# ASBMB today

December 2010


American Society for Biochemistry and Molecular Biology

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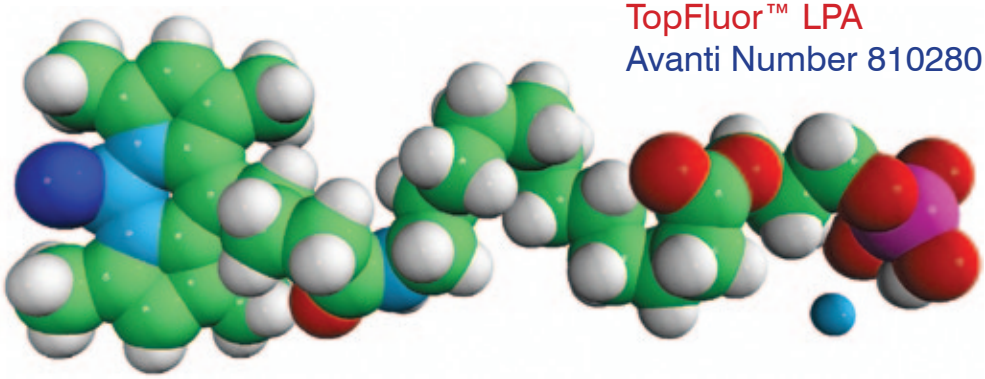

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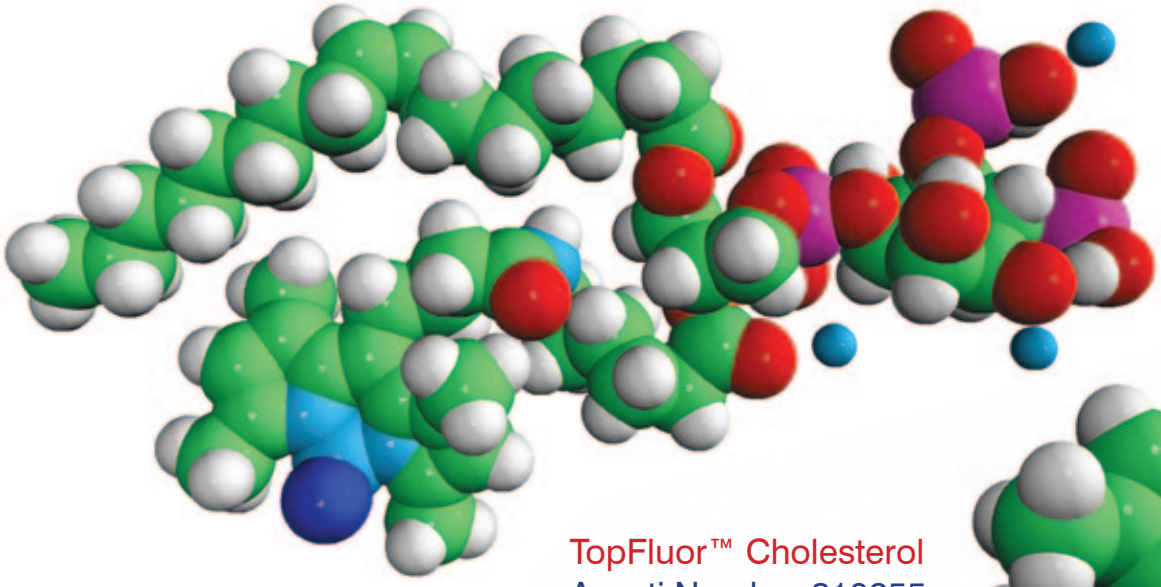

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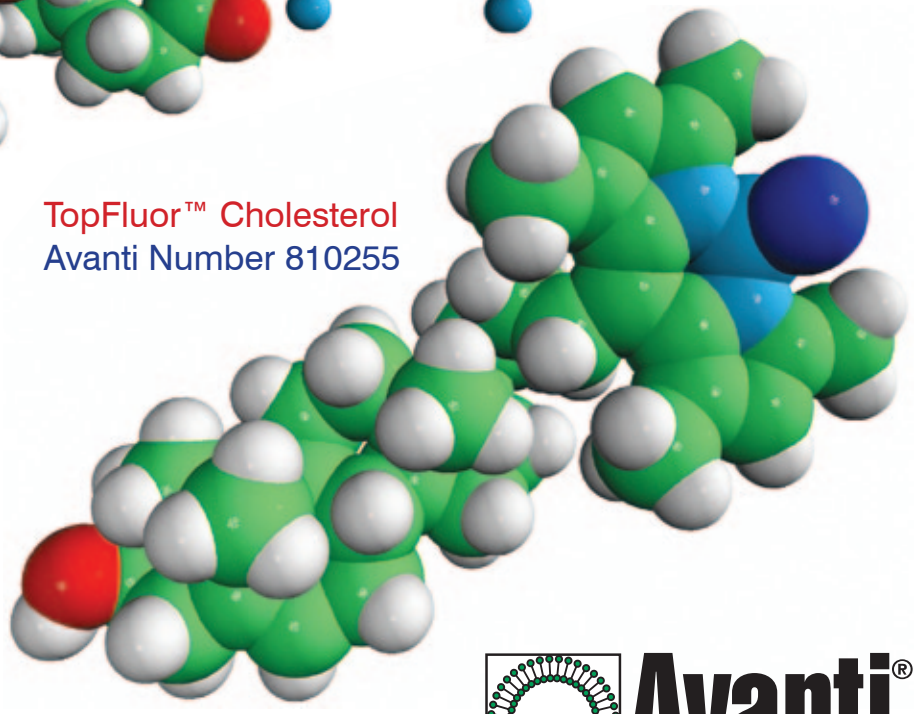

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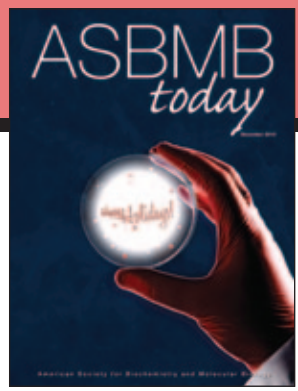


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**www.asbmb.org/asbmbtoday**

ASBMB today

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2008 APEX® AWARDS FOR PUBLICATION EXCELLENCE

# letters to the editor

## Molecular Visualization Survey

***Dear Colleagues,***

Many of us use molecular visualization as we teach our courses. If we do, it is likely that we also have discussed our approaches with friends and colleagues over the Internet and as we gather at conferences.

Bob Bateman, Lea Michel and I have created a survey for the molecular visualization community to get a more systematic idea of how we use molecular visualization in education. We are planning to present our results at the April 2011 ASBMB annual meeting and hope to also submit a manuscript to Biochemistry and Molecular Biology Education.

We would very much appreciate it if you could take the time to participate in our survey, at www.surveymonkey.com/s/62TL6ZJ.

The survey includes 11 multiple-choice questions and three open-ended questions. We anticipate it will take you 15 – 25 minutes to complete.

We appreciate your time.

*Paul Craig*
Rochester Institute of Technology
Rochester, NY

## Be Merciful to Ph.D. Students

***Dear Suzanne,***

I am Zhongzhou Yang, a professor at the Nanjing University of China.

Recently, I received my monthly ASBMB Today and read the President's Message with great enthusiasm. I completely agree with you on the key point: to be merciful to Ph.D. students for their publications (especially the first one). Science/research or training Ph.D. students is going astray in pursuing publications. Publishing a paper is the first priority of young Ph.D. students, not resolving a scientific problem or answering a scientific question. My first Ph.D. student has been terrified by the long-term back-and-forth (or submission-and-rejection) process in the past two years. Eventually, his first research paper was accepted by Developmental Biology. Nonetheless, the bad experience is hurting.

We appreciate your faithful service in the ASBMB and I wish all the best to our ASBMB.

*With my best regards,*
*Zhongzhou Yang*
Nanjing University
Nanjing, China

# Tennis in Biochemistry

BY SUZANNE PFEFFER

About three years ago, I took up competitive tennis. I had never played any competitive sports as a kid and wanted to return to tennis after a 20-year break. I signed up for lessons from one of the terrific Stanford University women's team coaches, and after a year of relearning my ground strokes (topspin!), I joined a local United States Tennis Association adult league team. Immediately apparent was the fact that my opponents were much more competitive than me. How was that possible? The world of science can seem like a very competitive place, and I am not usually thought of as a shrinking violet.

Unlike in science, in tennis there always is one winner and one loser. When I started, I was happy winning some great points, out-rallying an opponent and keeping him or her at the baseline. Winning matches was something quite different — and it was clear that some of my opponents REALLY wanted to win by any means possible. How I hated their lobs and dink shots! Match toughness gets easier with experience, and now, after a few years of practice, my nerves are a little calmer at the start of most matches. Confidence also comes from previous wins and hard work on my skill set. There has been improvement, after hours of continued instruction and practice, but it comes much slower at this stage of my life. I try to remind myself that my game is now much more multifaceted than it ever has been, and it really does continue to get better at a slow but steady pace.

How is it possible that tennis is more competitive than science? A good aspect of science is the fact that the corroboration of important results by multiple labs benefits our field tremendously. When two labs are working on the same question, they often will take independent approaches to come to a similar conclusion. That doesn't mean I like the idea of two students staying up into the wee hours to load the same gels on opposite sides of the country. That being said (journal editors take note), it is important when two labs obtain similar findings; we suffer when multiple labs fail to reproduce a published finding, because no one ever learns that a published result may not be correct.

As a discipline, there are important things we can learn from tennis. Consider the top tennis professionals who hone their skills through four to six hours of practice every day. They have training coaches and psychological coaches and couldn't succeed without them. We all are professional biochemists. What are we doing to stay at the very top of our game? Probably not enough. Any time we attend a lecture outside our field, we are broadening our horizons and increasing our chances of learning a new approach to apply to our own work. The very best scientists are taking cues from neighboring disciplines and keeping their ears open for any new technology to streamline the path to discovery. Attending meetings also is an important way to keep up with the latest findings and ideas in a field.

What about courses? Younger scientists take courses at Woods Hole and Cold Spring Harbor laboratories, but we all could benefit from additional courses in the newest technologies available to us. Offering courses is something that the American Society for Biochemistry and Molecular Biology might consider, and if you have ideas for courses that would benefit our members, please let us know. We are trying to offer breadth at the annual meeting, and our special symposia series are designed to benefit our members. Spending a week learning a new software package or experimental approach could benefit all of us. A fresh perspective can raise our performance to our full score advantage.

How many of our students and postdoctoral fellows consider faculty members to be their coaches? Maybe if we thought of ourselves more as coaches, we would do a better job as mentors. A coach would be sure that

students and postdocs were learning all the skills they needed to be successful in the future, including picking important questions, reading the literature and learning the techniques needed for their projects. A coach would take the time to help them improve their writing and speaking skills and explain how manuscripts are reviewed. And, of course, we need to cheer on our students the most when experiments aren't working and guide them back onto a path to success.

More experienced scientists need coaches as well. Career coaches exist, but senior scientists should continue to seek out mentors to help them be successful in their programs and achieve the success they are hoping for. Would a Match.com for scientific mentors be helpful to our members? Members could offer their services by discipline and experience and provide guidance in grant writing, project development, career advancement, etc. I would like to believe that our members would be happy to step forward to answer requests for guidance in these areas.

I recently watched a U.S. Open semifinal tennis match between Venus Williams and Kim Clijsters. The two superb athletes played at the top of their games; their shots hit every corner of the court, and their skills were simply amazing. But it was mental focus that distinguished the players and led to Clijsters' win. Williams lost her serve in a key tie-breaking second set; the wind didn't help, but it is hard to explain how such a strong server suddenly lost five points while at serve.

How often do we really focus on identifying the most important questions rather than on making this week's experiments work? No matter how much I may complain, it is while I am writing a grant that I am the most creative and spend the most time thinking hard about my science. On regular days, one tends to focus on the day's experiment rather than a longer term vision. It is important to get back to the big picture, as well. The very top scientists are successful because they identify the most important problems in science and use the most powerful approaches to address them. In times of limited research dollars, it is more important than ever to identify the most important areas for future work.

