit our website or contact our offices if you would like to learn how you can be a part of these efforts. ☺☺☺



Julie McClure (jmcclure@asbmb.org) is the science policy fellow at ASBMB.

REFERENCES

1. Budget data obtained from the NIH Research Portfolio website: <http://report.nih.gov/index.aspx>.
2. Statics based on 2007 data from "In Your Own Backyard: How NIH Funding Helps Your State's Economy" (2008). Families USA: Washington, D.C.

The Capitol Hill cohort

Nineteen young ASBMB members, along with a handful of Public Affairs Advisory Committee members and the main office's policy staffers, took to Capitol Hill in late

March to advocate for adequate and sustained federal funding for biomedical research. Here are snapshots of the young participants and their research interests.



VALERIE O'SHEA

University of California, Berkeley, postdoc
Structure and function of molecular machines involved in bacterial DNA replication initiation



KAUSTUBH BHINGE

University of Louisiana at Monroe, Ph.D. candidate
Role of glucosylceramide synthase in the regulation of breast cancer metastasis and cell-cycle regulation



ROBERT LINDER

University of Southern California, Ph.D. candidate
Mechanisms through which the proteasome is regulated during the adaptive response to oxidative stress



CHERIE RAMIREZ

Harvard University, Ph.D. candidate
Ensuring that our technology for editing the genetic code of living cells — zinc finger nucleases — has the lowest risk of unwanted side effects possible so that it can be used most effectively for curing human disease



KRISTY LAMB

Yale University, Ph.D. candidate
How subtle variation in DNA repair genes changes the efficiency of DNA repair and how that affects an individual's risk of developing cancer or his or her response to chemotherapy



MATTHEW SHIRLEY

Johns Hopkins University School of Medicine, Ph.D. candidate
Identifying genomic causes of childhood neurological diseases, such as autism, using human genome resequencing and DNA microarray technology



CHRIS CARMEAN

University of Chicago, Ph.D. candidate
Regulation and physiological significance of brown adipose tissue carbohydrate metabolism during fasting followed by refeeding



CHRIS PICKETT

Washington University in St. Louis, postdoc
Degenerative changes that cause age-related reproductive complications



MELISSA HARGREAVES

University of Montana, graduate student
 Characterizing ribosome biogenesis from an unusual ribosomal RNA operon in the Lyme disease bacterium *Borrelia burgdorferi*



GEORGE JULES

Meharry Medical College, Ph.D. candidate
 How benzo[a]pyrene exposure in utero alters the cardiovascular system to contribute to cardiovascular disorders in later life



ANNE MCCABE

Princeton University, graduate student
 Outer membrane biogenesis in *E. coli*, focusing on members of the BAM complex responsible for assembling Beta-barrel proteins within the outer membrane



REBECCA JOHNSON

University of Texas Health Science Center, Ph.D. candidate
 Cancer biology



JOSHUA ROXBY

University of New Mexico, Ph.D. candidate
 Characterizing a novel PARP inhibitor to be delivered to ovarian cancer cells with Cisplatin using silica-supported lipid nanoparticles



CLINTON COPELAND

Norfolk State University, postdoc
 Reproductive biology



CHRISTINE LEROY

New York Medical College, Ph.D. candidate
 Human DNA replication enzyme DNA polymerase delta, including its implications in the DNA damage response and its roles in the maintenance of genomic integrity



ABIGAIL SCHINDLER

University of Washington, Ph.D. candidate
 Biochemical and molecular basis of stress-induced depression and potentiation of cocaine reward



JOHN LACAVAL

Rockefeller University, postdoc
 Specializing in applied scientific research on molecular interaction dynamics



MELINDA HOUGH

University of Washington, postdoc
 Understanding the molecular mechanisms of bacterial cell death caused by antibiotic treatment in order to provide fundamental insights and future avenues for drug development



JONATHAN PROTO

University of Pittsburgh School of Medicine, Ph.D. candidate
 Nuclear factor Kappa B signaling in the regulation of muscle stem cell phenotype and the possible implications this may have for the aging process

Become a fellow

ASBMB is now accepting applications for its 2012–2013 Science Policy Fellowship program.

Visit www.asbmb.org for more information.

The deadline is April 15.

Recommendations for engaging basic scientists in translational research

BY ANNE M. DESCHAMPS

The Federation of American Societies for Experimental Biology released a report last month describing how research institutions, funding organizations, professional societies and scientific publishers can facilitate the participation of basic scientists in translational research. The report, "Engaging Basic Scientists in Translational Research: Identifying Opportunities, Overcoming Obstacles," is based on the proceedings of a two-day symposium held in March 2011 that brought together more than 150 basic, clinical and translational scientists, scientific journal editors and leaders from private and public research organizations. The report addresses the benefits of conducting translational research, challenges basic scientists face in developing translational research programs and practical recommendations for overcoming those challenges.

Basic scientists are the foundation of the biomedical research enterprise. Their work is key to understanding fundamental biological processes and mechanisms of disease pathogenesis, and it has been critical to preventing, diagnosing and treating diseases and conditions that afflict millions of people. FASEB's symposium featured a number of basic investigators who benefited from pursuing the translational applications of their work. They described how they learned new methods, expanded their insights into biological mechanisms of disease and even improved their publication rates.

In spite of these benefits, numerous factors can impede or prevent basic researchers from embarking on translational research projects. The physical and cultural separation of basic and clinical departments limits opportunities to interact and collaborate, basic scientists may not have access to the research resources, funding and support systems needed to conduct translational science, and unfamiliar and complex regulatory issues can deter them from moving a project forward. In addition, tenure and promotion committees may not accord the same value to participation in translational research, which tends to be goal-directed, interdisciplinary and team-based, as they do to hypothesis-driven basic science conducted by individual investigators.

Conference participants were asked to identify ways to address these challenges, with a focus on helping basic scientists acquire translational research training, facilitating collaborations, receiving recognition and rewards, and defining the role of funding organizations. These discussions provided FASEB's Translational Research Steering Committee with the material to shape the set of realistic recommendations below.

Funders should

- continue to support basic research to ensure a deep and broad reservoir of new knowledge upon which translational and clinical science can grow,
- provide specific funding for investigator-initiated translational research and
- ensure that grant application reviewers have appropriate expertise to review translational research projects.

Research institutions should

- provide didactic and experiential learning opportunities that place basic research in the context of pathophysiology and pathobiology,
- create opportunities for interdisciplinary collaboration:
- connect basic scientists with the infrastructure, equipment, and technical and administrative support necessary to move their discoveries from the bench to the bedside and
- revise tenure and promotion policies to recognize interdisciplinary, team-based translational work.

Scientific publishers should

- ensure that the roles of individual authors are clearly articulated in publications and
- encourage editors to identify and highlight the contributions that basic research findings could make to medicine and public health.

Professional scientific societies should

- spark interest in translational research by raising its profile in featured symposia, workshops and sessions at professional meetings;
- provide resources and opportunities to facilitate interactions among basic and clinical researchers;
- provide awards for exceptional contributions to team, interdisciplinary and translational science and
- advocate for policies and programs that facilitate participation of basic scientists in translational research.

continued on page 9



BERMAN



HONIG



LEMMON



LINDQUIST



SMERDON

Berman, Honig, Lemmon lauded by Protein Society

Helen M. Berman of Rutgers University won the Carl Brändén Award, given to an outstanding protein scientist who has made exceptional contributions in the areas of education and/or service. In a statement, the society said Berman was recognized for her work toward enabling a freely available, worldwide archive of 3-D structural information. "Dr. Berman's passion for making structural data accessible and understandable by a broad community has driven the development of the Protein Data Bank into a vital and accessible international resource for biology. Berman in the early 1970s was a champion of the open access of scientific information; albeit obvious today, the concept at that time of open access was truly visionary." Barry Honig of Columbia University won the Christian B. Anfinsen Award for significant technical achievements. Honig was singled out "for his contributions to our understanding of the electrostatic properties of proteins and the development of DelPhi and GRASP,

which are among the most widely used programs in structural biology." The society also emphasized the value of Honig's discoveries related to cell-cell adhesion and sequence-dependent protein-DNA recognition. Mark Lemmon of the University of Pennsylvania Perelman School of Medicine won the Dorothy Crowfoot Hodgkin Award for his significant contributions to the field of signal transduction and transmembrane signaling mechanisms of receptor tyrosine kinases. The society said: "Crystallographic, biochemical and genetic studies from his laboratory have provided sophisticated mechanistic understanding of EGFR cell signaling. His discoveries of the mechanisms for the epidermal growth factor receptor family offer new venues for developing novel therapeutic approaches targeting cancer and other human diseases." ❧❧❧

Lindquist earns lifelong EMBO honor

Susan Lindquist of the Whitehead Institute at the Massachusetts Institute of Technology was one of three U.S. scientists who became associate members of the

European Molecular Biology Organization late last year. Lindquist, who is also a Howard Hughes Medical Institute investigator, will now have a lifetime membership. Lindquist's work on protein folding was featured in the Feb. 15 issue of *Nature* and the Feb. 16 issue of *New Scientist*. ❧❧❧

Smerdon wins top faculty award

Michael J. Smerdon of the School of Molecular Biosciences at Washington State University has won the 2012 Eminent Faculty Award, the highest honor the university offers, for career-long excellence. Smerdon, one of the first researchers to analyze how repair is influenced by the way DNA is packaged and to recognize that the repair response to genetic signals is turned on and off by environmental conditions, has served as a *Journal of Biological Chemistry* editorial board member and is a fellow of the American Association for the Advancement of Science. In 2006, he was recognized as among the top 5 percent of extramural NIH grant awardees over the past 25 years. ❧❧❧

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Individual researchers should

- learn to define a health need with the same precision as a basic science hypothesis,
- seek mentors/collaborators from different disciplines and
- negotiate concurrence with departments as to how translational research will be evaluated in the tenure and promotions process.

FASEB's goal in developing these recommendations is not to turn basic scientists into clinical trialists. Rather, it is to encourage them to consider the translational potential

of their work and to create an environment that provides them with opportunities to translate their discoveries into human health applications. The conference proceedings and the complete set of recommendations are available here: <http://www.faseb.org/Policy-and-Government-Affairs/Publications.aspx>. ❧❧❧



Anne M. Deschamps (adeschamps@faseb.org) is a science policy analyst in the Office of Public Affairs at FASEB.

TABOR/JBC LECTURESHIP

Kornfeld's contributions recognized for their 'rigor and scientific breadth'

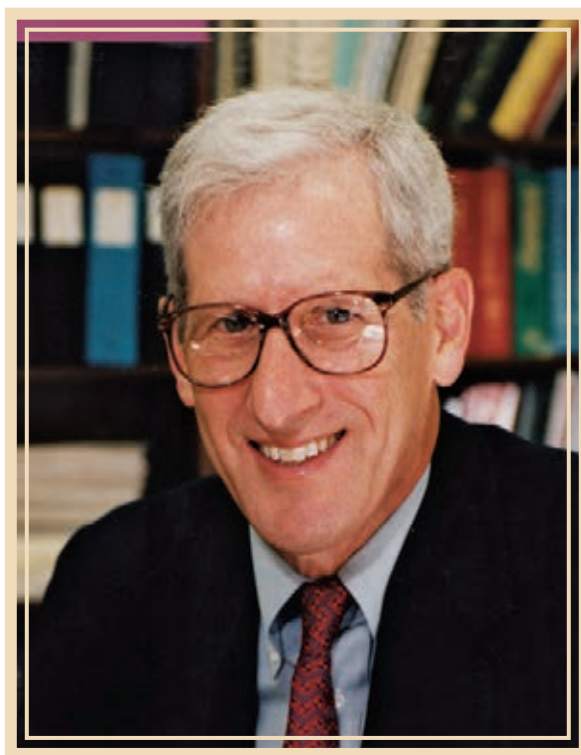
BY GEOFF HUNT

The American Society for Biochemistry and Molecular Biology has named Stuart Kornfeld, professor of medicine in the School of Medicine at Washington University in St. Louis, the winner of the society's Herbert Tabor/Journal of Biological Chemistry Lectureship.