Hopefully, we play the game of biochemistry because we share the same passion for science as tennis players do for their game. We usually aren't paid the million-dollar purses won by professional tennis players. But the satisfaction of important discoveries during a career of research far surpasses the pleasure that any cash award can bring us (okay, cash awards aren't all bad). We all can benefit from any activity that will improve our games, whether we are biochemists or world-class tennis champions.

# Society Headquarters to Be Relocated

## *Leaving historical Beaumont Campus will be exciting and bittersweet, staffers say*

BY ANGELA HOPP

The leadership of the American Society for Biochemistry and Molecular Biology has announced that the society's headquarters, located for the past five decades in a historical house and one of its outbuildings in Bethesda, Md., will be relocated in May to a more modern commercial space a few miles away.

Barbara Gordon, the society's executive director, said the decision to leave the charming Beaumont House was difficult but necessary. She said the new space, which will be reconfigured this spring to meet the society's needs, will foster more efficient workflows and allow for growth.

"It's been obvious for some time that we've simply outgrown this dear old house," Gordon said of the stone mansion constructed in 1929 and acquired by the Federation of American Societies for Experimental Biology in 1954. "We are spread out between Beaumont House and the annex. That's a couple dozen people across two buildings and five floors. In the new space, we'll all be in the same building, all on the same floor, and it's going to make a world of difference in how we get things done."


**The new ASBMB headquarters will be housed on the third floor of the CRI Building, a property built in 1986 and occupied by attorneys, financial services groups and health care providers.**

The 15,000-square-foot headquarters will be housed on the third floor of the CRI Building in Rockville, a property built in 1986 and occupied by attorneys, financial services groups, health care providers and the like. The building is about half a mile away from a metro stop and on the bus line. It's also close to restaurants and retail stores.

For Nancy Rodnan, ASBMB's director of publications, the move means finally having the entire publications staff in close proximity and giving the editorial support team, in particular, more room to grow if needed.

"We are a very close-knit group on a personal level, and we work very well together on a professional level, despite the fact that we're housed all over the place. I'm looking forward to having my department all together. It will be really nice," she said.

Still, leaving the lush 11-acre Beaumont Campus, named after distinguished American physician and pioneer physiologist William Beaumont, will not be easy, staffers said.

Its landscaping, architectural details and wildlife contribute to a warm, even homey, work environment that probably can't be duplicated, said Gordon, who has worked at Beaumont House in one capacity or another for more than three decades. But, she said, old buildings also have their challenges, and the new space is going to be far more functional.

"The FASEB campus is quite beautiful, but the offices have a frat-house feel right now," said ASBMB President Suzanne Pfeffer. "ASBMB's terrific staff deserve a more professional work environment that will enable them to work optimally on behalf of all members."

Angela Hopp (ahopp@asbmb.org) is managing editor for special projects at ASBMB.

# Election Roundup

BY GEOFFREY HUNT

The 2010 midterm elections brought massive change to Congress. Republicans reclaimed the U.S. House of Representatives, whereas the Democrats retained control of the Senate but saw their majority vastly reduced. These results promise to bring change to the approach of the legislative branch; what will their effect be on science?

## Tightening the Purse Strings

As the federal deficit climbs past $1.5 trillion, leaders on both sides of the aisle are trying to create ways to move the country's balance sheet back toward the black. These efforts, mostly centered on spending cuts, come as a great concern to scientists, who have become increasingly worried about their ability to obtain the funding and grants necessary to perform their research. In June, the U.S. Office of Management and Budget recommended that federal agencies, including the National Institutes of Health and National Science Foundation, prepare their fiscal 2012 budget requests anticipating a 5 percent decrease in appropriations from fiscal 2011. Recently, more revolutionary strategies aimed at reducing the federal deficit have included proposals from a bipartisan commission to eliminate the NSF.

Additionally, in their recent "Pledge to America," House Republican leaders John Boehner, R-Ohio, and Eric Cantor, R-Va., outlined their intentions to cut government spending almost 20 percent, rolling back funding to fiscal 2008 spending levels. For scientists used to budget growth that at least mirrors inflation, this would represent an enormous decrease in financial resources that potentially would leave numerous researchers struggling to survive. In a talk given at the annual American Society of Human Genetics meeting, NIH Director Francis Collins suggested that such policies would lead to so much of the NIH budget being tied up in committed grants that the success rate for new proposals, already precipitously low at 20 percent, would be reduced to barely 1 in 10.

In contrast, other signs point to a better-than-expected outcome for the global funding of scientific research. In the United Kingdom, the newly elected Conservative government recently released its spending review, which proposed average cuts of 19 percent across governmental programs. However, the budget for science funding was spared and will remain flat under the plan, leading some to envision a similar situation happening in the U.S. Meanwhile, some analysts have looked to the past as an indicator of the future. In 1994, a similar wave of voter discontent gave Republicans control of Congress, sparking fears of massive spending cuts. Yet thanks to steady advocacy efforts and a receptive audience in the form of Speaker of the House Newt Gingrich, science came out as a big winner. Congressional scientific champions, including Republicans John Porter and Mark Hatfield, were at the forefront of a push that led to the doubling of the NIH budget between 1998 and 2003. Although repeating such a scenario in the current fiscal environment is unlikely, the episode does provide scientists with a glimmer of hope.

## Leaders Past and Present

As for the legislators themselves, the passing of the 111th Congress sees the loss of several long-serving scientific champions. In the Senate, Sen. Arlen Specter, D-Pa., is retiring after being defeated in the Pennsylvania democratic primary back in the spring of 2010. During his 30 years in Washington, Specter, a cancer survivor, has been one of the staunchest proponents of science and research in Congress. As a member of the Labor, Health and Human Services, and Education subcommittee of

the Senate Appropriations committee, Specter consistently fought for increased funding for biomedical research and was instrumental in overseeing a nearly tenfold increase in the NIH budget, from $3.5 billion to $31 billion, between 1980 and 2010. Moreover, Specter was one of the Senate's earliest supporters of human embryonic stem cell research, holding hearings on the topic within weeks of the first report of their derivation in 1998 and even introducing the Stem Cell Research Act of 2000 that would have permitted federal funding for this line of research.

Even more change comes in the House. Rep. Bart Gordon, D-Tenn., has stepped down after 26 years in Congress. As chairman of the Science and Technology committee, Gordon was hugely influential in commandeering bipartisan support for numerous scientific issues: One of his signature achievements was the passage of the America COMPETES Act in 2007. In a recent email, Gordon thanked scientific societies, including the American Society for Biochemistry and Molecular Biology, for their support and advice on scientific issues and emphasized his and the committee's role in making "progress in increasing the investments in our research enterprise and education for our human capital."

Also retiring is Rep. David Obey, D-Wis., who served as chairman of both the powerful Appropriations committee and the LHHS subcommittee. Known for his decades-long dedication to health care, Obey teamed up with the White House to pass the Affordable Care Act (aka the health care bill) in March 2010. Furthermore, Obey was instrumental in passage of the 2009 American Recovery and Reinvestment Act, which supplied an additional $10 billion over two years for the NIH on top of its regular yearly appropriations of approximately $31 billion.

Finally, with the recent controversy surrounding embryonic stem cells, it is with a touch of irony that Congress loses Rep. Mike Castle, R-Del., who lost in his bid to win the Delaware Senate seat once held by Vice President Joe Biden. Castle teamed with colleague Rep. Diana DeGette, D-Colo., to sponsor legislation that would have expanded federal funding for human embryonic stem cell research. In both 2005 and 2007, Congress approved the Stem Cell Research Enhancement Act only for it ultimately to be vetoed by President Bush. A current version of the bill was introduced in September but is unlikely to be acted upon before the end of the current Congress.

Clearly, the loss of these scientific proponents leaves a void that will be felt throughout Congress as well as by scientific enterprises nationwide. Unfortunately, identifying new champions in the 112th Congress to replace these esteemed leaders will be a difficult task. Sen. Tom Harkin, D-Iowa, remains chairman of the Senate Health, Education, Labor and Pensions committee as well as the LHHS Appropriations subcommittee, where he consistently has demonstrated his strong support for science. A new potential Senate ally for scientists comes in the form of Rep. Mark Kirk, R-Ill., who was elected to President Obama's former seat. Kirk was first elected to Congress in 2000 to succeed former LHHS chairman John Porter, for whom Kirk worked. Like his former boss, he has been a vocal supporter of funding for biomedical research and human embryonic stem cells.

Less clear are champions in the House. DeGette will remain at the forefront, as will Rep. Rosa DeLauro, D-Conn., a member of the LHHS subcommittee who has been a staunch NIH supporter. However, with such a large freshman class, supporters from the Republican side of the aisle will likely only emerge after the new Congress has sprung into gear.

With such uncertainty lingering, it is imperative that scientists make their voices heard if they hope to maintain federal support for basic biomedical research. Legislators old and new will be relying on their constituents to help them decide how to proceed in this era of uncertainty. The silent will be left behind.

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

THE WILLIAM C. ROSE AWARD

# Melissa J. Moore Recognized for Research and Mentoring

BY ANGELA HOPP

The American Society for Biochemistry and Molecular Biology has named Melissa J. Moore, a professor at the University of Massachusetts Medical School, the winner of the society's 2011 William C. Rose Award.

Moore, a Howard Hughes Medical Institute investigator, is noted for her work with gene splicing and messenger RNA. She was nominated for the award in recognition of her outstanding contributions to biochemical and molecular biological research and her demonstrated commitment to the training of younger scientists.

*"It's truly an honor to be recognized for work that I so completely enjoy doing. Everyone should be so lucky to have such a compelling job, dedicated team and supportive community."*

**MELISSA J. MOORE**

"Melissa Moore is a paradigm for the Rose Award," said UMMS professor and chairman C. Robert Matthews in nominating Moore. "She is an outstanding scientist, a caring mentor and a terrific colleague. When she perceives a need – from her students, her colleagues or her institution — she always steps forward to fill that need."

Moore, who arrived at UMMS only a few years ago and today is a co-director of its RNA Therapeutics Institute, has initiated and led several programs there that will affect the development of translational research, Matthews said.

Intrigued by enzymes while working on her undergraduate thesis at the College of William and Mary, the Virginia native applied to only one school for graduate studies — the Massachusetts Institute of Technology — and went on to earn her doctorate in biological chemistry and complete postdoctoral research there. Under the supervision of Nobel laureate Phillip A. Sharp, she focused on RNA metabolism and developed a widely adopted technique for manipulating RNA molecules. Soon thereafter, she joined Brandeis University as a faculty member.

"Melissa's success in mentoring is derived from her uncanny ability to enthusiastically promote cutting-edge science while providing an invigorating and supportive setting for that work," said Melissa Jurica of the University of California, Santa Cruz. "She understands that successful science is carried out by secure and confident people. When I visited her lab as a postdoctoral candidate, everyone in her group underscored her people-managing skills while proclaiming her brilliance."

James E. Dahlberg of the University of Wisconsin-Madison School of Medicine and Public Health said one of Moore's strengths is "her willingness to take provocative and controversial stands on scientific issues, which then serve as a basis for designing clever tests that can either support or rule out her models."

Dahlberg said he appreciated Moore's ability to acknowledge and respond when change is needed: "Often she is right, but on those occasions when she learns that her proposals are incomplete or incorrect, she gladly accepts the facts and does not stubbornly hold to the old ideas just for their own sake."

Angela Hopp (ahopp@asbmb.org) is managing editor for special projects at ASBMB.

## About the award

**The William C. Rose Award was established to honor the legacy of Rose, an authority on protein nutrition and former president of ASBMB. The award consists of a plaque, a $3,000 prize and travel expenses to present a lecture at the ASBMB annual meeting. Moore will present her award lecture, titled "Pre-mRNA Processing and mRNA Metabolism" at 8:30 a.m. on April 12, at the 2011 annual meeting in Washington, D.C.**

THE AVANTI AWARD IN LIPIDS

# Yusuf Hannun Wins Award for Pioneering Work with Bioactive Sphingolipids

BY ANGELA HOPP

The American Society for Biochemistry and Molecular Biology has named Yusuf Hannun, professor and department chairman at the Medical University of South Carolina in Charleston, S.C., the winner of the 2010 Avanti Award in Lipids.

The award recognizes Hannun's work on bioactive sphingolipids, a class of lipids that have emerged as critical regulators of a multitude of cell functions and, when defective, can cause disorders with significant medical effects.

"For more than a century, sphingolipids were an obscure class of molecules whose metabolism and functions were poorly characterized," explained Robert C. Dickson of the University of Kentucky College of Medicine, who nominated Hannun for the award. "Indeed, their very name derives from the Greek sphinx, because they presented an enigma to their discoverer, Johann Thudicum. Dr. Hannun's work has pioneered the way in deciphering this enigma by establishing the field of bioactive sphingolipids."

Those supporting Hannun's nomination described his team's approach as a rigorous and concerted one that combines chemistry, biochemistry, cell and molecular biology and yeast genetics to unravel the sphingolipid mystery.

Hannun, author of hundreds of peer-reviewed publications during the past few decades, including 133 publications in the Journal of Biological Chemistry, also was lauded for being a tireless mentor. Indeed, one of his past trainees, Charles Chalfant, is the recipient of the 2011 ASBMB Avanti Young Investigator Award.

"The research group that he founded at the Medical University of South Carolina is now one of the best-funded lipid research groups in the U.S. Indeed, the cadre of young scientists he recruited is developing into one of the leading lipid research groups in the world," said Christopher R. McMaster of Dalhousie University in Nova Scotia, Canada.

*"This is a great honor and privilege, and I thank my many colleagues for their nomination and support. Work on sphingolipids has represented a long and highly rewarding journey. I am also gratified that the field of sphingolipids is coming into its own with increasing recognition of its significance not only in the world of lipids but also in overall biochemistry and cell biology."*

**YUSUF HANNUN**

Hannun earned his bachelor's and medical degrees from American University of Beirut, Lebanon, in 1977 and 1981, respectively. He spent nearly two decades working in multiple capacities at Duke University and its medical center. Today, he is the Ralph F. Hirschmann professor, chairman of the department of biochemistry and molecular biology and deputy director of MUSC's Hollings Cancer Center. He has edited seven books and published five patents.

"Dr. Hannun is a friendly person who cares about relationships in science and is willing to help the careers of others," said George Carman, director of the Rutgers Center for Lipid Research and associate editor for the JBC.

Angela Hopp (ahopp@asbmb.org) is managing editor for special projects at ASBMB.

## About the award

**The Avanti Award in Lipids recognizes outstanding research contributions in the area of lipids. The award consists of a plaque, $3,000 and travel expenses for the recipient to present a lecture at the ASBMB annual meeting. Hannun will give his award lecture, titled "Network of Bioactive Sphingolipids," at 8:30 a.m. on April 11, at the 2011 annual meeting in Washington, D.C.**

# Retrospective: Henry A. Lardy (1917–2010)

BY PAUL D. BOYER

Henry Arnold Lardy, one of our most respected biochemists and past president of the American Society for Biochemistry and Molecular Biology, was born Aug. 19, 1917. He died Aug. 4 from prostate cancer, a few days before his 93rd birthday. He was raised on a farm near Roslyn, S.D. After graduating from high school, Henry received permission from his father to attend one semester at South Dakota State University. Henry found acquisition of knowledge to be addictive and spent the rest of his life in its pursuit. In the fall of 1939, Henry and I started graduate studies at the University of Wisconsin-Madison, launching a lifelong friendship.

Henry's outstanding qualifications already were evident. After receiving his doctoral degree in 1943 and completing a year of postdoctoral study, he was recruited to the faculty of the Wisconsin biochemistry department. He later had a key role in the establishment of the well-recognized Enzyme Institute, and in 1966, he became a prestigious Vilas professor. Although he reached emeritus status in 1988, he continued his research until he was incapacitated by cancer this summer.

Known to associates as Hank, he mentored more than 60 graduate students and 100 postdoctoral fellows over the years. He had an unselfish interest in their training and welfare and deservedly gained their respect and affection. It is likely that more of his past colleagues regard him as one of their best friends than anyone else I know.

His group contributed importantly to a wide swath of enzymology and metabolism, in part because he wanted his students and associates to have their own problems and challenges. Some of Henry's notable accomplishments included the characterization and crystallization of 10 phosphate-transferring enzymes, the demonstration that many antibiotics inhibit oxidative phosphorylation, recognition that the rate of respiration could be controlled by the availability of acceptors of phosphate from ATP and the finding that biotin functions in the uptake of carbon dioxide. His introduction of an egg-yolk buffer for storage of spermatozoa (which was adopted widely) reflected his farm background. In addition to pioneering this technique, he became a leading contributor to the understanding of sperm metabolism.

When invited to contribute a "Reflections" paper for JBC, Henry chose the title "Happily at Work" in accordance with his status at the time.

Some personal aspects of Henry's life warrant mention. Henry and I both have had happy, 70-year marriages. He will be warmly remembered by his charming wife Annrita and his many friends. The Lardys and the Boyers have enjoyed many activities and travels together, such as a month of bicycling in France. In 1963, the Lardys acquired a farm some 30 miles from their home in Madison, Wis. They built a welcoming house from trees on the property and made a pond for swimming as well as a tennis court. Many days have been passed in this attractive setting.

The field of biochemistry has been enriched remarkably by Henry A. Lardy's contributions. He is one of the few intellectual giants of our profession.

Paul D. Boyer is a professor emeritus at the University of California, Los Angeles.

## To read more online:

- Remembrances from Lardy's friends and colleagues: http://bit.ly/ATodayLardy
- Lardy's ASBMB president page: http://bit.ly/ASBMBLardy
- Lardy's JBC Reflection and Classic: http://bit.ly/RefLardy and http://bit.ly/ClassicLardy

# Retrospective: Bernard L. Horecker (1914–2010)

BY NICOLE KRESGE

Bernard Leonard Horecker, best known for his contributions to elucidating the pentose phosphate pathway, died on Oct. 9, 2010. He was president of the American Society for Biochemistry and Molecular Biology in 1968.

Horecker was born in Chicago in 1914. He began his training in enzymology in 1936 as a graduate student at the University of Chicago in the laboratory of T. R. Hogness, searching for an enzyme that would catalyze the reduction of cytochrome *c* by reduced NADP.

After earning his doctoral degree, Horecker got a job at the National Institutes of Health in Frederick S. Brackett's laboratory in the Division of Industrial Hygiene. As part of the war effort, he was assigned the task of developing a method to determine the carbon monoxide hemoglobin content of the blood of Navy pilots returning from combat missions.

When the war ended, Horecker remained at the NIH and returned to research in enzymology. He began to study the reduction of cytochrome *c* by the succinic dehydrogenase system, which led to a collaboration with Arthur Kornberg in which the two studied the effects of cyanide on the succinic dehydrogenase system.

Two years later, Kornberg invited Horecker and Leon Heppel to join him in setting up the new Section on Enzymes in the Laboratory of Physiology at the NIH. Their section eventually became part of the new Experimental Biology and Medicine Institute and was later renamed the National Institute of Arthritis and Metabolic Diseases.

Horecker and Kornberg collaborated again, this time on the isolation of NAD (DPN) and NADP (TPN). Horecker also collaborated with Heppel on the isolation of xanthine oxidase from milk, which unexpectedly reduced cytochrome *c* only in the presence of oxygen, an observation that eventually led to a widely used assay for the detection of the superoxide anion.

Horecker's research interests turned to enzymes involved in the oxidation of 6-phosphogluconate, and he demonstrated that this pathway generated ribulose 5-phosphate. He played a key role in the elucidation of the pentose phosphate pathway, which included the discovery of the enzymes transketolase, transaldolase and pentose phosphate 3-epimerase and the identification of sedoheptulose 7-phosphate and erythrose 4-phosphate. His laboratory also was the first to prepare ribulose bisphosphate and ribulose bisphosphate carboxylase.

In 1958, Horecker assumed the microbiology chair at New York University School of Medicine, and in 1963, he moved to Albert Einstein College of Medicine as chairman of the newly formed department of molecular biology. In 1972, he moved to the Roche Institute of Molecular Biology. Eventually, he became dean of the Weill Cornell Graduate School of Medical Sciences as well as associate dean for research and sponsored programs and professor emeritus of biochemistry at Weill Cornell Medical College.

*Feel free to add your reflections on Bernard L. Horecker to the online version of this article at http://bit.ly/ATodayHorecker.*

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

## To read more online:

- Horecker's ASBMB president page: http://bit.ly/PresHorecker
- Horecker's JBC Reflection: http://bit.ly/RefHorecker
- Horecker's JBC Classic: http://bit.ly/ClassicHorecker

# asbmb member spotlight

## Bennett Awarded Beutler Prize for Translational Research

Joel S. Bennett, professor of medicine at the University of Pennsylvania, has been awarded the Ernest T. Beutler Lecture and Prize by the American Society of Hematology. Bennett will share the prize with Barry S. Coller of The Rockefeller University.

According to the ASH, Bennett and Coller were awarded the prize for "enabling advances in basic science as well as in clinical science and translational applications in hematology." The award is named for the late Ernest Beutler, past president of ASH and physician-scientist for more than 50 years. It is presented to two individuals and is intended to recognize major advances related to a single topic.

Bennett's research focuses on the structural basis of platelet integrin regulation. He has found that helix-helix interactions involving the transmembrane and membrane-proximal cytoplasmic domain segments play an essential role in regulating the function of both beta 1 and beta 3 integrins. The current focus of his studies is using biophysical and molecular biology techniques to characterize these interactions in detail and employing this information in designing potential antithrombotic agents.

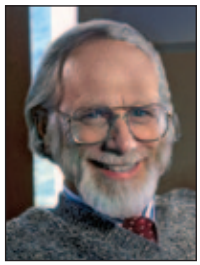
## Roeder Receives Salk Medal for Research Excellence

Gene expression pioneer Robert G. Roeder, the Arnold and Mabel Beckman professor of biochemistry and molecular biology at The Rockefeller University, is the recipient of the Salk Institute's Medal for Research Excellence.

"Robert Roeder's contributions to the understanding of RNA synthesis in animal cells are unparalleled in modern science," said Salk President William R. Brody in a press release. "The institute's 50th anniversary is the perfect moment to recognize the extraordinary contributions of our medalists. The Salk Institute medals are a fitting tribute to their ongoing, vital contributions to science and society. And our founder, Jonas Salk, would have been absolutely delighted by the medalist selection."

Roeder is known for his research on eukaryotic transcriptional regulation. In 1969, he showed RNA polymerases I, II and III directly copy DNA in animal cells. Later, he developed cell-free systems composed of purified RNA polymerases and components extracted from cell nuclei and used these cell-free systems to identify accessory factors essential for the RNA polymerases (e.g., TFIIA, TFIIB, TFIID, etc.) to read target genes. Roeder also was involved in the discovery of coactivators, large protein complexes that provide a bridge between the activators and repressors and the RNA polymerases and other components of the general transcription machinery.

## Bishop Honored with Advocacy Award



J. Michael Bishop, chancellor of the University of California, San Francisco, has been named the recipient of the 2011 Research!America Raymond and Beverly Sackler Award for Sustained National Leadership. Bishop will receive his award at the Research!America Advocacy Awards event this March in Washington, D.C.

The annual Research!America Advocacy Awards program was established in 1996 by the board of directors to honor outstanding advocates for medical, health and scientific research. Recognized individuals and organizations are those whose leadership efforts have been notably effective in advancing our nation's commitment to research

Bishop is best known for his Nobel Prize-winning research on retroviral oncogenes. Working with Harold E. Varmus, he discovered the first human oncogene, c-Src. These findings allowed the understanding of how malignant tumors are formed from changes to the normal genes of a cell. Bishop shared the 1989 Nobel Prize in physiology or medicine with Varmus for this work.

Today, Bishop continues to work on the genetic underpinnings of cancer, using mouse models based on anomalies of proto-oncogenes found in human cancer.