Kornfeld received the award for his seminal research in the field of glycobiology, in particular his work describing multiple novel pathways involved in oligosaccharide biosynthesis, processing and maturation. These actions subsequently were shown to be critical in mediating proper folding and transport of major cellular proteins, including those that regulate activity of the lysosome, a critical organelle involved in the degradation of macromolecules. Kornfeld also showed that disruptions in these processes could cause a range of metabolic diseases that have severe effects on organ systems.

The award has special meaning for Kornfeld. "Herb Tabor has been one of my heroes since I first met him at the National Institutes of Health in the 1960s," he said. "I am very honored to be selected."

Karen Colley, professor at the University of Illinois-Chicago, said she remembered "feeling very special when Stuart, at the beginning of a seminar years ago, announced to the audience that, by virtue of having worked for Jacques Baenziger (his first graduate student), I was therefore his granddaughter in science!" She was quick to reciprocate the pride Kornfeld expressed for



her that day. "His incredibly significant contributions to glycobiology and cell biology, elegantly simple scientific approach, and ability to ask the most important questions and solve complex problems make this amazingly humble man an extraordinary scientist and human being."

University of Chicago professor Ben Glick agreed. "Dr. Kornfeld's contributions are spectacular in their combination of rigor and scientific breadth."

Kornfeld was an undergraduate at Dartmouth College and earned his M.D. from the Washington University in St. Louis medical school, where, save for a brief stint at the NIH from 1963 to 1965,

he has remained his entire career. He ran the school's hematology division for more than 30 years.

Kornfeld will receive his award during the Experimental Biology 2012 conference in San Diego, where he will deliver the opening lecture of the conference. The presentation will take place at 6 p.m. April 21 in the San Diego Convention Center. XXXX

About the award

The Herbert Tabor/Journal of Biological Chemistry Lectureship recognizes outstanding lifetime scientific achievements and was established by the ASBMB to acknowledge the many contributions of Herbert Tabor to the society and the journal, of which he served as editor for nearly 40 years and now serves as co-editor.

WILLIAM C. ROSE AWARD

Marqusee lauded for protein-folding research and ‘encouragement of the next generation’ of scientists

BY GEOFF HUNT

The American Society for Biochemistry and Molecular Biology has named Susan Marqusee, professor of molecular and cell biology at the University of California, Berkeley, and director of Berkeley’s California Institute for Quantitative Biosciences, the winner of the society’s William C. Rose Award.

“I’m honored to receive an award that recognizes the sum total of what I love about my job — science, mentorship and training,” said Marqusee. “For me, it’s the melding of all three areas that gives me the greatest satisfaction.”

Marqusee received the award in recognition of her extensive thermodynamic and kinetic studies using hydrogen-exchange, nuclear magnetic resonance, and single-molecule methods to study protein structure and behavior at increasingly sharper resolution. According to Walter Englander, professor at the University of Pennsylvania, “this work convincingly revealed that proteins are composed of cooperative natively-like foldon units and demonstrated their key role in protein-folding pathways.”

Professors Carlos Bustamante and Jennifer Doudna of the University of California, Berkeley, nominated Marqusee for the award. “The fundamental nature of Dr. Marqusee’s work has had, and will continue to have, significant impact on many areas of research, ranging



from the physical chemistry of macromolecules to the design of therapeutics that prevent the aggregation of proteins which lead to common diseases such as Alzheimer’s,” they wrote in their nominating letter.

Marqusee’s mentorship efforts also are recognized by the Rose Award. Her colleague Jane Clarke from the University of Cambridge hailed Marqusee as “an all-too-rare example of an academic who is not simply a stellar scientist but someone who explicitly factors into her way of doing science dedication to encouragement of the next generation. Her students simply adore her.”

Marqusee will get her award and deliver her lecture at 9:05 a.m. April 24 at the Experimental Biology 2012 meeting in the San Diego Convention Center. ☺☺☺

About the award

The William C. Rose Award recognizes outstanding contributions to biochemical and molecular biological research and a demonstrated commitment to the training of younger scientists as epitomized by the late Rose, an authority on protein nutrition and former president of the ASBMB. The award consists of a plaque, \$3,000 and transportation to the 2012 ASBMB annual meeting to present a lecture.

EARL AND THRESSA STADTMAN SCHOLAR AWARD

Sabatini honored for ‘providing critical insights into the linkages between energy, nutrient metabolism and cancer’

BY GEOFF HUNT

The American Society for Biochemistry and Molecular Biology has named David Sabatini, associate professor of biology at the Massachusetts Institute of Technology and a Howard Hughes Medical Institute investigator, the winner of the society’s inaugural Earl and Thressa Stadtman Scholar Award.

Sabatini received the award for his work identifying the mTOR pathway, a major regulator of mammalian cell growth and a central component of pathways relating to metabolism and aging. Susan Lindquist, a professor at MIT, praised Sabatini’s work on mTOR for “providing critical insights into the linkages between energy, nutrient metabolism and cancer.”

The work done by Sabatini’s lab has led to the development of several drugs aimed at treating cancer. His lab also recently has demonstrated the ability of diet to affect aging and cell growth.

Solomon Snyder from Johns Hopkins University was not bashful in his praise for his former graduate student. “Virtually all of the major breakthroughs relating to signaling pathways whereby growth factors and nutrient amino acids regulate protein translation can be attributed to one individual: David Sabatini,” Snyder said.

Upon completing his M.D./Ph.D. at Johns Hopkins, Sabatini was invited to become a fellow at the prestigious Whitehead Institute in 1997. He was elevated to full member in 2002. Sabatini also began a professorship in the department of biology at MIT in 2005.

In addition to his experimental insights, Sabatini has



earned praise for his technological inventions, including the reverse transfection microarray, a rapid, high-scale throughput technique in which cells expressing defined cDNAs are screened for select phenotypes, thereby enabling investigation into the effects of varying gene expression levels on a cellular rather than population level. This technology also allows for simultaneous screening of the efficacy of multiple small-molecule compounds that serve as potential drug candidates.

“I am delighted to receive this honor from my colleagues and am humbled to receive an award named for pioneering biochemists whose work has influenced all of us who pretend to be one,” said Sabatini.

Sabatini will receive his award during the Experimental Biology 2012 conference in San Diego, where he will deliver an award lecture. The presentation will take place at 8:30 a.m. April 23 in the San Diego Convention Center. XXXX

About the award

The Earl and Thressa Stadtman Scholar Award was established by their friends and colleagues to preserve their legacies as scientists and mentors. It is awarded to a scientist with 10 or fewer years of post-doctoral experience, including medical residency and fellowship. The award is given every other year, alternating with the Earl and Thressa Stadtman Distinguished Scientist Award. The award consists of a plaque, a \$10,000 cash award and travel expenses for the ASBMB annual meeting to present a lecture.

RUTH KIRSCHSTEIN DIVERSITY IN SCIENCE AWARD

‘No one has been more dedicated to increasing the pipeline of minority scholars than Lovell Jones’

BY GEOFF HUNT

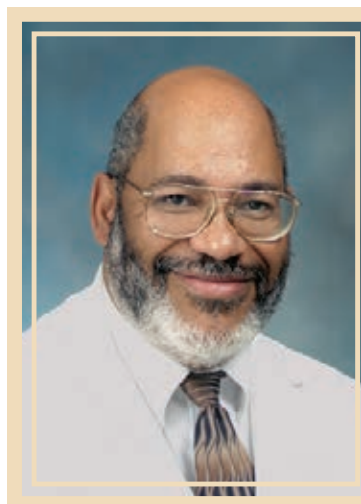
The American Society for Biochemistry and Molecular Biology has named Lovell Jones the winner of the society’s Ruth Kirschstein Diversity in Science Award. Jones is a professor at both the University of Texas MD Anderson Cancer Center and the University of Houston as well as director of the joint Center for Health Equity & Evaluation Research.

Throughout his career, Jones has focused on minority health issues. He was a co-founder of the Intercultural Cancer Council, the nation’s largest multicultural health policy group focused on minorities, the medically underserved and cancer; chaired the first Biennial Symposium on Minorities and Cancer in 1987; and was among the leaders who worked with members of Congress to designate the third week of every April National Minority Cancer Awareness Week.

Thomas Landefeld, professor at California State University–Dominguez Hills, praised Jones for being “totally devoted to diversity issues in the scientific community, with a major emphasis on both addressing the underrepresentation of minorities at all levels in academia, industry and government, as well as the overwhelming issue of health disparities in our nation.”

Jones also has shown great dedication to mentorship of underrepresented groups. In supporting his nomination for the award, Marian Johnson-Thompson, professor emerita of the University of the District of Columbia, cited his “attention to promoting diversity in training programs, which has led to the next generation of health-disparities researchers and policy leaders.” Judith Kaur, from the Mayo Clinic, agreed: “No one has been more dedicated to increasing the pipeline of minority scholars than Lovell Jones.”

In addition to his efforts involving minority health disparities, Jones is also a pre-eminent scientist. He holds both M.S. and Ph.D. degrees in zoology from the University of California, Berkeley, and has worked in the department of biochemistry at MD Anderson since 1980,



“Perception is reality to those who perceive it... Until you address the perception, you will never be able to truly address the reality. In setting up the minority training programs, Ruth took both aspects into account. It is truly an honor receiving this award in her name.”

LOVELL JONES

focusing primarily on the role of estrogen and environmental estrogenic agents in tumor induction in hormonally responsive tissues.

Jones will receive his award during the Experimental Biology 2012 conference in San Diego, where he will deliver an award lecture. The presentation will take place at 2:55 p.m. April 23 in the San Diego Convention Center. ❧❧❧



Geoff Hunt (ghunt@asbmb.org) is ASBMB’s public outreach coordinator.

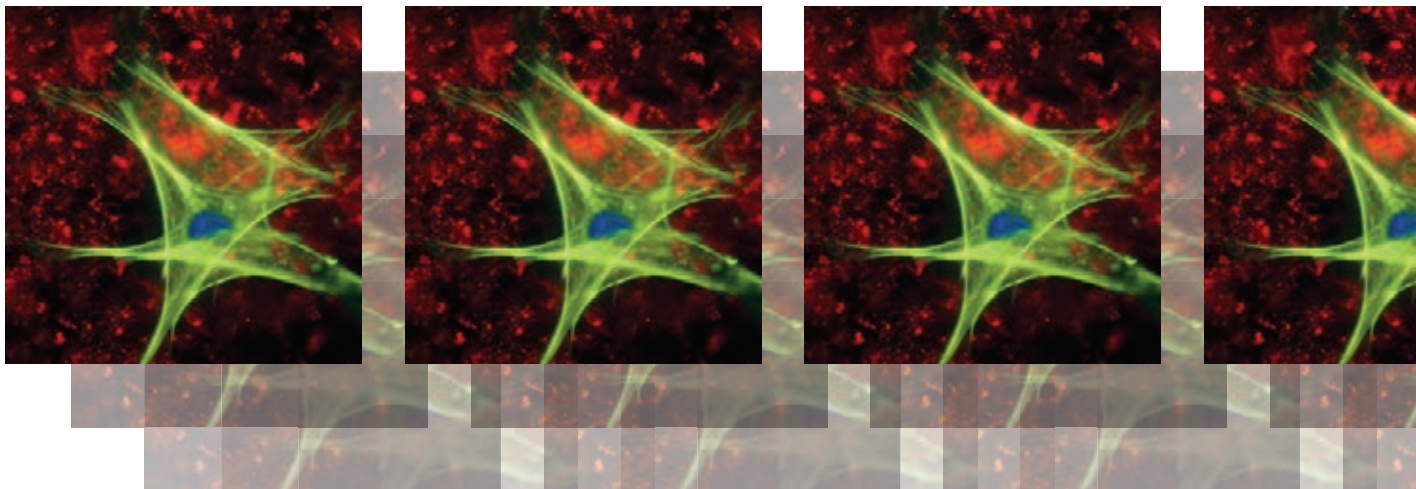
About the award

The Ruth Kirschstein Diversity in Science Award was established to honor an outstanding scientist who has shown a strong commitment to the encouragement of underrepresented minorities to enter the scientific enterprise and/or to the effective mentorship of those within it. The award consists of a plaque, a cash prize of \$3,000 and transportation expenses to present a lecture at the ASBMB annual meeting.

VALID -OMICS

With the massive quantities of -omics data being produced today, how should they be validated?

BY RAJENDRANI MUKHOPADHYAY



Genomics, transcriptomics, proteomics — the list of fields with “-omics” as the suffix has ballooned, and so has the excitement and anticipation of what these fields can deliver. When so many biomolecules are tracked at once, scientists can get more detailed and complete pictures of the complex connections between different molecular pathways, cellular and tissue conditions, and pathologies. With the more detailed pictures, researchers can deepen our understanding of biology and even develop novel clinical diagnostic tests or therapeutic treatments to improve public health.

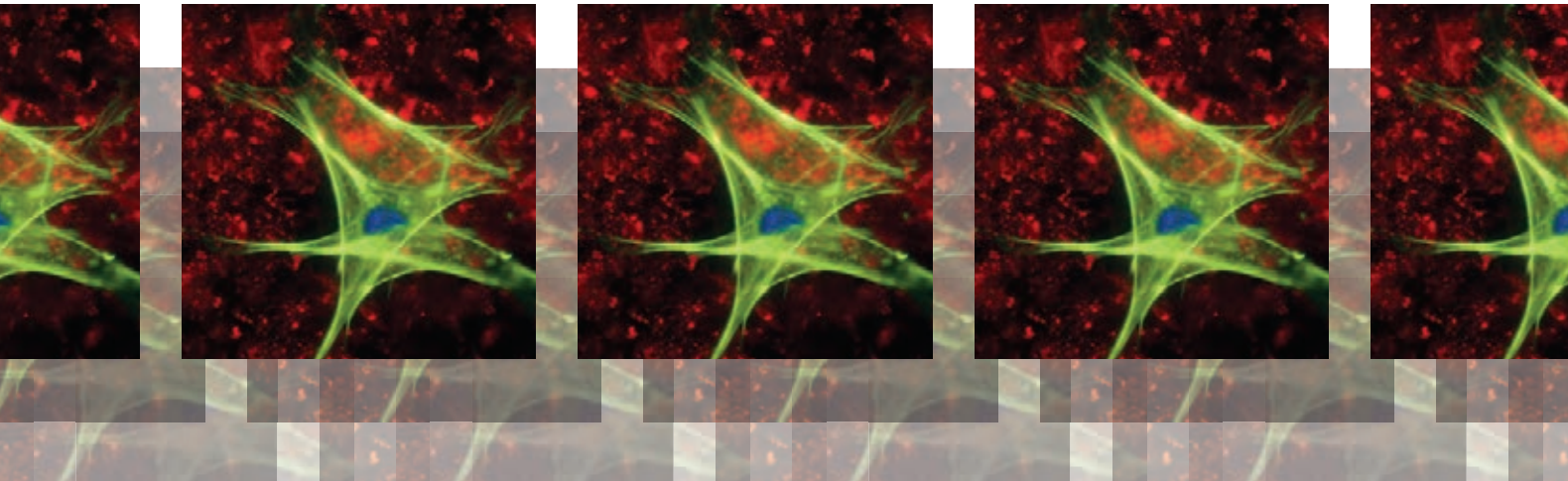
But in the excitement over the promise of -omics technologies, “the issue of validation, an important one, has been a bit neglected,” says James P. Evans at the University of North Carolina at Chapel Hill. He and other researchers, whose expertise range from fundamental research to clinical epidemiology, are worried that if data validation is not properly done, discoveries from -omics endeavors will be pointless.

The notion of validation is not anything new. “The process of replication is a hallmark of science,” says John Ioannidis of Stanford University. Scientists “don’t just blindly trust results, because trust belongs to dogma.”

But experts say that validation of -omics data is a

different beast. “For -omics research, the complexity is so immense that we cannot really afford to just go for discovery without validation,” says Ioannidis. “Validation should be built into the process of discovery.”

Hypothesis-generated research — when one or two variables are tested against one or two others — tends to produce a few results, which are relatively easy to validate with simple statistical tests. But -omics data sets contain thousands, even millions, of molecules. Because of the sheer quantity of data, Keith Baggerly at the University of Texas MD Anderson Cancer Center says, “I no longer believe that we have good intuition about what makes sense.” Because of this lack of intuition to grasp what large data sets are



revealing, Baggerly says these data sets need to be independently verified and checked in multiple ways.

The need for validation is growing increasingly urgent, especially when a significant number of -omics studies are targeted for medical applications. “There is plenty of research that focuses on the initial discovery phase but not enough research on replication, validation and translation,” argues Muin Khoury at the Centers for Disease Control and Prevention, who with Ioannidis recently made some recommendations about the validation of -omics data for clinical studies (1).

Experts all brought up the two cautionary tales of what can go wrong when -omics data are not scrutinized: Correllogic’s OvaCheck test of 2004 and Anil Potti and Joseph Nevins’ clinical trials at Duke University (see sidebar). The Institute of Medicine has reviewed how -omics data should be validated for clinical trials (see <http://iom.edu/Activities/Research/OmicsBasedTests.aspx>).

The need for validation is growing increasingly urgent, especially when a significant number of -omics studies are targeted for medical applications.

Much of the emphasis has been on validating -omics data relevant for clinical applications, because patient safety is of utmost importance. But Ruedi Aebersold at the Swiss Federal Institute of Technology in Zurich points out that validation also has significant repercussions in fundamental research. “True, patients aren’t hurt if someone misassigns a protein in a yeast project,” he says. “But it’s still an enormous waste of resources and effort. It’s generally bad for science if the data are poorly reproducible or misassigned.”

BUILDING FROM THE GROUND UP

Like a tower, validation is made of a stack of bricks. The first brick is analytical confirmation. This is the type of validation for which researchers have to ask themselves whether they get the same result from the same experiment done all over again or if a dif-

ferent method on the same sample set gives them the same answer.

Next are the bricks of independent repeatability and replication. Researchers not connected with the original group must see if they can carry out the same experiments and get the same answers. If the analysis has clinical implications, it should also be carried out in larger cohorts to see if the same results emerge.

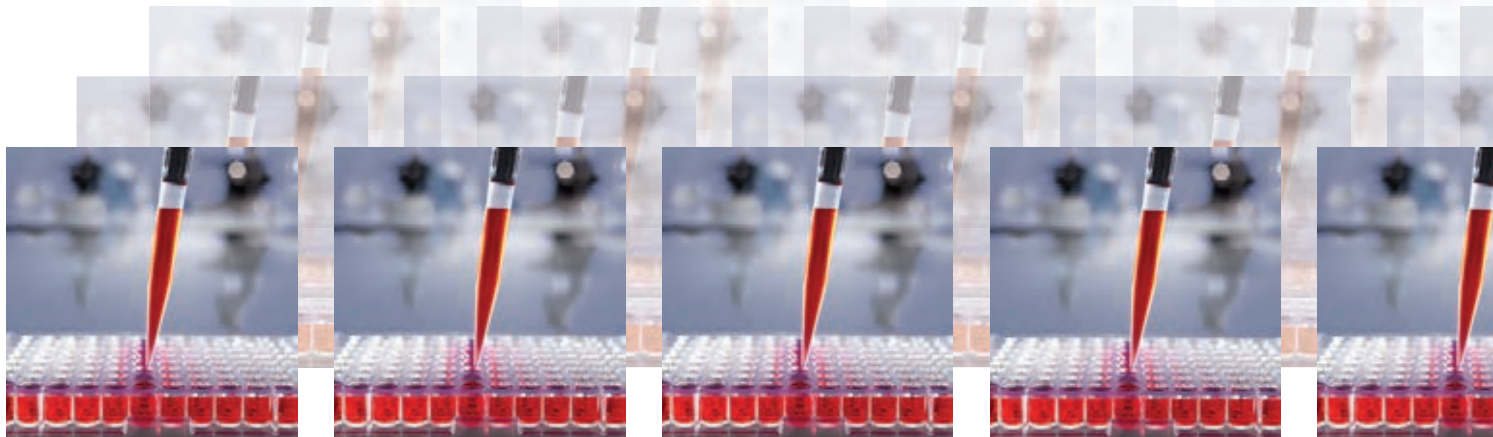
The next brick of validation is interpretation, and this one “is the toughest of all,” says Ioannidis. “Even when everything has been repeatable, reproducible and replicable, there is some room for differences in opinion.” Ioannidis says that, while he believes in the freedom of researchers to interpret data as they see fit, some standards need to be set in how to interpret data for different fields.

The final brick is asking whether the newly discovered information helps us. “Even if you know what a variant means, and even if it is one you can act on, does acting on it actually improve public health?” asks Adam Felsenfeld at the National Human Genome Research Institute. “It is a huge issue that has to be tackled not just by the clinical community but by health-care economists” and others. He gives the example of the prostate cancer screening test, whose true clinical utility in reducing the burden of disease has been debated. He says that kind of consideration for clinical utility should be built into -omics research as early as possible.

NO ONE-SIZE-FITS-ALL SOLUTION

In discussing validation, it’s important to appreciate that the different -omics fields can’t be lumped together. The information gleaned from these fields “encompasses so many different kinds of data. Each one of them has its own technical challenges with respect to validation,” says Ralph Bradshaw at the University of California at San Francisco and co-editor of *Molecular & Cellular Proteomics* with Alma Burlingame at the same institution. (MCP is published by the American Society for Biochemistry and Molecular Biology.) “If you really want to talk about validation, you have to start piecemeal,” he says, taking each field on its own with its quirks and challenges.

Ioannidis agrees that validation has to be tailored according to the needs of each particular field and the types of measurements available. Just take proteomics. It may have the mission to use large sets of



proteins to understand various biological phenomena, but the data come in a variety of forms, ranging from mass spectrometric methods to difference gel electrophoresis. Validation issues for various techniques have to be dealt with in different ways.

As Bradshaw points out, “Validation carries with it the connotation of replication.” He explains that for some -omics fields, such as genomic sequencing, “the replication of the data, both from the terms of technical and biological, is in fact really quite exact.” However, for shotgun proteomics, which identifies by mass spectrometry a large number of proteins from a sample containing millions, “the reproducibility of an experiment, even in the same laboratory on the same sample, is only partial,” says Bradshaw. “You can’t talk about validation [in that case] because of the nature of large-scale mass spectrometry experiments.”

Gilbert Omenn at the University of Michigan, the chairman of the IOM committee on -omics data validation, agrees with Bradshaw. “It’s extremely important to recognize you may not get the same result if you repeat the experiment in the same lab with the same hands with the same samples, because there is a certain stochastic aspect to detection of peptides in mass spectrometry,” he says. But he adds it simply means that there is an even greater need for replication with these types of experiments. While there isn’t a one-size-fits-all procedure for ensuring accuracy of -omics data, Omenn says that no matter the experimental platform, the principles of validation cut across all -omics fields.