IMAGE COURTESY OF THE UNIVERSITY OF CALIFORNIA, SAN FRANCISCO.

## Epstein Selected for ASHG Leadership Award

The American Society of Human Genetics' board of directors has selected Charles J. Epstein, professor emeritus of the department of pediatrics and Institute for Human Genetics at the University of California, San Francisco, as the recipient of its 2010 McKusick Leadership Award.

The award, named in honor of Victor A. McKusick and his contributions to the field of human genetics, is presented to an individual whose professional achievements have fostered and enriched the development of various human genetics disciplines. According to ASHG, recipients of this award must exemplify the enduring leadership and vision required to ensure that the field of human genetics will flourish and assimilate successfully into the broader context of science, medicine and health.

Epstein was selected as this year's recipient of the McKusick Leadership Award for his exemplary and inspiring contributions to the field of human genetics. In addition to setting up a model medical genetics clinic and enhancing the fields of biochemical and clinical genetics, he helped establish and legitimize the profession of genetic counseling in the late 1970s.

Throughout his career, Epstein also has been a prominent leader in the ASHG community, serving as president of the society and as editor of the American Journal of Human Genetics.

## Ja and Verdin Receive Biology of Aging Awards

JA

VERDIN

William Ja and Eric M. Verdin have received Glenn Awards for Research in Biological Mechanisms of Aging. The awards, initiated in 2007, provide unsolicited funds to researchers investigating the biology of aging. Award recipients are selected from nominees provided by an anonymous scientific advisory committee.

William Ja, an assistant professor at Scripps Florida, studies longevity-enhancing manipulations and their impact on aging and metabolism in drosophila. Among these manipulations are dietary restriction and the effects on their hosts of certain types of bacteria that live in the gastrointestinal tract.

Eric M. Verdin is a senior investigator at the Gladstone Institute of Virology and Immunology and a professor of medicine at the University of California, San Francisco. He looks at the biology of reversible protein acetylation. Specifically, he focuses on the enzymes that remove acetyl groups from proteins, the histone/protein deacetylases.

## Nine ASBMB Members Elected to IOM

Nine members of ASBMB were among the 65 new members and five foreign associates elected to the Institute of Medicine of the National Academies. Election to the IOM is considered one of the highest honors in the fields of health and medicine and recognizes individuals who have demonstrated outstanding professional achievement and commitment to service.

**The newly elected ASBMB members are**

**SYDNEY BRENNER**, senior distinguished fellow, Crick-Jacobs Center, Salk Institute for Biological Sciences, La Jolla, Calif.

**RICCARDO DALLA-FAVERA**, Percy and Joanne Uris professor of clinical medicine, professor of pathology and genetics and development and director, Institute of Cancer Genetics, Columbia University Medical Center, New York City

**TITIA DE LANGE**, Leon Hess professor, Laboratory of Cell Biology and Genetics, The Rockefeller University, New York City

**JENNIFER A. DOUDNA**, investigator, Howard Hughes Medical Institute; and professor, department of molecular and cell biology, University of California, Berkeley

**CAROL W. GREIDER**, Daniel Nathans professor and director, department of molecular biology and genetics, the Johns Hopkins University School of Medicine, Baltimore

**IRA H. PASTAN**, co-chief, laboratory of cell biology, National Cancer Institute, the National Institutes of Health, Bethesda, Md.

**PETER J. POLVERINI**, professor and dean, School of Dentistry, University of Michigan, Ann Arbor

**KEVAN M. SHOKAT**, investigator, Howard Hughes Medical Institute; and professor and chair, department of cellular and molecular pharmacology, University of California, San Francisco

**CARL WU**, chief, laboratory of biochemistry and molecular biology, Center for Cancer Research, National Cancer Institute, the National Institutes of Health, Bethesda, Md.

## Three ASBMB Members Receive National Medal of Science

Three American Society for Biochemistry and Molecular Biology members were among the 10 researchers named by President Obama as recipients of the National Medal of Science.

**The ASBMB members are**

BENKOVIC

**STEPHEN J. BENKOVIC**, Evan Pugh professor and Eberly chairman in chemistry at The Pennsylvania State University

LINDQUIST

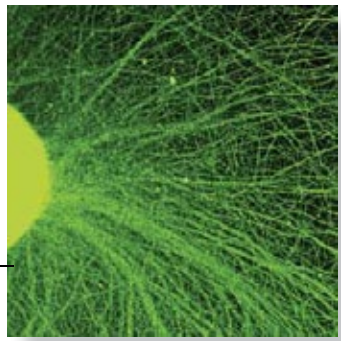
**SUSAN L. LINDQUIST**, Howard Hughes Medical Institute Investigator, Whitehead Institute for Biomedical Research member and professor of biology at the Massachusetts Institute of Technology

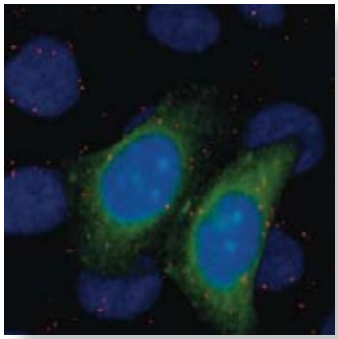
PRUSINER

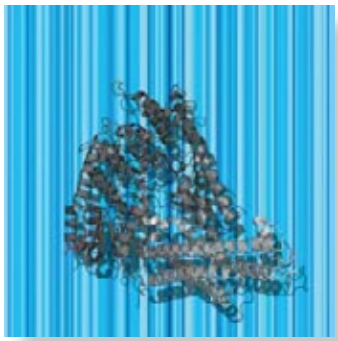
**STANLEY B. PRUSINER**, professor of neurology and director of the Institute for Neurodegenerative Diseases at the University of California, San Francisco

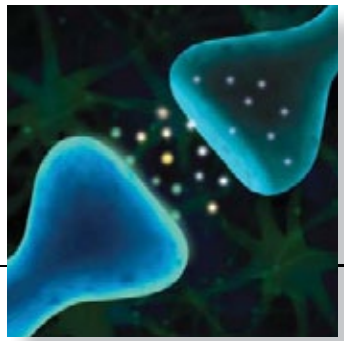
This is the highest honor bestowed by the United States government on scientists, engineers and inventors. The recipients will receive their awards at a White House ceremony later this year.

The National Medal of Science was created by statute in 1959 and is administered for the White House by the National Science Foundation. Awarded annually, the medal recognizes individuals who have made outstanding contributions to science and engineering. Nominees are selected by a committee of presidential appointees based on their extraordinary knowledge in and contributions to the biological, behavioral/social and physical sciences, as well as chemistry, engineering, computing and mathematics.









2012

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**PROPOSALS DUE MARCH 1, 2011**

# Inaugural USA Science and Engineering Festival a Rousing Success

BY NICK ZAGORSKI

This past October, the American Society for Biochemistry and Molecular Biology joined 850 other science organizations and universities at the inaugural USA Science & Engineering Festival. Under beautiful fall skies, more than half a million visitors attended the festival, spread out at four different locations around the National Mall in Washington, D.C., to participate in the 1,500 different exhibits and performances.

Among the countless informative and interactive booths, visitors could speak with astronauts, play soccer using robots, look at cells under a microscope and even touch a squid. In between visiting the booths, they could take time to watch some science comedy, magic shows, juggling and other stage acts that both entertained and educated.

ASBMB's two exhibits, "Molecular Machines" and "A Taste of Genetics," were extremely well-received — more than 2,000 curious individuals stopped by during the two-day event to learn more about the molecules of life and make a tasty DNA treat.

"While it was disheartening that no one under the age of 15 has ever heard of Watson and Crick, we are happy to report that more than 1,000 moms, dads and kids now know that life happens in water, or more specifically, that proteins fold in the polar, watery media of the cell, following basic principles of chemistry and physics," said Tim Herman of the Center for BioMolecular Modeling at the Milwaukee School of Engineering, who oversaw the "Molecular Machines" booth.

"Overall, it was a wonderful experience for all the CBM staff, who had the opportunity to ponder questions like, 'How does the cell remember the exact amino acid sequence of each of our 30,000 proteins?' with the visitors who came to the ASBMB booth," he continued.

The festival's mission was to reinvigorate our youth (and our adults as well) with the wonder of science and engineering while also sending a message about the value and importance of science for the continued success of our nation. Based on the size and excitement of the crowd, the festival succeeded tremendously, and ASBMB is proud to have been a part of this groundbreaking event.

At the ASBMB "A Taste of Genetics" exhibit, participants made DNA out of licorice and marshmallows.

However, the mission goes beyond that singular weekend. The turnout and participation clearly demonstrate that children are eager to learn about science, and the challenge now is sustaining the festival's effect year-round and spreading it to other parts of the nation.

ASBMB will continue to do its part in promoting science education at all levels and certainly encourages all of its members to plan and/or participate in local events that promote science through activity.

Nick Zagorski (nzagorski@asbmb.org) is a science writer at ASBMB.

**For more information:**

Go to http://bit.ly/ATodaySciFest for photo and video recaps of the festival.

# Ajit Varki: *The Seductive Science of Sialic Acids*

BY NICK ZAGORSKI

Ajit Varki studies the biochemistry, molecular biology and genetics of sialic acids.

It's not uncommon for scientists to shift their research focus in new and different directions during the course of their careers, whether to separate themselves from their mentors or to follow up on unexpected discoveries, which sometimes results in unusual research trajectories.

Even so, in 1975, when Ajit Varki first set foot on U.S. soil to pursue his interests in hematology research, he couldn't possibly have envisioned that someday he would be taking a sabbatical at the Yerkes National Primate Research Center to learn about chimpanzees or requesting fossil samples of Neanderthals while at the same time emerging as a leading expert in glycobiology. He also never imagined that his work would be recognized by such honors as election to the American Academy of Arts and Sciences and the Institute of Medicine of the National Academies.

But it's a journey Varki is thrilled to have made. Currently a distinguished professor in the departments of medicine and cellular and molecular medicine at the University of California, San Diego, as well as co-director of both the UCSD/Salk Center for Academic Research and Training in Anthropogeny and the Glycobiology Research and Training Center, Varki studies the biochemistry, molecular biology and genetics of sialic acids, a diverse family of glycans, while using that information to answer broader questions about human origins, disease and evolution.

"I could not have written a better script for myself," he says. "I can keep doing basic research in the ASBMB mold but also apply that to answer philosophical questions like, 'What makes a human a human?' while studying the implications for human disease."

## Unconventional Origins

Ajit Varki, whose own origins trace to Kerala in southwest India (along the fabled spice coast that Columbus was trying to reach in his journeys), recalls wanting to be a physician from a very early age; thus, he developed strong academic interests, particularly in biology. "Having two rather famous grandfathers (Pothan Joseph, a renowned Indian journalist and newspaper editor, and A. M. Varki, who founded one of Southern India's first English-medium colleges) greatly raised the stakes on performance expectations in my childhood, though generally in a positive way," he says.

The positive reinforcement helped, driving him to be the top student from Bishop Cotton Boys' School Bangalore, often called the "Eton of the East," and from Christian Medical College at Vellore, one of the leading medical schools in India. "Although my first love was medicine and I even spent a year working at a small rural hospital after graduation, my exposure to scientific research at CMC convinced me to try a career as a physician-scientist," he says. However, India's research infrastructure was not as well developed — Varki says he was fortunate to attend one of the few Indian schools that blended research, science and medicine — and he knew he had to leave the country to pursue further research training.

"It's much different today in India," says Varki, who returns to his native country each year to serve as a visiting professor at the Indian Institute of Technology Madras and to help enhance academic excellence at CMC. "The government has invested heavily in R&D, and new research institutes are now springing up everywhere."

But back then, the one country where physicians seemed to conduct research on par with doctorates was in the United States. So Varki arrived stateside, like many before and since, with a suitcase, $6.00 in his pocket and a dream (in his case, doing great research).

"Now, I knew my research opportunities would improve if I first finished my medical training," he says. "But despite having been the number one student throughout my schooling, I could not even get an interview at any major university; at that time in the 1970s, there was a good deal of prejudice against foreign doctors," he says. "Today, I get bemused whenever I get invited to present an honorific lecture at some of these institutions and think back to when they wouldn't even talk to me."

So Varki had to claw his way up the academic ladder, starting at a small community hospital in Philadelphia, then moving to the University of Nebraska and finally entering a hematology-oncology fellowship at Washington University in St. Louis.

There, he ended up joining the lab of Stuart Kornfeld. "Honestly, I didn't know much about glycobiology (which was Kornfeld's area of expertise), but I decided that this guy was so extremely smart and that I should go work for him."

The timing was fortunate, as Kornfeld's group was just making their first of many discoveries about the mannose 6-phosphate pathway, wherein mannose moieties on lysosomal enzymes are phosphorylated in the Golgi, which in turn acts as a signal to target them to the lysosome.

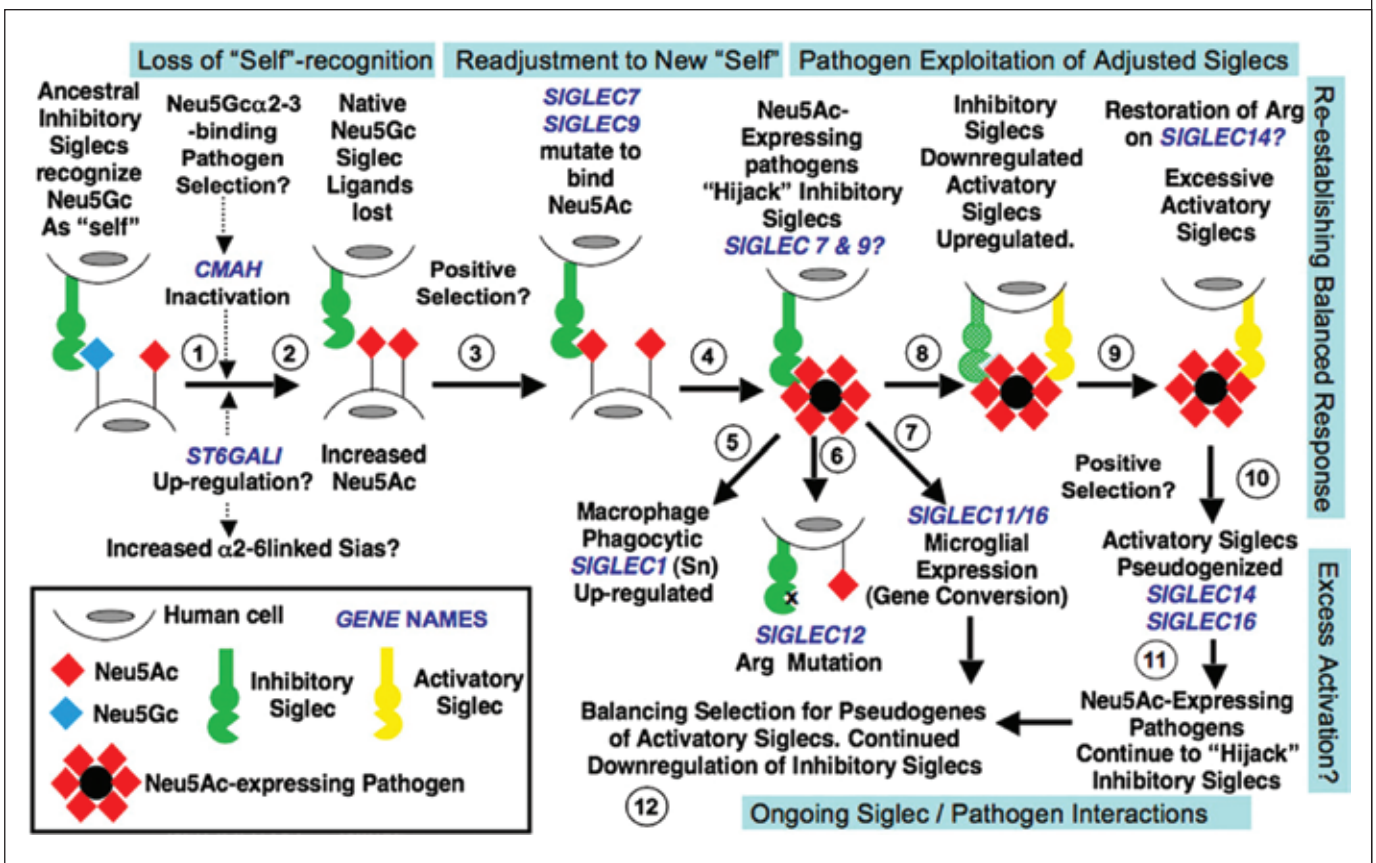
"It was an exciting time," notes Varki, who identified the enzyme responsible for the second step in the two-step pathway, the phosphodiester glycosidase. "The lab was uncovering the first known biological function for the sugar in a eukaryotic system. And not only a function; we soon identified the M6P receptor and showed that I-cell disease was brought on by a deficiency of phosphotransferase, the enzyme that catalyzes the first step of the pathway."

## Spreading His Wings

In 1982, Varki completed his work with Kornfeld and joined the faculty at UCSD, where, in a move he wouldn't advise for a young investigator today, he completely dropped all his M6P work and decided to prove himself by doing something completely different.

The question was what avenue to pick. His appointment at UCSD coincided with a national surge in molecular biology, but he made a conscious decision "not to jump on that bandwagon." He wanted to remain in glycobiology, and given that it was an underrepresented field — and still is today, though Varki notes that increased enthusiasm among young scientists is spurring a slow but steady growth — he had plenty of options.

"I had written one paper on sialic acids with Stuart," he says. "And I was intrigued that this family of sugars included over 50 different varieties, but no one really




**Proposed evolutionary scenario linking human-specific changes in sialic acid-related genes; from Varki, A. (2010).** *PNAS* **107**, 8939–8946.

knew much about this diversity or its functions."

During the next 15 years, Varki and his team set out to characterize essential features of sialic acid structure, biochemistry and biology and the connections of these molecules — which dot the surface of every cell — to infections, the immune response and cancer.

Among his many important contributions, which can be evidenced by the more than 50 Journal of Biological Chemistry articles he published during this period, he worked on *O*-acetylation, a tightly regulated yet poorly understood sialic acid modification, and conducted numerous studies with the receptor protein CD22, which is found on B cells and is one of several lectin-like proteins that bind to sialic acids. That led him to coin the term by which these receptors are now known — Siglecs (Sialic acid binding Ig-like Lectins) — and to define the larger family they belong to, which he called I-type lectins.

During this period, Varki also followed his journalistic heritage (his mother writes articles for newspapers and magazines in India) and became chief editor of the Journal of Clinical Investigation, shepherding it through the transition to electronic publishing and simultaneously making it the first major journal to go to full open access in 1996. More recently, he collaborated with the National Center for Biotechnology Information and Cold Spring Harbor Laboratory Press to edit the first-ever major open access textbook, the second edition of "Essentials of Glycobiology." In both instances, he demonstrated financially viable models of free access to knowledge, something in which he ardently believes. Another cause Varki advocates for is having on-site infant care facilities for women scientists, having watched the experiences of Nissi Varki, his CMC classmate, spouse and longtime collaborator, whom he also credits greatly for any successes he has had.

In 1998, he made perhaps his signature breakthrough when he examined blood samples from humans and several ape species, including chimpanzees, for their sialic acid composition. The impetus for this project had occurred years earlier, when Varki witnessed a case of serum sickness in a patient he was treating with immunosuppressive serum therapy. Varki had assumed the response was due to an immune reaction against foreign proteins in the horse serum but then read studies suggesting that sialic acids on the proteins might be the antigen.

This seemed odd, given sialic acids' ubiquitous presence, so he conducted a chromatographic analysis of the different primate species and found that humans alone lacked a particular sialic acid called *N*-glycolylneuraminic acid, or Neu5Gc. A follow-up study showed that the cause was a human-specific exon deletion/frameshift mutation in the gene for the enzyme that converts CMP-*N*-acetylneuraminic acid, or CMP-Neu5Ac, into CMP-Neu5Gc, rendering it inactive.

"I realized we had found the first known functionally significant genetic difference between humans and chimps," Varki says of that moment. "One that produced a distinct structural difference with a clear biochemical readout; you could analyze any human or ape cell and identify whether it was human or not." But remarkably, he later found that this nonhuman sialic acid could sneak back into the human body from dietary origins — something he proved by drinking a sample of Neu5Gc himself (with institutional review board permission, of course).

## On Human Nature

The lack of Neu5Gc turned out to be just the first of many genetic changes that have occurred in sialic acid biology during the course of human evolution, which has raised many intriguing questions. "If you compare mice and rats, you might find a couple of differences in sialic acid biology, the same if you compare different ape species," Varki explains. "Yet, between humans and our closest relatives, chimps, we've already uncovered a dozen alterations, most in Siglec receptors, despite less than 60 identified genes involved in sialic acid biology.

"So, something has happened over the past few million years that really spurred a rapid evolution of these particular genes in the human lineage."

In a recent review, Varki points out that sialic acids on the cell surface are common recognition targets by pathogens and that selective pressure by infectious agents is important. "A lot of diseases specific to humans, like falciparum malaria or cholera, are caused by pathogens that target sialic acids," he says. "On the other hand, many other human pathogens disguise themselves by expressing surface sialic acids."

"At the same time, human evolution is like a murder mystery," he adds. "Each change only occurred once, so you can't recreate the crime. And if you just use logic to deduce an answer, you may be wrong. After all, every single cell in a human is covered with sugars, and research has now shown biological roles for glycans that range from the sublime to the ridiculous. So if you mess around with sialic acid biology, you end up changing a lot of functions."

Like any good mystery, the key, says Varki, is to follow all of the available clues to the answer. To do that requires comprehensive and comparative studies of the "sialome" (another term he coined) in humans, other living primates and fossil samples from hominid precursors using chro-

matography and mass-spectrometry as well as employing both "humanized" and "chimpanized" mouse models to compare functions of genes involved in sialic acid biology. And clues that many uniquely human diseases may have some basis in sialic acid changes have brought him full circle back to his roots in medicine.

Of course, sialic acids alone will not answer the question of human origins. That's why Varki founded the Center for Academic Research and Training in Anthropogeny to provide a place where great minds and resources could be brought together to make connections and share ideas. The center is supported by the Mathers Charitable Foundation, which also was instrumental in funding Varki's early evolution projects, for which he is extremely grateful. "I probably couldn't have pursued my research without them, as I don't think probing the meaning of humanity through glycobiology would be high on the NIH funding list."

Varki hopes the efforts of CARTA and related places like the Leipzig School of Human Origins in Germany will help put human evolution in proper perspective.

"We've gone from the Victorian idea of humans as special creatures made in God's image to the other end of the spectrum," he says, where the influence of the popular press, and more recently genome sequencing, has pushed scientists to focus mostly on how humans and chimpanzees are similar.

"Humans are both remarkably similar and remarkably different from chimps," Varki says. "And I think the latter part of that statement needs to be addressed a little more, in a comprehensive way."

Nick Zagorski (nzagorski@asbmb.org) is a science writer at ASBMB.

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# Scenes from the 2010 ASBMB Special Symposia

BY JLYNN J. FRAZIER

This past fall, the American Society for Biochemistry and Molecular Biology held four special symposia as part of a series highlighting cutting-edge science in areas ranging from membrane trafficking to transcriptional regulation. Below are some highlights from the meetings.

Jlynn J. Frazier (jfrazier@asbmb.org) is conference manager at ASBMB.