WHO’S RESPONSIBLE?

Given the magnitude of -omics studies, the responsibility for ensuring that data are valid involves everyone, says Omenn. He doesn’t let anyone off the hook: Students, postdoctoral fellows, principal investigators, departmental heads, institutional review boards, journal editors and funding agencies

all have to take their roles seriously to ensure that data are sound.

But in discussing responsibilities, points of contention arise. To validate data, researchers need access to data collected by others. What kinds of data should researchers make available to others? It is important to note, says Robert Chalkley at UCSF, that not every researcher likes the idea of releasing his or her data. It’s not just the risk of scrutiny that alarms these researchers but the worry that someone else may discover something novel in the data that they missed, which can easily happen with -omics research because the data sets are so large.

But even if researchers see the need for releasing the data, what should they release? It shouldn’t be just raw data, argues Baggerly. He says researchers also should release the algorithms and codes of bioinformatics tools as well as the metadata, the types of information that denote which samples belonged to which groups and how researchers selected those samples. Baggerly explains that with -omics information, “The data are subject to several different types of pre-processing. . . . In many of these pre-processing steps, any one of several different algorithms could be employed. There is not yet a consensus as to which one is best.” Because there isn’t a consensus, Baggerly argues researchers have to be explicit in stating which ones they used.

Then comes the big question: Who should bear the responsibility of collecting, housing and making accessible all that data? In Baggerly’s view, journals should house the bioinformatics scripts through which researchers ran their data sets for a given publication, because those codes don’t take up much server room. But what about raw -omics data files, which can be gigabytes, even going onto terabytes, in size?

RAW DATA ACCESS

Access to raw data is a thorny subject. One way to illustrate why is to look at proteomics. “Over the years, [raw] data have never left the laboratory in which they were collected,” explains Bradshaw. “It has been clearly the opinion of a lot of people in the proteomics field, and certainly the opinion of the editors of MCP, that these data need to be put somewhere where they can be interrogated by others.”

The first cautionary tale in being too hasty with -omics technologies harks back 10 years. Scientists from the U.S. Food and Drug Administration, National Cancer Institute and bioinformatics company Correlologic Systems published a paper that described proteomic patterns in patients’ serum that seemingly indicated ovarian cancer even at early stages (1). Correlologic Systems licensed the technology to Quest Diagnostics and the Laboratory Corporation of America to develop a diagnostic test called OvaCheck.

But other scientists set off alarm bells, questioning the analytical validity of the study (2, 3). When Baggerly’s team analyzed the data from one of the sets in the paper, Baggerly says by “using electronic noise, we could separate cancers from controls. We should never be able to do that. The fact that we could was evidence they screwed up the [experimental] design.” The FDA, on hearing the reports, eventually stepped in and insisted on further validation before OvaCheck was commercialized.

The other cautionary tale involves outright fraud. In 2007 and 2008, Duke University launched three clinical trials based on research led by Joseph Nevins and Anil Potti that used microarrays to develop personalized treatments for breast and lung cancer patients based on genomic signatures (4). Baggerly once again was involved, along with his collaborator Kevin Coombes, in pointing out various mistakes in the data interpretation (5; to watch a lecture by Baggerly on this topic, go to http://videlectures.net/keith_baggerly/). But it soon appeared that Potti had lied about his qualifications on his curriculum vita and the data from his experiments were riddled with errors. In 2010, Duke University halted the clinical trials. So far, nine of the Nevin and Potti publications, including reference 4, have been retracted (6). CBS’s “60 Minutes” aired a segment on the Duke case on Feb. 12 (www.cbsnews.com/8301-18560_162-57376073/deception-at-duke/). ☹☹☹

REFERENCES

1. Petricoin, E.F. et al. *Lancet* **359**, 572 – 577 (2002).
2. Sorace, J.M. & Zhan, M. *BMC Bioinformatics* **4**, 24 (2003).
3. Baggerly, K.A. et al. *Bioinformatics* **20**, 777 – 785 (2004).
4. Potti, A. et al. *Nature Medicine* **12**, 1294 – 1300 (2006).
5. Baggerly, K.A. & Coombes, K. R. *Ann Appl Stat* **3**, 1309 – 1334 (2009).
6. <http://dukechronicle.com/article/ninth-potti-paper-date-gets-retracted>.

Websites like PRIDE collect processed proteomics data. But processed data, as Baggerly and Bradshaw are keen to emphasize, are not the same as the raw data spat out by analytical instruments.

So in 2010, MCP made it mandatory for its authors to deposit their raw data files in a repository designed specifically for the purpose. One example of a raw data repository is TRANCHE (<https://proteome-commons.org/tranche/>), operated by the laboratory of Philip C. Andrews at the University of Michigan.

“For some time, TRANCHE was basically the only show in town,” says Bradshaw. “The problem was that TRANCHE’s funding line eventually was dependent on a [federal] grant, which ultimately was not renewed.”

Over the past year, TRANCHE has struggled, because it hasn’t had funding to hire software engineers who are needed to maintain it. Because of TRANCHE’s technical and financial problems, MCP had to put a moratorium on its requirement for depositing raw data.

The lack of federal support for publicly accessible repositories for raw data has researchers vexed. TRANCHE isn’t the only example; Omenn, Baggerly and others also point to the Sequence Read Archive, a repository for next-generation sequencing data, which had its funding cut off by the National Center for Biotechnology Information at the National Institutes of Health last year because of budget constraints (2).

“Funding agencies wish to fund the initial discoveries,” says Evans. For research projects that aim to benefit patients, just producing those first discoveries doesn’t cut it. “You have to spend some time and money ensuring that validation can be done,” he explains. “It isn’t as sexy as funding discovery, but I think funding agencies do have a responsibility to encourage and enable validation. Otherwise, we’re never going to really know which of these discoveries will pan out.”



And unlike funding discovery-driven research, points out Aebersold, it's not going to cost federal agencies millions of dollars to build and maintain repositories for raw data. Creating infrastructure for data deposition is "not cheap but it's also not astronomical," he says. "It's certainly a serious effort, but it's not something that would bankrupt the NIH."

A great example that benefitted from public access to data is the Human Genome Project. The organizers of the federally funded project "demanded that data be uploaded, even at a time when the data were riddled with errors," says Omenn. "It helped clean up the data, because people weren't hiding it in their own computers!" Because other researchers were able to examine, test and validate the data, genomics has been able to move forward onto whole-genome sequencing, genomewide association studies and other endeavors.

When asked to respond to these views of academic researchers, Lawrence Tabak, a co-chair of the NIH Data and Informatics Task Force and the Advisory Committee to the Director, NIH Data and Informatics Working Group, provided a statement. "Data sharing is critically important to the advancement of biomedical research, and NIH is committed to supporting the collection, storage and sharing of biomedical research data. The astonishing increase in the amount of data being generated through NIH-funded research is an indicator of the extraordinary productivity of the research enterprise," he said. "Yet with this astonishing increase, the agency is facing significant data management challenges. Given how extremely beneficial the availability of large datasets is to advancing medical discoveries, ensuring its continued availability is a high priority for NIH."

Tabak, who is also the NIH principal deputy director, went on to say that the NIH director has formed an internal working group as well as a working group

to the Advisory Committee to the Director to help inform NIH policy on data management. The committee is expected to make its recommendations in June of this year.

But Bradshaw cautions that having access to the raw data won't be the entire solution to validation. Raw data access is "not a panacea, but it will make it easier to go in and look at what different people collected under different conditions," says Bradshaw.

MOVING AHEAD

Experts in this story all cited the volume of -omics data as a cause of concern for validation. But Matthias Mann of the Max Planck Institute of Biochemistry in Germany is hopeful that the data volume issue will someday be more manageable. Right now, the data volume is an indication of the complexity of biology, but some of the complexity of biology comes from interconnections between different molecular pathways, cells, tissues and organs. "I think we will see in the future that many of the biological changes are not independent of each other but they go together," he says. "That means the dimensionality of what we are measuring is actually lower... That inherently reduces the complexity." But he cautions, "Until we know more and have mapped it all out, we will be swimming" in data.

The boundaries of biomedical science can't be pushed forward without proper validation steps, which have to be integrated in all stages, from fundamental research to clinical trials and population studies, say Ioannidis and Khoury. Aebersold points out that researchers suffer from lost money, resources and time if they chase mirages in data. And the repercussions of improper validation are magnified if research has medical applications. As Evans puts it, "You get validation wrong, and people will literally suffer." ❧❧❧

Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the senior science writer for ASBMB Today and the technical editor for the Journal of Biological Chemistry.



REFERENCES

1. Ioannidis, J.P.A. & Khoury, M.J. *Science* **334**, 1230 – 1232 (2011).
2. www.nlm.nih.gov/pubs/techbull/jf11/jf11_ncbi_reprint_sra.html.



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SUNDAY, APRIL 22, AND MONDAY, APRIL 23 • 7 – 8 A.M.

CONVENTION CENTER, ROOM 11A, UPPER LEVEL

Join Kim Orth on Sunday and Bettie Sue Masters on Monday for breakfast to discuss science and scientific careers. The event is free but open to undergraduates only. Preregister at www.asbmb.org/breakfast.

Workshop on LIPID MAPS Lipidomics Tools

SUNDAY, APRIL 22 • 12:30 – 2 P.M.

CONVENTION CENTER, 11A, UPPER LEVEL

Lunch provided for first 35 attendees. This workshop should be of interest to lipidomics researchers and bioinformaticists. It will highlight the diversity and unique structural and biochemical challenges of the lipidome and will provide users with a suite of convenient online tools for the purpose of information retrieval and lipidomic data analysis.

Teaching Session with Stuart Kornfeld:

Modeling the Molecular Machinery of the Protein Trafficking Pathway

SUNDAY, APRIL 22 • 1:30 – 2:30 P.M.

CONVENTION CENTER, 6B, UPPER LEVEL

This informal session will provide students and postdocs the opportunity to meet and visit with Kornfeld and other researchers who have contributed to the field of protein trafficking. Physical models of key proteins involved in protein trafficking pathways will be available—and will frame these conversations about the recent discovery of essential features of the trafficking pathway.

ASBMB Welcome and Networking Reception

Sponsored by the ASBMB Minority Affairs Committee

SUNDAY, APRIL 22 • 6:30 – 8:30 P.M.

MARRIOTT MARQUIS HOTEL, MARINA BALLROOM D, SOUTH TOWER

The ASBMB Minority Affairs Committee welcomes primary investigators, industry professionals, educators, young scientists and students to enjoy this networking and mentoring reception featuring research posters by the 2012 Graduate Minority Travel Award recipients.

Effectively Communicating Your Science

Sponsored by the ASBMB Public Affairs Advisory Committee

MONDAY, APRIL 23 • 12:30 – 2 P.M.

CONVENTION CENTER, 6B, UPPER LEVEL

It has never been more important to communicate science and its value to the public. How can we make scientific discovery a high national priority? What can each of us do to make a difference? This panel features Nobel laureate Paul Berg, National Public Radio science correspondent Joe Palca, Deputy Director of Practices, Synthetic Biology Engineering Research Center (SynBERC), Megan J. Palmer, Huffington Post senior science correspondent Cara Santa Maria, and moderator and ASBMB President-elect Jeremy Berg.

Lipid Droplets:

Basic Working Principles

MONDAY, APRIL 23 • 12:30 – 2 P.M.

CONVENTION CENTER, 11A, UPPER LEVEL

Our partner for this workshop is Avanti Polar Lipids.

Lipid droplets, organelles found in cells of vertebrates, invertebrates and plants, have received much attention of late because of their importance in lipid-based diseases, in host–pathogen interactions and in the production of biofuels. This workshop will focus on the working principles and methodologies of lipid droplet research.



Events

ASBMB Scientific Fermentation Hour

MONDAY, APRIL 23 • 6 – 7 P.M.
CONVENTION CENTER,
WEST TERRACE (BAYSIDE), UPPER LEVEL

Relax at this casual post-session happy hour and continue the scientific discussion, meet the speakers and network with others in your field.

ASBMB Poetry Contest Reading

MONDAY, APRIL 23 • 7 – 7:30 P.M.
CONVENTION CENTER, 6A LOBBY AREA, UPPER LEVEL

Join us in support of our prize-winning poets and the runners-up, who will read their science-themed verses for all to enjoy.

Brewing Science, ASBMB Tweet & Meet

MONDAY, APRIL 23 • 7:30 – 9:30 P.M.
MISSION BREWERY, 1441 L. ST.

Looking to learn how to share your science in an Internet 2.0 world? Need practice communicating your science to lay audiences? Just like beer? Then join us for Brewing Science, an informal tweet-and-meet blend of scientists, communicators and concerned constituents.

Work-Life Balance and Time Management:

A Professional Development Workshop for Students, Postdocs and Junior Faculty

TUESDAY, APRIL 24 • 12:30 – 1:30 P.M.
CONVENTION CENTER, 11A, UPPER LEVEL

* Advance registration and fee required.

Suzanne Pfeffer, ASBMB's president, will engage participants in a discussion to address work-life balance and the practice of successful time management to achieve and sustain personal and professional satisfaction.

ASBMB Women Scientists Networking Event

TUESDAY, APRIL 24 • 6 – 8 P.M.
CONVENTION CENTER, 11A, UPPER LEVEL

Join fellow women biochemists and molecular biologists for a topical discussion of how women scientists can better support each other. Featured presenters: Ellen Daniell, author of "Every Other Thursday: Stories and Strategies from Successful Women Scientists," and Christine Guthrie, ASBMB-Merck Award lecturer.

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Science in stanzas

Congratulations to the prize winners and runners-up in the ASBMB Today poetry contest coinciding with the society's annual meeting and the Experimental Biology 2012 conference to be held April 21–25 in San Diego. We look forward to showcasing the top poems at a public reading at 7 p.m. April 23 in the convention center 6A lobby on the upper level.

FIRST PLACE

Lost in Translation

Andrew Brown, The University of New South Wales

The patient is resting and Hope attends
as a silent witness at her vigil.
Both can but wait. *Patiently.*
Her raw red eyes will
the bands to separate.
Her labcoat weighs heavy
on shoulders hunched over the apparatus.
Her gloved hands ache from pipetting.
Not long now.

Soon she will be in the darkroom
fixated on the developer
waiting two dry-mouthed minutes.

Soon the Moment of Truth
(*or at least something approaching it*)

Will the results herald a Miracle Cure? A Medical Breakthrough?
Snag her a slot on the Sunday news?

But she's dreaming
not of the lucre, the Lasker, Cell and celebrity.

She dreams only of...

Amongst the twinkling snoring machines
Her eyelids droop her head drifts down
And there is Hope that she won't drool

As she dreams (*from bench to bedside*)

only of Sleep.

SECOND PLACE

Angiogenesis

Cheryl Ainslie-Waldman,
University of Minnesota

A hiccup of the cells
mantelpiece clock that needs no winding
perfused by gears and cogs and wires
that drive their stake into the earth.

A tumor formed from two
and borne by one.

Alien at first
an invader welcomed with snakelike tendrils
curling up and in and around
to deliver maternal blood.

The DNA aligns itself
and reveals political intentions.

A being never to be seen or heard or touched
will kill by its love
and mistaken creation.

THIRD PLACE

Ode to the Lab

Jesus Manuel Ayala Figueroa, University of Puerto Rico at Humacao

O laboratory! How sublime is your splendor!
Microscopes, benches and gadgets garnish your space.
The smell of the agar, the color of your solutions—
Oh how magnificent this place is!
It is within these walls that I want my bed always to be.
The mere mention of your name evokes happiness,
For it is within these walls that great things occur.
Your inhabitants have sworn to advance humanity's greatness.
It is here that great minds concur.
Days, months or years; time matters not.
I can spend my life enjoying these blots.
O Morpheus, never wake me up from this dream!
Because here is where I want my bed always to be.
Rejoice if it's wrong, celebrate if it's right—
The thrill of experiment, the researcher and its might.
Ideas bend, change and collide.
My only desire is to have my bench to bedside.

HONORABLE MENTION

Song of Sanger

Gail S. Begley, Northeastern University

They fill my heart with joy,
These jagged peaks that cross my screen,
No mere Gs, Cs, As and Ts,
But mounts of blue, black, red, and green.
What mysteries will their sequence yield
About my very favorite gene?

HONORABLE MENTION

How... Understanding

Karen Hecht, University of Pittsburgh

How brightly do cells glow
In a dark field?
Winking back at the objective
What shapes do proteins take
In a CHARMMed sea?
Folding back that which was unknown
When do signals fire
In salty streams?
Shouting out all their potential
Where does a Drifter go
In fledgling flight?
Expressing what moves us forward
Why do these codes unfurl
In charged currents?
Spilling secrets to those who ask
Who devours these whispered words
With swelling thirst?
Living life through understanding

EDITOR'S CHOICE

Consistent with this, cell extracts from the *iba57* Δ strain showed virtually no aconitase activity (Fig. 2A).

Cristy Gelling, University of Pittsburgh

In a well-lit, windowless cupboard alone
with a chirping machine,
a bucket of melting ice
and a persistent smell,
I danced.

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Meeting Attendees

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Beauregard, a 13-year-old snow leopard, arrived at the San Diego Zoo over the winter to breed with the zoo's 8-year-old female snow leopard, Anna.

PHOTO: KEN BOHN, SAN DIEGO ZOO

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Heather Doran, a Ph.D student in medical sciences at the University of Aberdeen, will be the society's official EB2012 meeting blogger. She is a passionate science communicator, writer and editor for Au Science Magazine. Keep an eye on her blog at <http://ausm.org.uk> or follow her on Twitter at www.twitter.com/hapsoci.



Tribute to midlevel scientists

Let's acknowledge and reward the burgeoning class of highly skilled, underpaid and highly stressed workhorses in our nation's research laboratories

BY LYNN ZECHIEDRICH

They are not often the first or last authors on publications. They are not usually the ones traveling to meetings to present their work. They do not often get to interact with the public or the press. Their jobs are tenuous, and their titles rarely reflect their talent, intellect or hard work. In the U.S., they are known variously as instructors, nontenure-track faculty, postdoctoral fellows, research faculty, senior technicians or staff scientists.

They were always a part of laboratory groups, but as the economy has stumbled and the job market has tightened, fewer postdoctoral fellows have landed the previously typical positions befitting their training. As a consequence, increasing numbers of highly skilled workers have become stuck in their training laboratories. The reasons people get stuck often include life events that can strike anyone at any time: illness, divorce, natural disaster, or long-term or challenging projects that failed to yield sufficient numbers of publications.

Sometimes it's a matter of choice. Trainees observe the stress on the boss, particularly the lack of time, and they choose not to progress to that next step — not if that step means less time with family and loved ones, neglecting outside interests that are meaningful to them or giving up a long-term project with potential high impact.

In my group, Jamie Catanese chose to stay. He wants nothing to do with my “crazy hours, stress or constant grant-writing.” Now a senior staff scientist, Jamie trains graduate students and postdoctoral fellows while carrying out several of his own long-term research projects. One of these projects, new potential therapies for lung cancer, is personal for Jamie: His mother died from the disease.

While jobs have become harder to find, the demand on the people in those jobs has increased. Unable to

offer him a raise last year because of a wage freeze, I asked Jamie what I could do to let him know how much I appreciate him. I expected to hear something like “an office,” “a closer parking spot” or “a better title.” His reply illustrates why he, and those like him, are so valuable to research laboratories and institutions: “I would like to give a lecture in one of your classes. I love teaching.”

Although they were not likely hired purposefully to occupy this niche, without people like Jamie in the middle ranks, less work would be done, fewer grants would be written, trainees would be less well trained and more

laboratories would be closing. The middle ranks bring their knowledge and expertise. They bridge the gaps between the more transient laboratory members and the boss, and they bring the freedom to work on long-term goals, those that might not lead to immediate or as frequent publication but that eventually might have greater impact.

Especially in today's find-the-next-superstar job searches that tend to select those few people who have not yet been struck by normal life events, a lot of great talent is accumulating in the middle ranks of institutions. Both those who have become stuck and those who have purposefully chosen not to move on bring much good to our nation's laboratories and institutions.

Why not consider today what these scientists bring to your group, department or institution and then ask them what you can do to help make them feel valued? Being aware of the advantages and rewarding their dedication and skill just makes sense. ∞∞∞



Jamie Catanese



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Are we doing a good job of teaching the groundbreaking research of our predecessors?

BY DENNIS VANCE

Some time ago, I was presenting a lecture on cholesterol biosynthesis in an advanced course on lipid and lipoprotein biochemistry. I mentioned that Konrad Bloch did key research from the 1940s to the 1970s. "Have any of you ever heard of Konrad Bloch?" I asked. I was rather surprised that the students did not know about Bloch or his contributions.

Of course, it is possible that Bloch's fundamental contributions were taught and the students simply forgot. Alternatively, they may never have been taught about his important discoveries. In either case, this is very unfortunate. In my view, as teachers of biochemistry, we are not instructing our students properly.

Some will argue that there is already too much to cover when we teach biochemistry and we don't have time to provide a historical perspective. I don't buy this argument. We need to bring lipid biochemistry to life for our students. The students should appreciate the key scientists who laid the foundations for the current developments in the subject. It is also instructive to describe some of the experiments these scientists did. Bloch conducted very elegant experiments using heavy isotopes and radioisotopes to delineate the pathways of cholesterol biosynthesis. If one or two of these experiments were described, it would help the students understand how tracers are used in biochemistry.

In the last millennium, I contributed the lipid chapters to the textbook "Biochemistry" edited by Geoffrey Zubay. We made an effort to present a historical perspective. A unique feature of the textbook was a com-



To read the *Journal of Biological Chemistry* Classic article "The Biosynthetic Pathway for Cholesterol" about Konrad Bloch, visit <http://bit.ly/ys2FKN>.

panion paperback collection of key papers in biochemistry. Thus, it was easy for students to read and digest the experiments that led to key findings. In 2012, such a collection of papers is not necessary. All we need to do is provide the references, and students will be able to access most of these papers on the Internet. Most students probably will not bother to review these original papers. However, shouldn't we provide guidance to those students who do care?

While we need to teach the basic language of lipid research (i.e., structures, pathways, enzymes, genes, regulation), one of our major objectives should be to convey to the

students the sense of discovery and awe in lipid biochemistry and expose students to how we know what we know. We need to reiterate the scientific method for testing hypotheses. It seems to me the best way to start the teaching process is to introduce the stars of the past. Who were these scientists? What questions did they ask? How did they obtain the answers?

If this teaching approach were introduced, we might be pleasantly surprised the next time we asked students, "Who was Konrad Bloch and what did he do?" ∞∞∞



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jbc THE JOURNAL OF BIOLOGICAL CHEMISTRY

Worm protein provides insight into aging and neurodegeneration

BY RAJENDRANI MUKHOPADHYAY

Humans carry an RNA-processing protein called the transactive response DNA-binding protein, or TARDBP/TDP-43. The protein has been linked to a number of neurodegenerative disorders that involve protein misfolding, such as amyotrophic lateral sclerosis and frontotemporal lobar

degeneration. In a recent “Paper of the Week” published in the Journal of Biological Chemistry, Jiou Wang at The Johns Hopkins University and colleagues described a *Caenorhabditis elegans* model in which they removed the worm version of the TDP-43 protein, called TDP-1 (1).