## *Transcriptional Regulation by Chromatin and RNA Polymerase II*

***Sept. 30 – Oct. 4, Tahoe City, Calif.***

**Far left, top, meeting organizer Ali Shilatifard (center) with best-poster awardees Hidehisa Takahashi (left) and Lu Chen, all from Stowers Medical Research Institute. Far left, bottom, Johnathan Whetstine (left) of the Massachusetts General Hospital Cancer Center and Harvard Medical School chats with Simon Elsaesser from The Rockefeller University. Left, Ohio State University scientist Devi Nair presents her research at the poster session.**

## *Post-translational Modifications: Detection and Physiological Evaluation*

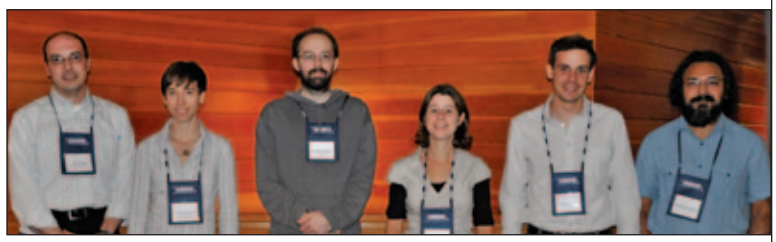
***Oct. 21 – 24, Tahoe City, Calif.***

**Right, Ohio State University scientist Thushani Rodrigo-Peiris (left) presents her poster. Below, Joshua Alfaro of the Pacific Northwest National Laboratory (second from left) presents his poster to meeting co-organizer Gerald Hart of the Johns Hopkins University School of Medicine (middle).**

## *Biochemistry and Cell Biology of ESCRTs in Health and Disease*

***Oct. 14 – 17, Snowbird, Utah***

Top left, meeting organizers (from left) Phyllis Hanson of the Washington University School of Medicine and James Hurley of the National Institutes of Health pose with best-poster awardees Sabrina Simoes of the Curie Institut, Justin Keener of the University of Utah and Julien Guizetti of ETH Zurich. Bottom left, David Katzmann (left) of the Mayo Clinic networks with Markus Babst of the University of Utah, and Jennifer Lippincott-Schwartz of the National Institutes of Health presents her keynote lecture. Below, Graduate/Postdoctoral Fellow Travel Award recipients (from left) Eric Weiss, University of Massachusetts Medical School; Viola Baumgaertel, Ludwig Maximilian University of Munich; Matthew Russell, University of Colorado at Boulder; Natalie Elia, the National Institutes of Health; Julien Guizetti, ETH Zurich; and Kaushik Choudhuri, New York University School of Medicine.



## *Biochemistry of Membrane Traffic: Secretory and Endocytic Pathways*

***Oct. 28 – 31, Tahoe City, Calif.***

(Below, clockwise from top left) Alumni from the Schekman and Rothman Labs reunite (from left): Peter Novick, Elizabeth Miller, Greg Payne, Sandra Schmid, Paul Melançon, Benjamin Glick, Randy Schekman, Vladimir Lupashin, James Rothman, James McNew, Fabienne Paumet, Claudio Giraudo, Nava Segev, Suzanne Pfeffer and Scott Emr. Meeting attendees enjoy a keynote lecture by Scott Emr of Cornell University. ASBMB President Suzanne Pfeffer presents a birthday cake to James Rothman of Yale University. Meeting attendees pose for a group photo.

# A Remedy for a National Ailment

BY ARTHUR GUTIERREZ-HARTMANN

Despite modest increases in the number of underrepresented minorities earning doctoral degrees in the biomedical sciences, the number of tenure-track, funded URM faculty members essentially has remained unchanged for the past 40 years. It is not only a moral imperative but also the responsibility of the entire scientific community to promote, support, nurture and mentor URM trainees. Only when we achieve equality in the diversity of the nation's work force will the full potential of these URM populations optimally impact the progress of the U.S.

## Increasing the Number of Visible Minority Investigators

We only can achieve these goals through synergistic actions by academia and government. The most critical component is to have minority investigators in key positions with high visibility for our undergraduate, graduate and postdoctoral URM trainees.

Historically, the National Institute of General Medical Sciences has provided significant funding, approximately $4 billion for nearly 40 years, through the Minority Biomedical Research Support and Minority Access to Research Career programs (1, 2). These programs have positively affected the number of URM students entering biomedical research training programs and resulted in increased numbers of URM graduate students — from approximately 2.3 percent in 1973 to 3 percent in 1985 and 7.2 percent in 2003.

However, the number of URMs attaining tenure-track, National Institutes of Health-funded, research-oriented faculty positions remained disappointingly bleak during this period (3 – 5). Indeed, a National Research Council panel and NIGMS working group reviewing the NIH's URM efforts concluded that simply obtaining a doctoral degree is too narrow a definition of success and that the NIH needs to increase its efforts if true progress is to be made in increasing URMs in principal investigator-type faculty positions. It is crucial that URM students meet URM investigators who are successful and able to sustain a career that is both intellectually and financially rewarding (2, 6).

From 1966 to 2003, the total number of doctoral degrees awarded in the life sciences increased threefold, yet the total number of tenured scientists essentially has remained constant during this period (5). Only about 39 percent of the most competitive majority doctoral students supported by NIH predoctoral fellowship grants or T32 training grants, and less than 30 percent of those trained at non-NIH institutions, gain tenure-track faculty appointments (5, 7). Thus, given the dramatically reduced number of annual URM doctoral graduates (only 294 of the 4,200 degree earners in 2003) (4, 8), it is clear that even if 30 percent of this URM pool attained tenure-track research faculty positions, it would have little effect. The very limited number of tenure-track faculty positions makes these extremely competitive (8) and is, no doubt, a key contributor to the severe shortage of URMs in research-oriented faculty positions (4).

## Holistic Training Approaches

What makes a graduate student the most fit for a PI faculty position? Specifically, what are the features that most reliably correlate with success? Is it personality, critical transition choices, training history, the role of mentors, the impact of the graduate program or the postdoctoral experience? Are the features the same for URM students as for majority students?

Clearly, there are factors separate from purely academic issues that contribute to overall URM success. The University of Maryland, Baltimore County Meyerhoff and the University of California, Berkeley Biology Scholars programs, two of the most successful college programs in graduating URMs with science degrees, have been successful precisely because they specifically address nonacademic issues (9, 10). For example, these two programs have strong leaders who address social, academic and scientific enculturation; establish high expectations for performance and goals; establish URM peer support groups, tutors and mentors and actively engage in making institutional culture more inclusive and minimizing covert prejudices.

While the above nonacademic factors contribute to college success, several additional factors likely have contributed to the very low rate of URMs obtaining faculty positions. These include a focus by the NIH and graduate programs on simply priming the URM pipeline without a

clear plan to shepherd URM trainees to faculty positions, a lack of appreciation of the critical importance of URM mentors, ineffective enculturation of an elitist scientific attitude in URMs and poor advising on the importance of the postdoctoral experience with regard to obtaining a research faculty position. In summary, a strong case can be made that these hidden curricular and institutional cultural factors may be the most important in successfully leading URM, and even majority, graduate students to independent PI positions (11).

## Postdoctoral Training

Although graduate training is formative, postdoctoral training is defining, because it delineates the work that a trainee will use to start his or her laboratory. Not surprisingly, about 20 of the most elite, research-intensive

> **"We only can achieve these goals through synergistic actions by academia and government."**

institutions have generated the vast majority of PIs who currently hold tenure-track, research-oriented faculty positions. Unfortunately, the critical importance of postdoctoral training with a top-notch scientist is not adequately emphasized to URM graduate trainees, who are less likely to move far from home for training, due to financial, cultural, personal and/or family reasons. (9, 10)

A key priority for graduate programs should be leading URM predoctoral students to postdoctoral positions with world-class scientific leaders. Trainees should pursue postdoctoral training with someone who not only does cutting-edge, world-class science but also is a good mentor. Moreover, graduate programs should set high expectations for performance and goals but also establish URM peer support groups and tutors, provide forums for substantive interactions between the most successful scientists and trainees, continuously emphasize the importance of the postdoctoral experience and provide a group of successful URM mentors as role models. It is imperative to establish a growing cadre of URM trainees who will continue to help one another through their careers, much as the Pew Scholars and Howard Hughes Medical Institute investigators have done, in order to optimize for career success.

## Senior Minority Faculty

Typically, URMs lack faculty role models of the same ethnicity throughout their training, yet this is a critical attribute for success. No doubt this is due to the severe paucity of URM faculty in tenure-track, research-oriented positions. Moreover, URM faculty frequently are asked to participate and provide the diversity voice and perspective on national and local committees, but this typically is uncompensated and unrewarded by promotion committees. In this regard, this group is particularly vulnerable and increasingly faced with the difficult decision to reduce their URM volunteer training activities in order to survive. Faculty members who are in this position should be afforded salary support so that they can serve as role models, fully participate in the experience and provide career advice. Perhaps funding agencies should invest more resources at the other end of the pipeline: it may be time for a URM merit award for that most rare breed of all — the highly successful, senior URM faculty.

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# Defining the Boundaries

## *JBC associate editor is working to improve scientific ethics education in China*

BY NICK ZAGORSKI

Xiao-Fan Wang, the Donald and Elizabeth Cooke professor of experimental oncology at Duke University and a Journal of Biological Chemistry associate editor, certainly had heard about and witnessed some unusual article submissions. He recalls one instance in which a colleague rejected an article because the author had apparently copied material straight from another paper only to come across another article for review by the same author a few days later; it was the exact same paper, still containing the copied text, submitted to a different journal.

Although such anecdotes can be humorous, they also can be distressing, particularly if the authors involved are from Wang's home country of China, a rapidly emerging scientific power but one where publishing output seems to be outpacing publishing knowledge.

Of particular concern was a recent news story in Nature describing an anonymous survey in which one-third of Chinese researchers reported that they had committed some form of scientific misconduct. "If someone hears that, they might think Chinese science is corrupt," Wang says, "which is not true. Of the reported incidents, true fraud only accounted for a tiny minority. The most common issue was that Chinese authors had plagiarized sentences or paragraphs."

The underlying problem, as others have noted, is the language barrier Chinese scientists face when publishing internationally, particularly given that Chinese characters are fundamentally different from the English alphabet. Another, less publicized factor is cultural: Wang points out that Chinese secondary education has long placed a stronger emphasis on being able to memorize and recite previously written material (like famous poems) than on coming up with original writings.

"Now, I'm not excusing these actions," Wang continues, "but I think it's important to understand the reasoning behind it. Of course, it's more important to remedy it. Scientists in China want to do the right thing; the country doesn't have the proper system in place."

Wang has been taking an active approach to trying to help China better educate its researchers about the rules and responsibilities of scientific publishing. This educational effort is beneficial for his homeland as it becomes a science power but also serves JBC's interests. "China is going to be a big market for the journal, and we want more submissions, but we don't want any retractions."

Wang figured funding agencies would be the best places to start, so he approached the president of the Chinese equivalent of the National Science Foundation and mentioned that they had a responsibility to push for changes that would promote good ethics, similar to the way the National Institutes of Health requires an ethics class for some of its grantees.

Not long after, he got a call from the Chinese foundation's deputy director of biological sciences and was asked to identify an ethics textbook that could be translated into Chinese. So, he found a book on scientific integrity written by Francis L. Macrina, the vice president for research at Virginia Commonwealth University. "Macrina was supportive of my proposal and sent me a copy of the book so I could see if it's current enough for translation; he's writing a third edition now, but China is hoping to introduce the course into next year's curriculum, so hopefully the second edition will work."

Wang also penned a letter to the vice minister of the Chinese Ministry of Science and Technology, asking him about changing the way the funding system works. Specifically, he was concerned with the megaproject grants that generally are awarded to laboratory consortia with the best ability to network with bureaucrats, thus making schmoozing more valuable than doing research or properly training students. He also encourages individual institutes to stop creating extra pressure to produce high-impact papers through practices such as financial incentives or graduation requirements.

Wang also hopes that the Chinese funding agencies can take a stronger role in punishing individuals when the rare cases of true data fraud arise. "Maybe it could be something like a loss of funding for three to five years, or even a lifetime ban on receiving government funding if the offense is very serious — something that will show to everyone that if you get caught, you have to face the consequences," he says. "But don't leave misconduct issues

**JBC Associate Editor Xiao-Fan Wang of Duke University has been taking an active approach to trying to help China better educate its researchers about the rules and responsibilities of scientific publishing.**

in the hands of university administrators, because they can drag their feet in such situations."