Why the worm? “Although mammals such as mice offer important models for human diseases,

sometimes the complexity of the mammalian systems prevent the unraveling of basic functions of a molecule,” explains Wang. “For example, the TDP-43 knockout mice die in early embryogenesis, making it difficult to tease out the physiological functions of the protein.”

Wang’s team showed that the worm and human versions of the RNA-processing protein were very similar. Worms missing TDP-1 suffered from problems with fertility, growth and movement, but, intriguingly, they lived longer. The mutant worms were also more resilient against the toxic effects of misfolded proteins. The investigators concluded that TDP-1 regulates protein homeostasis and aging through RNA processing.

Because protein homeostasis and aging are common themes in many age-dependent neurodegenerative diseases, “we are hopeful that interventions that improve protein homeostasis or delay aging might eventually turn

out to be effective strategies to treat these devastating conditions,” says Wang. But, he cautions, first “we need to learn more about normal functions of TDP-43.” ☺☺☺

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REFERENCE

1. Zhang, Tao et al. *J. Biol. Chem.* **11**, 8371 – 8382 (2012).



JLR THE JOURNAL OF LIPID RESEARCH

From the inside out

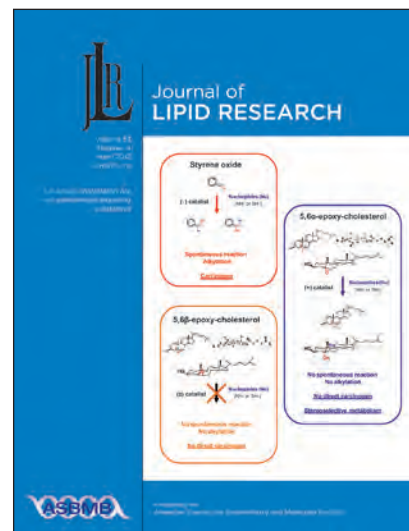
New study gives clues on how the only FDA-approved drug to treat primary biliary cirrhosis works in the liver

BY MARY L. CHANG

A small amount of ursodeoxycholic acid, also known as UDCA or ursodiol, has been a component in Chinese traditional medicine treatment for liver disorders for centuries. In the Western world, UDCA is the only approved drug to treat primary biliary cirrhosis, an autoimmune disorder characterized by progressive damage to the bile ducts within the liver, causing a buildup of cholesterol in the liver and subsequent liver damage.

Without treatment, most patients with this condition will need a liver transplant later in life, and a quarter of patients who have had the condition for more than 10 years will suffer liver failure. UDCA also has been shown to prevent the progression of colorectal cancer and the recurrence of colonic dysplasia, the development of precancerous, abnormal cells in the colon. But the mechanism by which UDCA counteracts these liver problems hasn’t been completely elucidated.

In their paper entitled “Ursodeoxycholic acid binds



ileal bile acid binding protein” to be published in the April issue of the Journal of Lipid Research, Changming Fang and colleagues at the Cancer Research Center at the Sanford-Burnham Medical Research Institute in La Jolla, Calif., set out to determine if ileal bile acid binding protein, or IBABP, a cytosolic protein believed to be involved in the absorption of bile acids associated with the processing of dietary fat, is involved with UCDA’s activity in the human body (1).

Major human bile acids bind to two sites on IBABP and act in a cooperative manner in healthy individuals. In contrast, they found by tryptophan fluorescence spectroscopy that UCDA only binds to a single site. Further, when IBABP was saturated with UDCA, the affinity of IBABP for major human bile acids increased two- to five-fold, and UDCA was shown to bind cooperatively with a major human bile acid bound to the other binding site just as two bile acids normally do while sitting in these binding sites.

IBABP also associates with farnesoid X receptor alpha, or FXR α , and had been assumed as a mediator of this receptor’s activity. While it is still not clear how this mediation occurs, Caco-2 cell culture results from this study indicate IBABP is involved in UDCA’s effect to increase the activation of this receptor. Further research is needed to determine IBABP’s precise mechanism of action.

This article highlights the importance of considering IBABP’s activity and role in UDCA’s potential benefits in patients with liver damage. UDCA increases the binding of major human bile acids; this decreases the number of free bile acids in cytosol, reducing stress on the gastrointestinal system and preventing bile acid-induced mutations and the development of bile acid resistance seen in colorectal cancer. The authors suggest that, based on their observations, when FXR α ’s activation is enhanced in the presence of UDCA bound to IBABP, more major human bile acids are released from cells called ileocytes, which are otherwise held back in liver disease and can cause cirrhosis. XXX

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REFERENCES

1. Fang, C. et al. *J. Lipid Research*. doi: 10.1194/jlr.M021733 (2012).

MCP MOLECULAR & CELLULAR PROTEOMICS

Serum antibodies as biomarkers

BY RAJENDRANI MUKHOPADHYAY

The scientific literature contains more than 100,000 reports of biomarkers, but only 43 have been approved by the U.S. Food and Drug Administration for clinical diagnostics (1). A problem is that most biomarkers are so dilute in blood that detecting them becomes a needle-in-haystack issue. Phillip Stafford and colleagues at Arizona State University and the University of Arizona have instead been pursuing antibodies as disease indicators, an idea first proposed by Abner Notkins of the National Institutes of Health (2).

Antibodies are abundant and stable in serum and easily detected. Stafford says his group had discovered that with antibodies they could predict a number of infectious, chronic and autoimmune diseases. “We could even predict transplant rejection,” says Stafford. “I’ve no idea why this [notion] didn’t catch on earlier.”

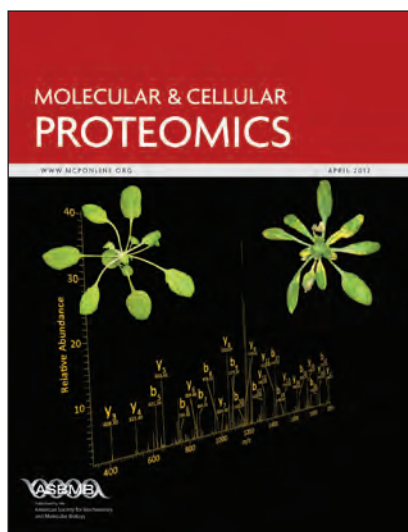
Because antibodies readily cross-react with random peptide sequences, Stafford and colleagues demonstrated in a recent Molecular & Cellular Proteomics article that microarrays with 10,000 random peptides served as an effective and simple way to capture antibodies from serum to reveal a patient’s health history (3). For instance, they found antibodies against a newly developed disease or a recent vaccination dominated over antibodies from an older disease.

“I hope people start to use this technology, because it holds enormous promise for diagnostics,” says Stafford. The group is now working on making microarrays with tens of millions of peptides because “the more peptides you can examine, the better you can dissect a disease, and you gain a measure of sensitivity as well,” explains Stafford. He adds, “We’re also working on field units so you can take this technology on-site for rapid diagnosis or biothreat detection.” XXX

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REFERENCES

1. U.S. Food and Drug Administration. www.fda.gov/Drugs/ScienceResearch/ResearchAreas/Pharmacogenetics/ucm083378.htm.
2. Notkins, A. L. “New Predictors of Disease.” *Scientific American*, March 2007.
3. Stafford, P. et al. *Mol. Cell. Proteomics*. doi: 10.1074/mcp.M111.011593 (2012).



Navigating the NIH grant-application process

BY SONIA C. FLORES

If your career goal is to perform biomedical research, then you should read this article. Here, I'll try to help you navigate the grant application and review process and hopefully guide you to a successful submission. I will address only applications to the National Institutes of Health, because, frankly, this is what I know. There are many more funding agencies, but the NIH is where the bulk of the money is.

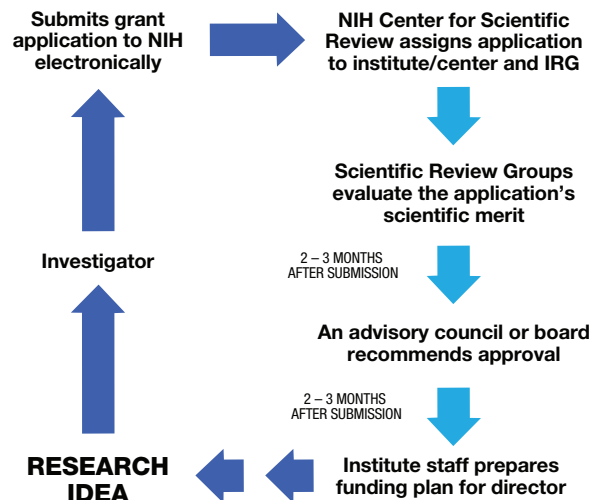
The NIH has a complex organizational structure (www.nih.gov/icd) made up of institutes or divisions with their own research interests. When the application is submitted, it is first reviewed by the Center for Scientific Review; based on the content of the abstract, a program officer at the CSR assigns the grant to an Integrated Review Group (a study section) and an institute or center. If you want your application to be assigned to a specific institute or study section, make sure the first or last sentences of the abstract have keywords aligned with those research interests. There may be some overlap between study sections, and you are allowed to request a study section in the cover letter.

About two to three months after submission, the Scientific Review Groups evaluate the scientific merit of the grant. After another two to three months, an advisory council or board recommends the grant for approval. After approval, the institute staff prepares a funding plan for the director, the institute allocates the funds and the grantee begins conducting his or her research. (See figure.)

Writing a cover letter to request a study section

Your cover letter should include the following: application title, institute request (it's best to choose three, but you need to prioritize), IRG request (get advice from your program officer on this), and any other special requests. Information on institute requests can be found at www.nih.gov/icd and on study sections at www.csr.nih.gov/Roster_proto/sectionl.asp.

Having your application assigned to the right study section ensures that the appropriate people review your application. The NIH generally honors requests for study sections. It is important to frame your request in positive terms. Mentioning that a study section has several people



interested in your area and qualified to judge your work is essential. While gathering the information to make an informed request takes work, many investigators feel it's worth it. Research the interests of each study section to see where your application would fit best, and look at review rosters to see who is on the committees. Remember that it is not easy to tell who will review the application, because many applications are now reviewed by fluid ad-hoc, special-emphasis panels.

Meeting deadlines

The NIH has three grant cycles that may vary depending on the type of grant. It is important to observe the deadlines. If your grant is submitted after the deadline, it may not be reviewed until the next review cycle. Find grant deadline information at www.nih.gov/grants/funding/submissionschedule.htm.

Strategies for planning a grant

Write an outstanding application that will appeal to reviewers, who serve as judge and jury. Write from the perspective of a screenwriter and not from the perspective of a novelist. A grant is presented to a panel of peer reviewers by one primary person and two helpers, so you want to write a script that will facilitate presentation of your proposal to the rest of the panel.

There are eight main steps to follow when planning your grant.

1. Check out the competition and see which projects in your field are being funded. Search the NIH RePORTER database at <http://projectreporter.nih.gov/reporter.cfm>.
2. Evaluate yourself: How do your strengths match the topics found in step 1? Can you capitalize on your expertise and fill in gaps with mentors, collaborators or consultants? Do you have a niche? If not, find one!
3. Determine available resources and support from your school.
4. Brainstorm with colleagues and mentors, and have knowledge of the relevant literature!
5. Write a hypothesis for your proposal in 25 words or fewer; edit, edit and then edit again.
6. Give yourself time to write and rewrite the application.
7. Utilize any form of pre-peer review that you can find (e.g., a mock study section, a class).
8. Follow all instructions to the letter: Poor formatting, illegible figures, wrong fonts and poor grantsmanship will turn reviewers off!