"I know some universities in the United States have not been immune to such problems in recent years," he continues, "so I know how difficult it can be for one institution to punish its own and publicize it."

Still, although effective punishing of severe cases is required, Wang believes in an education-first approach, and he believes that China will be responsive to his, and others', recommendations. "One element of the Chinese government that works in our favor is that much of Chinese science is run by technocrats and not by politicians."

"They tend to think very academically and logically," he says, "and that makes necessary transitions quicker. Two years ago, I organized a letter-writing by more than 50 scientists in the U.S. and China to the prime minister about the exodus of students to foreign graduate programs and stated that the main problem was that compensation at Chinese graduate schools was very low. And he recognized the problem and raised stipends threefold. So I'm quite hopeful we will see meaningful changes soon."

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## Online

Go to http://bit.ly/ATodayChinaEthics to view a video of Xiao-Fan Wang speaking more about improving ethics in China.

# ASBMB Introduces Website for Summer Undergraduate Research Programs

BY ANN STOCK

Most bioscientists first experience laboratory research as undergraduate students, and many look back on this experience as an important factor in their decision to pursue a career in science. Some departments incorporate independent research or research theses into the required curriculum, but at many institutions, undergraduates are left on their own to find research opportunities. Many routes are available for finding part-time research positions at one's home institution during the academic year, often on a volunteer basis or for academic credit. Finding a paid position for the summer can be more challenging. This especially is true for undergraduates who seek positions outside of their home institutions, such as students at primarily undergraduate institutions with limited research opportunities and out-of-state students who need to return home during the summer.

Students looking for summer research opportunities outside of their home institutions should consider applying to some of the many summer undergraduate research programs hosted by institutions throughout the country. Most of these programs are advertised through websites at each institution, but finding them can be tedious. To assist undergraduate students in finding summer research programs and vice versa, the American Society for Biochemistry and Molecular Biology has created a website (www.asbmb.org/SummerResearch) for the cumulative listing of summer undergraduate research programs. We hope that this will prove to be a useful resource for both students and host institutions.

## The Website

The summer research program listing resides within the Careers & Education pages of the ASBMB website. Programs listed on the website have been self-identified through a request sent to all ASBMB members this past September. The response has been strong, with more than 120 programs in approximately 40 different states listed so far. The completeness of the list relies entirely on the participation of program representatives at host institutions. It is not too late to have your program added to the list — just go to www.asbmb.org/SummerResearch.

Visitors to the website will find summer undergraduate research programs organized by state and will include the name of the institution, the 2011 application deadline and, most importantly, a link to the program's website where specific details about the program and the application procedure can be found.

## Summer Research Opportunities

Summer research internships provide an excellent opportunity for students to pursue research on a full-time basis. This complete immersion is extremely valuable, especially for students who are just beginning to do independent research. Following experiments from start to finish provides a clearer and deeper understanding of research than can be gleaned from a few hours interspersed with classes during the academic year. Additionally, daily repetition of procedures allows for quicker assimilation and mastery of technical skills. Thus, a summer research experience can significantly increase the productivity of part-time research pursued in subsequent academic years.

There are two basic routes for summer research


**The ASBMB summer research program listing includes information on application deadlines and links to the programs' websites.**

experiences: independent arrangements with an individual laboratory or participation in an organized summer research program. For students already working in a research laboratory or for those who plan to continue working in a laboratory at their home institutions throughout the academic year, individual arrangements are a logical choice. For students seeking summer research opportunities outside of their home institutions, formal programs offer some advantages.

## Program Benefits

Summer research programs vary greatly from one institution to another, but all are designed to make research opportunities more accessible to students. Programs usually provide access to many different laboratories through a single application, eliminating the need for students to initiate multiple contacts to individual laboratories. Furthermore, stipends provided by the program often enable research in laboratories that would otherwise be unable to fund undergraduate research fellows. In addition to an individual laboratory research experience, programs typically offer activities aimed at providing an orientation to the campus environment, an overview of different research projects and development of research and career skills. Importantly, programs bring together undergraduates working in different laboratories to discuss research as peers, to network with students from other institutions and to promote camaraderie that creates an enjoyable and memorable summer experience.

Summer research programs also benefit host laboratories and institutions. Undergraduates can make valuable contributions to research programs. Their perspectives are fresh and unconstrained by knowledge of how difficult a project might be. They tackle projects with enthusiasm and optimism, occasionally producing results that have eluded more experienced researchers. Additionally, guiding an undergraduate can be a rewarding training activity for graduate students and postdoctoral fellows, providing an important — and often first — mentoring experience. Summer programs are also a great way to showcase the research and graduate programs at an institution to undergraduate students who have an interest in research and future graduate studies.

As this year draws to a close, it already is time to start thinking ahead to the summer of 2011. Start exploring options now for an exciting summer research internship, and check out the ASBMB website if you are looking for a program outside of your home institution to enhance your research experience.

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### Looking for a summer research opportunity?

- **Visit the ASBMB website:** If you are looking for a research opportunity outside of your current academic institution, our Web-based resource (www.asbmb.org/SummerResearch) can help you find programs throughout the country.
- **Start early:** Most programs have application deadlines in February or March, but some are as early as January. Positions in individual laboratories usually are filled long before summer begins.
- **Submit a competitive application:** Whether applying to a program or an individual laboratory, provide a complete and professional application. This might include a curriculum vitae, transcripts or a summary of coursework and GPA, a digest of any relevant experience and a statement about your interest in the specific research pursued by the laboratory.
- **Research the research:** Check out individual laboratory websites to find research that is especially interesting to you. Your application to an individual laboratory will be stronger if you are familiar with the research pursued in the laboratory.
- **Network:** Ask your mentor, adviser or instructor at your current institution for help in finding a summer research position. A letter, e-mail message or phone call from another principal investigator can be a very helpful introduction.
- **Be persistent:** Apply to multiple programs or laboratories and do not get discouraged by rejection. A negative response often simply indicates lack of space or funds rather than dissatisfaction with the applicant's qualifications.

# Distracters or Detractors? What's the Catch?

BY PETER J. KENNELLY

## Synthesizing versus Selecting

Perhaps the most important transition that any student of science must make is the leap from consumer to producer. Most students majoring in science, technology, engineering and math areas have the capacity to become quite adept at absorbing and utilizing existing information and methodologies. Although such technical knowledge and proficiency generally is sufficient to obtain a degree and become gainfully employed as a member of the supporting cast, becoming an originator of new facts, new concepts and new technologies requires the capacity to engage in creative and analytical thought on a routine basis.

**"If Charles Darwin had been trained in a system overly reliant on multiple-choice testing, would he ever have conceived of natural selection?"**

I generally like to initiate a discussion on the nature of science by asking, "How can a scientist have confidence in the answer they obtain when asking a question that never has been raised before?" Because students are all about getting the "correct" answer, this question places the issue in a very practical and familiar context. How do you prepare for an exam or complete a homework assignment in a course for which no assigned text or answer key exists, and no authority figure is available to confirm or deny the validity of your answer?

As science teachers, our most important goal should be to guide students in developing their ability to apply fundamental scientific principles and logical reasoning to formulate and test scientific hypotheses, as well as the analytical and critical reasoning skills to interpret the results. It therefore would appear reasonable to expect STEM curricula to be replete with exercises and questions that challenge students to draw upon these skills to synthesize an original response. Unfortunately, the pressures of large class sizes and doing more with less frequently induce instructors to employ multiple-choice tests as their primary, and sometimes exclusive, format for assessing student progress.

## I Thought You Were Trying to Trick Me

Unfortunately, picking from a list of prepared responses falls well short of providing students with a chance to exercise their abilities to draw upon their knowledge and reasoning skills to generate an answer whose origins are indigenous to their own intellect. Moreover, in attempting to increase the sophistication of the thought processes required to select the correct answers on a multiple-choice test, instructors often exacerbate the situation by choosing inappropriate "distracters" (the alternative answers from which the student must select).

One form of distracter that can do more harm than good is to append some mysterious condition such as, "Choose the most correct answer from the choices given below." What is the definition of "most correct"? Doesn't the perception of which of the correct answers is the "most" correct depend upon (frequently unmentioned) circumstances? Another common distracter is the "parade of permutations": a), b), c); both a) and b); b) and c) but not a); none of the above or all of the above. Both of these rubrics share the property of transforming normally correct answers into incorrect ones. In the first case, one can select a perfectly correct answer and receive no credit because it was not the "most" correct. Similarly, if both a) and b) are correct, a student who recognizes that a) is correct or b) is correct, but not that both are, receives the same zero score as a person who marked c) or "none of the above" even though the former responses betray greater insight into the correct answer.

The use of deception or misdirection as a means for differentiating amongst the top performers in a class can be counterproductive at a number of levels. First, such a format tends to reward the memorization of minutiae and the ability to recognize the subtle semantic cues indicating that a particular question has some "twist" to it. While these qualities may correlate to some degree with a student's capacity for critical thinking and intellectual synthesis, differentiation through deception neither encourages nor stimulates the development of these higher-level skills. When instructors become overly reliant on differences in form rather than substance when constructing a multiple-

choice examination, some students become alienated from science, seeing it as a "game" they can never "win."

### Trust, but Verify

As a research mentor, I always am on the alert for the occurrence of what now is popularly referred to as a "teachable moment". In my best Socratic style, I will begin asking the student questions, "How can a protein bind to an ion-exchange column in the presence of the large excess of counter ions present in a low-salt loading buffer?" "How does our laboratory refrigerator work?" If the student encounters difficulty with my opening question, I emulate my mentors and ask a follow-up question that generally is more focused and simple than the initial one. "When a gas is allowed to expand, where does the energy to support this process come from?" With frightening regularity, I encounter students unable to formulate the answer to even a simple question or who provide bizarrely complex answers. When, in my frustration, I ask the student why they are having so much trouble answering even extremely basic questions, an increasingly common response is, "The question was too simple. I thought you were trying to trick me."

When students are fed a steady diet of "trick" questions and distracters that rely on disguise rather than substance, an insidious form of conditioning occurs. To protect themselves against being fooled by the various forms of misdirection and camouflage encountered among the distracters, many students soon learn to consider every question to be a trick question until proven otherwise. This adaptive mechanism can have insidiously unfortunate consequences. The practice of habitual skepticism requires that students condition themselves to distrust their powers of observation, to view their initial reasoning as suspect and to reject their instincts, as these constitute the prime targets of the deceptive distracter.

Tragically, such conditioned skepticism selects against several of the most important attributes of the successful scientist — the ability to correctly utilize and trust in logic, reason, the experimental method, careful observation and measurement. If Charles Darwin had been trained in a system as overly reliant on multiple-choice testing as most contemporary high schools and universities, would he ever have conceived of the process of natural selection? Or, upon first perceiving patterns of adaptation in the animals and plants around him, would he simply have rejected this as an anomaly arising from some catch hidden below the surface?

The multiple-choice examination will be with us for as long as "do more with less" remains the order of the day in public education. However, it is important that the menu of potential answers that we ask students to select from differ from one another in substance, with no attempt to hide that substance under some semantic disguise. If multiple possibilities are correct, tests should be constructed such that students can select amongst individual entities instead of selecting the one correct combination. Will this result in some score compression, as the culling effect of deceptive distracters and convoluted questions is lost? Perhaps initially, but this is a point that can, and should, be addressed by adding questions that are more challenging in substance rather than form.

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# UAN Chapter Educates about Organ Donation

BY RAY ROMANO AND ANN AGUANNO

Marymount Manhattan College's Undergraduate Affiliate Network chapter recently was invited to partner with the New York Organ Donor Network in its College Initiative program. The federally funded program aims to increase awareness and education about organ, eye and tissue donation on college campuses. Due to the efforts made by their biology students during the past four years through their annual Halloween-themed "Give us your organs!" awareness event, the NYODN has awarded the MMC UAN chapter a two-year, $1,000 grant to continue and expand these efforts.

According to the NYODN website, more than 100,000 people need life-saving organ transplants in the United States. However, the number of registered donors is decreasing. It has become the network's mission to shed light on organ donor issues to college-age students, and MMC has stepped up to the challenge. In fact, the MMC UAN chapter has pledged that it will help enroll 200 new organ donors.