Writing a solid hypothesis

Most top-notch grant applications are driven by strong hypotheses rather than advances in technology. Applications should ask questions that prove or disprove a hypothesis rather than use a method to search for a problem or simply collect information. If your application is not hypothesis-based, state that it isn't and give your reasons why the work is important (e.g., X-ray crystallography, or perhaps it's a training grant). Choose an important, testable, focused hypothesis that increases understanding of biological processes, diseases, treatments or preventions. A strong hypothesis should be based on previous research. Reiterate your hypothesis throughout the grant using different wording.

Planning your application

Ask yourself these questions: Why is this project important? Why are you the right person to conduct this research?

Required sections of a grant are "Specific Aims" (one page long) and "Research Strategy" (the new format has a 12-page maximum).

"Specific Aims" should include the following:

1. One to two paragraphs that develop the conceptual framework of the proposal. These should describe previous studies in the area, identify the gaps the research will address and end with a statement of your hypothesis or overall objective.
2. A set of aims designed to answer the questions posed by the hypothesis. The important word here is "specific"!

Each aim should be a specific test of the overall hypothesis. Organize and define your aims so that you can relate them directly to your research strategy.

The "Research Strategy" section includes the following:

1. Significance

- a. Explain the importance of the problem or critical barrier to progress in the field that the project will address.
- b. Explain how the project will improve scientific knowledge, technical capability and/or clinical practice in one or more broad fields.
- c. Describe how the concepts, methods, technologies, treatments, services or preventative interventions that drive this field will be changed if the aims are achieved.

2. Innovation

- a. Explain how the application challenges and seeks to shift research or clinical-practice paradigms.
- b. Describe novel theoretical concepts, approaches or methodologies, and instrumentation or intervention(s) to be developed or used and any advantage over existing methodologies, instrumentation or intervention(s).
- c. Explain refinements, improvements or new applications of theoretical concepts, approaches or methodologies, instrumentation, or interventions.

3. Approach

- a. Describe the overall strategy, methodology and analyses to be used to accomplish the specific aims. Provide evidence of feasibility — not a miniature version of the proposed study.
- b. Discuss potential problems, alternative strategies and benchmarks for success anticipated.

Crafting your biographical sketch

The bio sketch requires a personal statement that briefly describes why your experience and qualifications make you particularly well suited for your role in the project.

Having your application scored

The IRG will review your application and assign it a score from 1–9. A score of 1 is the highest, given to a grant considered exceptionally strong with essentially no weaknesses; 9 is considered poor, with very few strengths and numerous major weaknesses.

In summary, a great proposal is a solid, exciting idea that is well expressed with a clear indication of methods for pursuing the idea, evaluating the findings, making them known to all who need to know and — for the NIH — indicating the overall impact to the scientific community. ☺☺☺



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Indications of a bright future through science

BY MICHAEL J. BRADLEY

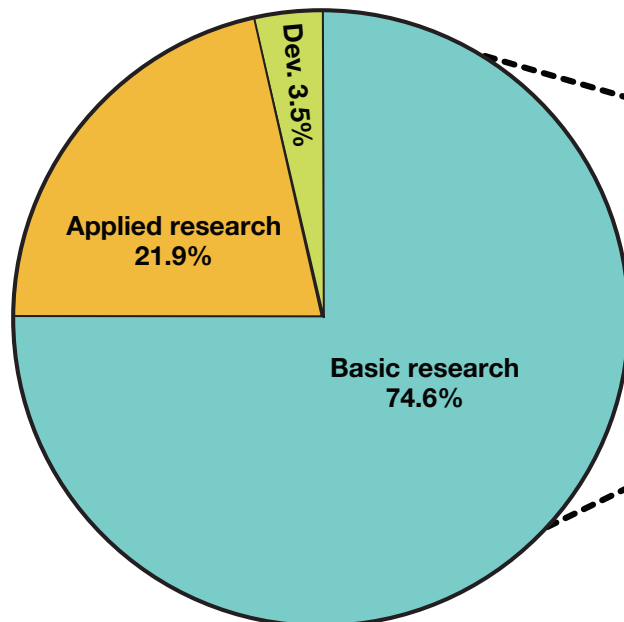
As scientists and science educators, we strongly value rational decision making based on reliable data. Both in and outside of academia, we depend on research and development and education funding from a variety of sources to conduct our work. As we perform research and teach science, we mentor and advise students at many levels of training and expertise on why and how to become a practicing scientist. One source of current and reliable data with which to reinforce both our funding justifications and our education and professional development advice is the biennial Science and Engineering Indicators from the National Science Board, the governing body of the National Science Foundation. The SEI are factual and governing policy-neutral. Here, I'll highlight a few points from the 2012 SEI that influence several aspects of my own scientific career development and the advice I give to aspiring scientists (1).

Scientific investment and the U.S. economy

In this election year, with tight budgets in both the U.S. government and private industry, how do we justify our investments in R&D? According to the 2012 SEI, the U.S. has spent about \$400 billion on R&D in each of the past few years, with industry contributing 62 percent, the federal government 31 percent, nonprofits 3 percent, colleges and universities 3 percent, and nonfederal governments 1 percent.

The most important justification for continuing and increasing these expenditures comes from considering that fields based in science, technology, engineering and mathematics, collectively referred to as "knowledge- and technology-intensive industries," or KTI, contributed about 40 percent of the \$14-trillion-plus U.S. GDP in each of the past few years (1). As today's KTI investments lead to tomorrow's breakthroughs, our nation's total annual R&D budget currently affords a 14:1 return on investment. That's comparable to the investment returns from building the U.S. interstate highway system (2). Today, our current R&D investments constitute 2.8 percent of U.S. GDP. To put this in perspective, several other countries, including the members of the European Union, have set goals of

Types of academic R&D expenditures, 2009



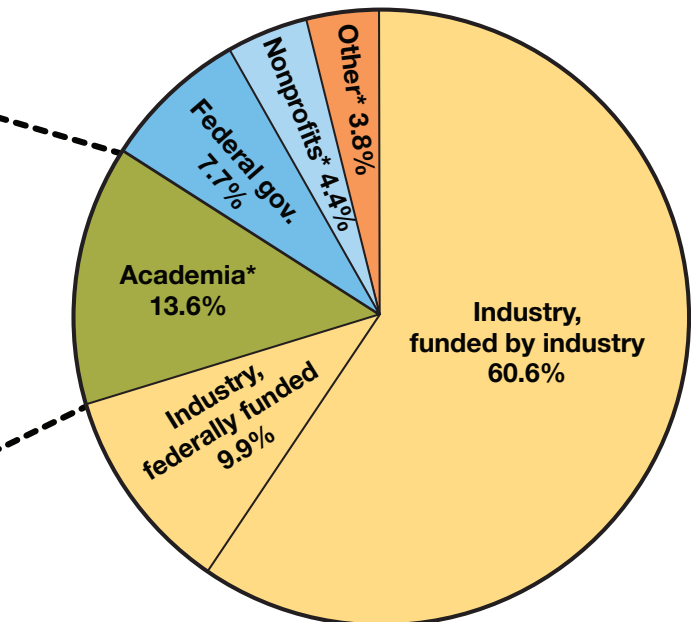
attaining and maintaining a level of R&D investment equal to 3 percent of GDP (1). As the U.S. competes globally for KTI market share and aims to attract, train and retain the best and brightest human capital, it is critical that our nation expand R&D expenditures at rates that will stay near or above 3 percent of GDP over the long term.

Educational investment on a personal level

In the early spring of my senior year in high school (14 years ago now), my parents and I visited several Midwest colleges to which I had been accepted. Given that my parents weren't in a financial position to put me through college, a difficult decision arose. I had a comparatively cheap option, thanks to scholarships, where the biochemistry professor assured my father that I would be a "big fish in a small pond." At a decidedly higher caliber but more expensive school, a biochemistry professor talked about the challenges and rigor of the program along with the high expectations of the faculty members and the superior capabilities and track records of typical students there. The clincher for my father was when he said, "Don't just consider the tuition costs over the next four years but also the opportunities that will help your son develop a satisfying and financially rewarding lifelong career."

I eventually chose both the more challenging school and a career in science, and I have remained very happy with

U.S. R&D expenditures, 2009 (% of \$400.5B)



both decisions, even with some lingering college debt. I've also recently written about weighing the costs and benefits of going to graduate school in the biosciences (3).

Scientific training: the human capital driving innovation

Well-trained human capital is vitally important for the sustained success of R&D initiatives in the U.S. Robust economic growth that outlasts financial-sector upheaval requires innovations that will be developed only if our highest-caliber students choose careers in R&D rather than financial derivative packaging and sales. The route to successful R&D careers includes undergraduate training with hands-on research experiences in STEM disciplines and possibly additional graduate school (1). Careers in R&D pay higher median salaries and historically exhibit lower unemployment rates than other jobs that require at least a bachelor's degree (1). Earning a STEM-discipline Ph.D. further increases the likelihood of landing and keeping R&D employment, along with even greater job security and a progressively higher wage distribution for many years after receiving the degree (1, 3). The majority of all STEM degree holders, including Ph.D.s, must ultimately develop careers outside of academia (1). Therefore it's critical to advise students and mentees to consider several career possibilities, conduct informational interviews,

* These sectors have significant federal funding to varying levels. In particular, the funding for R&D in academia breaks down as follows: 59.3 percent federal, 20.4 percent from within academia, 6.6 percent from state/local government, 5.8 percent from industry and 7.8 percent from other sources (private foundations, charities, etc.). SOURCE: SEI 2012

pursue internships and expand their nascent professional networks by all means possible. As China begins to train more STEM degree holders than the U.S., from bachelor's degrees to Ph.D.s (1), the U.S. must develop policies aimed at attracting and keeping large numbers of high-quality students on a scientific training and career path over the next decade (4).

Whether you're conversing with students, parents or U.S. senators, it's important to build and reinforce your advice and arguments with accurate data. Such information helps high school seniors make college choices, undergraduates select majors, graduates select areas of specialty and young scientists select career paths using rational logic. The 2012 SEI provides an excellent resource for understanding how STEM disciplines are impacting the U.S. economy and being shaped by fiscal and societal forces.

As many of us know, the initial stages of new discoveries are built upon the foundation of new knowledge attained through basic research. While industrial investment in basic research is an important component, for the past few decades federally funded academic investigators have conceived and conducted most of the basic research performed in the U.S (1). Although the majority of STEM undergraduates, graduate students and postdoctoral fellows ultimately will work outside of academia, during their training they have the opportunity to participate in formulating and solving the motivating questions that will increase our understanding of many important issues driving our economy and transforming our society. ∞∞∞



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REFERENCES

1. Science and Engineering Indicators 2012. www.nsf.gov/statistics/seind12/.
2. Surowiecki, J. *The New Yorker*. Published Feb. 14, 2011. Accessed March 11, 2012. www.newyorker.com/talk/financial/2011/02/14/110214ta_talk_surowiecki.
3. Bradley, M.J. *ASBMB Today*. (August 2011).
4. Drew, C. *The New York Times*. Published Nov. 4, 2011. Accessed March 11, 2012. www.nytimes.com/2011/11/06/education/edlife/why-science-majors-change-their-mind-its-just-so-darn-hard.html.

LETTER TO THE PRESIDENT

President's Message, March 2012

Dear Suzanne,

I read your recent President's Message titled "Branching careers in biochemistry" in *ASBMB Today* with great interest. The issue around professional and career development of biomedical trainees is one that is gaining more attention, and I enjoyed reading about the role the American Society for Biochemistry and Molecular Biology has taken. Sparked by your article, I thought you may be interested in hearing about additional opportunities for trainees occurring in the biomedical environment.

Here in Alberta, Canada, Alberta Innovates-Health Solutions, the provincial funding body for health research and innovation, also recognizes the importance of career and professional development for biomedical trainees along with the role mentorship plays in this process. AIHS strongly supports the training of highly skilled academic health researchers and also recognizes the need to provide opportunities to those considering nonacademic careers. As such, our newly designed Graduate Studentships now have a PLUS option associated with them, where the funded trainee can access up to one additional year of funding to gain valuable experience and additional skills beyond those acquired through their direct graduate research training. This may include internships in policy, government, industry or not-for-profit environments. It is designed to allow trainees to tailor the PLUS experience to their career goals. Also associated with all our Training and Early Career Development Opportunities is the requirement of a multifaceted mentorship advisory committee. This committee may be similar to or different from the trainee's supervisory committee and includes his or her primary research supervisor; a co-mentor to provide an alternate perspective from another discipline, research focus, sector or institution; and a career mentor to focus on the trainee's career development.

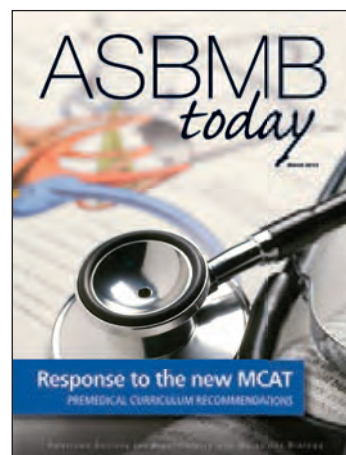
As an ASBMB member and scientist who has taken a nonacademic career path, I am pleased to see ASBMB recognizes that scientists contribute in a variety of meaningful ways beyond the walls of academe. We should support and reward biomedical trainees whether their career paths are academic or otherwise.

kindest Regards,
Ryan Perry

READER COMMENTS ONLINE

Response to the new MCAT, March 2012

We're pleased with the dialogue that our recommendations generated. There is broad agreement on teaching molecular genetics in the year of premedical biology. Indeed, arguments were made to exceed new MCAT standards in genetics and genomics. There also has been broad agreement that the MCAT core competencies in research methods and data analysis can be met by coursework in at least three different departments and that two semesters of biochemistry should be recommended. We are not surprised by the lively discussion of how to teach chemistry to premedical students and are pleased to learn about Jonathan Clayden's carbonyl-first "Organic Chemistry" textbook, I. David Reingold's organic-first approach at Juniata College, and Melanie M. Cooper and Michael W. Klymkowski's year of life-oriented chemistry at University of Colorado. These courses and others to be developed can provide the general chemical rigor demanded by our critics, effectively teaching chemical concepts with molecules found in living systems. —CHARLES BRENNER, UNIVERSITY OF IOWA, AND DAGMAR RINGE, BRANDEIS UNIVERSITY



This article has some good ideas, but item 2 is far too proscriptive to receive the general cooperation of chemists who are otherwise sympathetic to the recommendations. It does not even mention the Scientific Foundations for Future Physicians document produced by the Howard Hughes Medical Institute and (the) American Association of Medical Colleges. I and others are working with both the American Chemical Society Committee on Education and the HHMI Nexus Experiment Grant to address these concerns. In particular, the one-year chemistry part of recommendation, in my view, does not allow chemistry courses to adequately address the outcomes listed in the SFFP document. I could have endorsed this if recommendation 2 were revised to [read,] "The traditional sequence of general and organic chemistry should be revised to a course in life-oriented chemistry. There are a variety of ways in which this goal could be achieved." My views are my own and not intended to represent an official position of the ACS or HHMI. —MARC LOUDON, PURDUE UNIVERSITY

Of course, it is important to train students not just for the MCATs but also for medical college and beyond. The proposed curriculum change will be very helpful in providing a more uniform foundation of knowledge for incoming medical students. Teaching first-year medical students is very challenging when the class includes biochemistry majors alongside people who have not taken any biochemistry. I am concerned, though, that one year of chemistry is not sufficient, and I agree with Marc Loudon that the recommendation should be more flexible to allow adequate coverage of these materials.

—FRED MAXFIELD, BIOCHEMISTRY, WEILL CORNELL MEDICAL COLLEGE

As a practicing psychiatrist with a broad enthusiasm for the sciences, I welcome these recommendations. Hard-core organic chemistry is not in the working repertoire of any of the doctors I see, though it was a tough hurdle in their training, and it is a wonderful subject in its own right. The revised formulation suggests a much more relevant, lively line of study. I note that physics is not mentioned, though it forms the basis for a unified view of biochemistry. The medical students I meet are usually weak in this area. As far as “behavioral science,” I doubt that common psychology courses offer any richness compared to examined life experience or meaningful study of literature, sociology or anthropology. These comments are solely my own. —MICHAEL STITELMAN, YALE MEDICAL SCHOOL

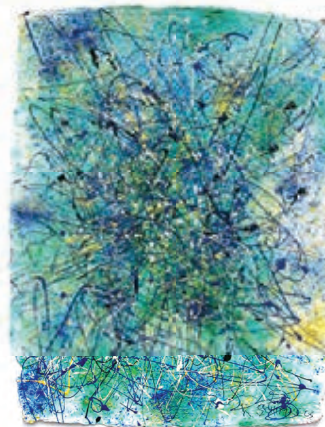
While I agree with Marc Loudon’s concerns about part 2 being quite proscriptive, I think that the ASBMB document is right on in regard to replacing much introductory organic chemistry with biochemistry (with a heavy emphasis on chemistry). As a biochemistry undergraduate (a long time ago) and a molecular biologist for many years, I am convinced that it must be possible to teach many organic chemistry principles in the context of biological molecules and thereby make orgo more interesting and useful for biology students. On the other hand, I would have liked to see more discussion of the place of thermodynamics. But overall, I congratulate the ASBMB committee with a report that should inspire tinkering in both chemistry and biology departments. —LASSE LINDAHL, UNIVERSITY OF MARYLAND, BALTIMORE COUNTY

CORRECTION

In the March 2012 issue of ASBMB Today, the article “The men behind Western blotting” incorrectly referred to RNA or DNA blotting as immunoblotting. The nucleic-acid detection methods don’t use antibodies like Western blots.

Next month in ASBMB Today

In May, ASBMB Today science writer Rajendrani Mukhopadhyay profiles Robert Schimke, who once was president of the American Society for Biochemistry and Molecular Biology and who served on the editorial board of the Journal of Biological Chemistry. Schimke is known for major contributions to at least four different areas of biology, and today he’s an artist.



What’s new on Wild Types

Here’s a snapshot of ASBMB Today science writer Rajendrani Mukhopadhyay’s blog. Follow it at wildtypes.wordpress.com.

- Khan Academy takes on biochemistry and molecular biology
- Science funding through crowdsourcing
- Leaf-cutter ants and their marvelous microbiomes
- Wild Types: blogging about molecular biology, biochemistry and anything in between!



PHOTO: BANDWAGONMAN AT EN.WIKIPEDIA

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Mitochondria: Energy, Signals and Homeostasis

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LOCATION: Kellogg Hotel & Conference Center at Michigan State University, East Lansing, MI

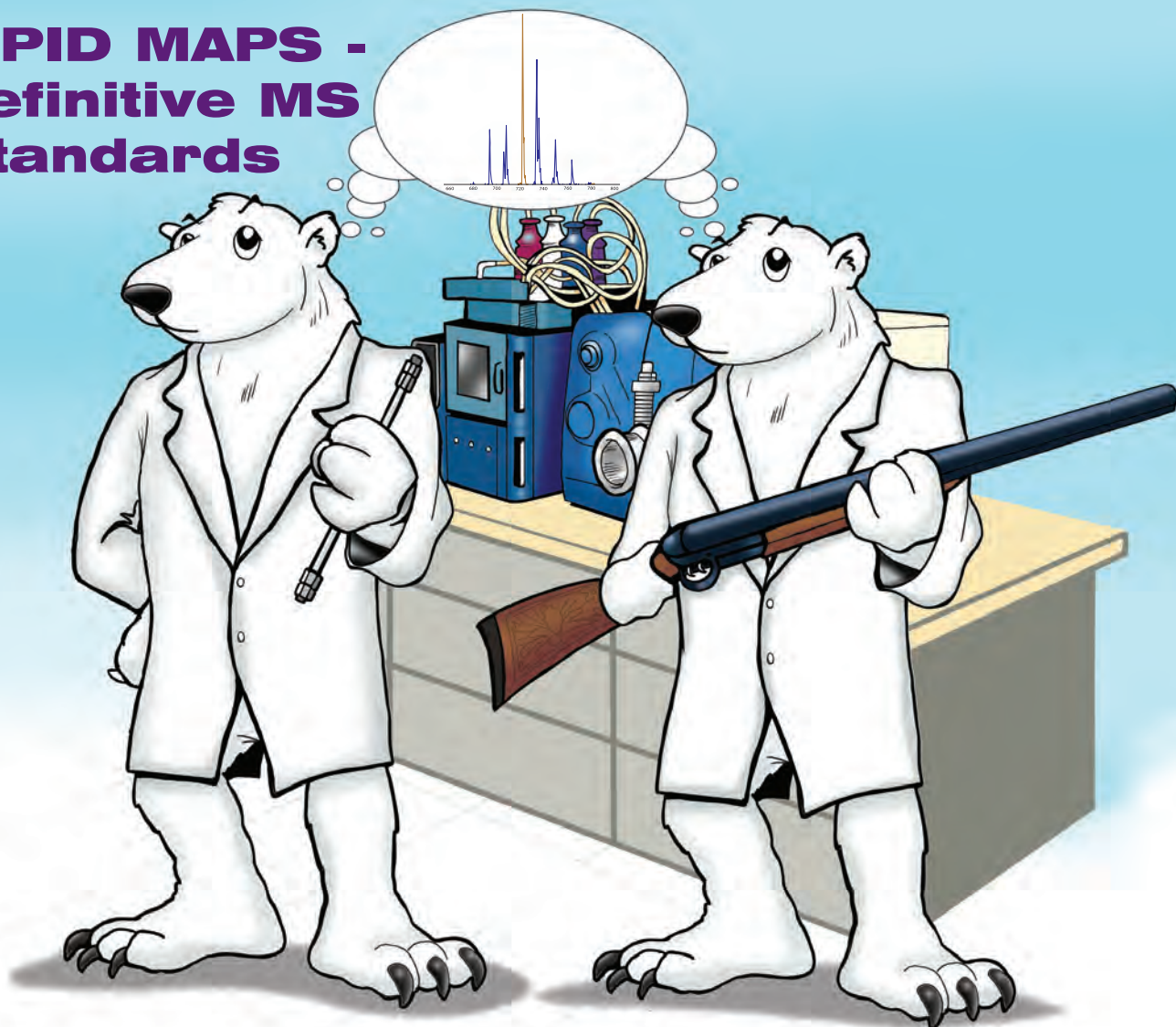
ORGANIZERS: Laurie S. Kaguni, Michigan State University and Howard T. Jacobs, University of Tampere, Finland

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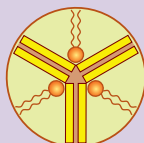
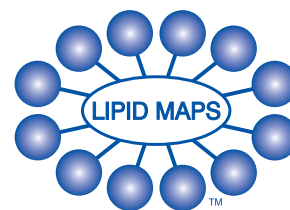
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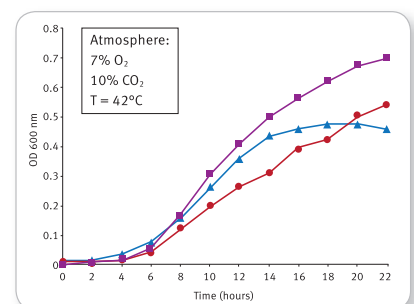
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