The chapter already has made great strides toward its goal. The club regularly sets up awareness tables where UAN members can educate classmates on the process, need and value of becoming an organ donor, and the club helps students enroll in the donor registry.

These events are a great success and will continue throughout the upcoming academic year. Future events include a continuation of the "Give us your organs!" event, a college-wide movie night and discussion about organ donation and a "Jeopardy"-style table at one of the college's major festivals where students can compete for prizes using their knowledge of organ donor information.


**Marymount Manhattan College Undergraduate Affiliate Network chapter members at their annual Halloween-themed "Give us your organs!" awareness event.**

Ray Romano is an undergraduate biology major and Ann Aguanno (aaguanno@mmm.edu) is an associate professor of biology and director of the Northeast Region of the UAN. Both are at Marymount Manhattan College.

## 2010 Graduation Survey

Since 1998, the American Society for Biochemistry and Molecular Biology has conducted an independent survey of schools to determine how many students are graduating in biochemistry and molecular biology.

The 2010 survey revealed that the ratios of female to male graduates at the baccalaureate and master's levels have remained essentially the same for the last two years. However, there was a significant increase in the reported number of American Indian or Alaskan Native women who received baccalaureate degrees.

View the full report at www.asbmb.org/2010survey.aspx

| 2010 ASBMB Graduation Survey Results | Female B.A./B.S. | Male B.A./B.S. | Female M.A./M.S. | Male M.A./M.S. | Female Ph.D. | Male Ph.D. |
|---|---|---|---|---|---|---|
| American Indian or Alaskan Native | 27 | 12 | 0 | 0 | 5 | 6 |
| Asian | 170 | 134 | 18 | 19 | 29 | 29 |
| Black, not of Hispanic origin | 25 | 49 | 11 | 8 | 6 | 4 |
| Hispanic | 30 | 26 | 3 | 2 | 3 | 4 |
| Pacific Islander | 4 | 0 | 0 | 0 | 1 | 5 |
| White, not of Hispanic origin | 482 | 501 | 43 | 40 | 70 | 85 |
| International students | 49 | 40 | 31 | 22 | 54 | 50 |
| Unspecified | 137 | 113 | 3 | 4 | 5 | 6 |
| TOTAL | 924 | 875 | 109 | 95 | 173 | 189 |

# Yes, I Can!

## Going from Industry to Academia and Back Again

BY SHAREL M. FIGUEREDO

### The Realization

A high school chemistry class with a teacher who encouraged me and recognized my potential led me to pursue a college degree in science. I completed my bachelor's degree in Mumbai, India and then worked at Kuwait University as a research assistant. I loved the three years that I spent there, investigating the effects of oil pollution from the Persian Gulf War on marine flora and fauna. The experience also made me realize that, to have a successful career in scientific research, I would need a higher degree. So, I enrolled in the masters program in chemistry at San Jose State University and spent the next two years doing research on chiral stationary phases using capillary electrochromatography.

### The Turning Point

After graduating, I remained in the U.S. and got a job doing research in microfluidics. This was my first taste of working in industry. I spent the next seven years working in industry and loved the fast-paced nature of the research and the excitement of inventions and novel discoveries. I learned to work both independently and as part of a team. I learned to meet tight deadlines and to manage multiple projects. However, there were times when I felt that having a doctoral degree would allow me to rise higher in my career, and, as the saying goes, the sky would be the limit.

### A New Decision

I applied and was accepted into the doctorate program for biological sciences at the University of California, Irvine. Going back to school was difficult. It involved sacrifices, long hours, multitasking and the support of my family. The hardest part was balancing my life: I was married and had two school-aged children. I wanted to be a great student, wife and mother.

But, having worked in industry, I also had the tools necessary for graduate school: persistence, endurance and a passionate drive for science. I spent four years and nine months in school, and I loved every minute of it. I gained friends along the way and earned the respect of my colleagues and adviser. My dissertation on the structural determinants of biological activity in mouse pro-α-defensins resulted in a few articles published in peer reviewed journals. My family is proud of me and I am truly thankful for their support.

### The Payoff

Now that I am working as a scientist for a multinational company in Carlsbad, Calif., one of my ambitions in life has been fulfilled. Five years ago, I had a dream that I thought was impossible to achieve with a family. But, when that acceptance letter from UCI came, I decided to take a leap of faith. I am happy with my decision, and I am ready to meet the new demands in my career. I am sure there always will be challenges along the way, but, just as before, all I will need to do is take leaps of faith.

Sharel M. Figueredo is a developmental scientist at Beckman Coulter Inc. in Brea, Calif. She has also worked at Ciphergen Biosystems Inc. and Aclara Biosciences Inc., both in California. Figueredo earned her doctoral degree in biological science from the University of California, Irvine and her master's degree in chemistry from San Jose State University.

# Combining Filmmaking and Science at Wesleyan University

BY MANJU HINGORANI AND JACOB BRICCA

"If you were asked to think about muscle development, the first thing that would probably come to mind would be hitting the gym." Rosemary Ostfeld's film opens with these words, accompanied by pounding music and scenes of toned bodies working out in a gym. However, the viewer is caught by surprise when the film reveals itself to be a documentary about Stephen H. Devoto's research into how muscle cells develop long before that trip to the gym.

Ostfeld was one of 12 students who enrolled in "Making the Science Documentary," an experimental cross-disciplinary course that we co-taught for the first time in spring 2007 at Wesleyan University. The course was designed to introduce undergraduate students to the life sciences (taught by Manju Hingorani) and to documentary filmmaking (taught by Jacob Bricca) in order to teach them the skill and art of communicating science-related topics through visual media. The students, for the most part, were nonscience majors with little or no prior filmmaking experience. Our expectation was that by the end of the course, they would be able to tell compelling stories about science through documentary films.

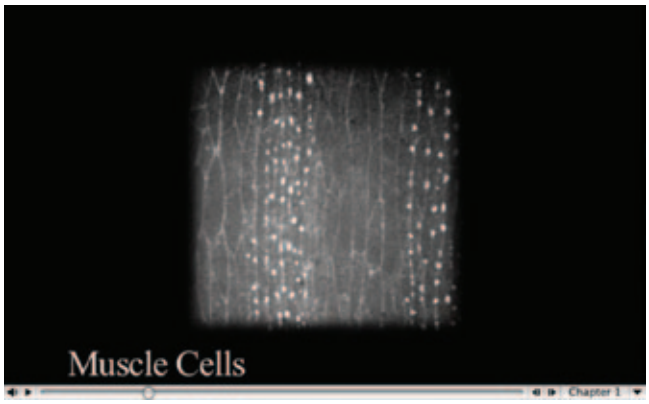
The challenge of creating a one-semester classroom experience in which students could both learn the filmmaking skills necessary to create professional quality documentaries and get a solid grounding in the scientific subject they had to communicate to an audience was daunting. Moreover, we could not find an analogous course taught elsewhere that might serve as a model. As we grappled with developing the course, the idea of focusing on research in the Wesleyan science community took hold in our minds.

We wanted students to learn about biology at the molecular through organism levels and, just as importantly, to learn about how science is done by getting an inside look at the fascinating world of life science research. In order to achieve this goal, Manju recruited four Wesleyan professors as potential subjects of the students' documentary films: Ishita Mukerji and Scott Holmes of the molecular biology and biochemistry department, who work on protein structure/function and transcriptional regulation, respectively, and Stephen H. Devoto and Janice R. Naegele of the biology department, who work on cellular development and neurodegeneration related to epilepsy, respectively. Manju taught students the scientific concepts and content necessary to engage intellectually with the research. Students also had full access to personnel in the scientists' laboratories, including their own undergraduate peers who worked there as research assistants.

Jacob taught students technical filmmaking skills such as composition, interviewing techniques, lighting and editing, and we viewed short science documentaries (e.g., from the NOVA scienceNOW series) to analyze relevant models of non-fiction filmmaking. Later in the course, students developed and refined proposals for film projects that reflected their particular interest in the research areas. They worked in groups of three to shoot hours of footage and interviews and then made individual six to ten minute documentary films. Since Manju had pre-arranged access to the potential subjects of their films, the students could spend a lot of time deciding how to present complex scientific concepts in a clear and direct manner and how to engage their audience with interesting characters through the use of visual information rather than verbal explanation. One of the most exciting aspects of the class was the degree to which it brought students into contact with the day-to-day lives of researchers. It is difficult for non-scientists to understand what doing science is really like, and our students had the opportunity — indeed the obligation — to carefully observe and understand the workings of a research group and then show this world to other people.

Just as important for our students' education was that they learned about the exciting possibilities of the documentary genre as well as its limitations. There is a great fascination these days with turning all forms of communication into easily digestible bits, supposedly the only kinds of stories that suit the YouTube generation, but it is not always obvious how much is lost along the way. We think that by experiencing firsthand the degree to which matters have to be simplified for a short documentary film and just how little scientific information might make it into the final product, our students became more critical consumers of the genre.







**An experimental course at Wesleyan University taught undergraduates how to make science documentary films.**

Another version of the course was offered in spring 2009 as a collaborative project with retired nurse and educator Ann Anthony, and, in this case, the focus was on the nursing profession. Two of our students' films were selected for showing at the 2009 Hartford Regional Nightingale Awards for Excellence in Nursing gala in Connecticut.

The students' learning experience in the course is best summarized by Chris Doucette, a molecular biology and biochemistry major and recipient of the 2009 American Society for Biochemistry and Molecular Biology Undergraduate Affiliate Network's Undergraduate Research Award, who said, "I have always been interested in how science has been represented through both still and moving images, and this class really taught me how documentaries can be effective tools for conveying information and educating the public about pressing social and scientific issues."

The course will be offered again in spring 2011, this time with Suzanne O'Connell of the earth and environmental sciences department, who will focus on environmental studies, specifically sustainability issues related to the production and distribution of food. We are looking forward to future iterations of the course that take on a variety of scientific disciplines.

*Initial development of "Making the Science Documentary" was supported by a Wesleyan Fund for Innovation, Wesleyan Service Learning Center, Howard Hughes Medical Institute and a National Science Foundation Early Career Development Award (Hingorani). Wesleyan continues to support development of collaboratively taught, cross-disciplinary courses through initiatives such as the Sciences Across the Curriculum project (for more information, see http://bit.ly/xdisciplinary).*

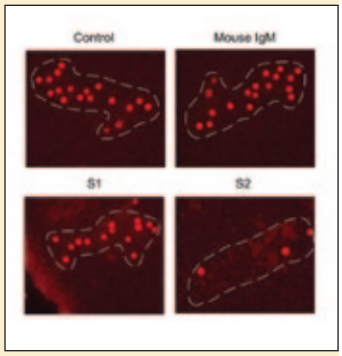
Manju Hingorani (mhingorani@wesleyan.edu) is an associate professor of molecular biology and biochemistry, and Jacob Bricca (jbricca@wesleyan.edu) is an adjunct assistant professor of film studies. Both are at Wesleyan University.

## For More Films:

To see some films made by students who took the "Making the Science Documentary" course, go to http://bit.ly/ATodayDocumentary.

## Generating Carbohydrate Antibodies

Cell-surface glycans play roles in a variety of immune functions, and to understand those functions, it is important to define which glycans are expressed on a cell surface at a given place and time. Monoclonal antibodies against glycans are problematic, however, as many different types of glycans are expressed intrinsically in animals. In this study, the researchers developed an efficient method of creating anticarbohydrate mAbs by immunizing mice that lack the enzymes to synthesize target glycans, specifically two *N*-acetylglucosamine-6-*O*-sulfotransferases. These mAbs, called S1 and S2, could bind to high endothelial venules in lymphoid tissue; S1 bound primarily to sulfated *O*-glycans, whereas S1 bound to both sulfated *N*- and *O*-glycans. The binding of S1 or S2 to leukocytes resulted in significant decreases in lymphocyte homing to lymph nodes and also decreased leukocyte adhesion to HEVs. These studies suggest that sulfated *N*- and *O*-glycans cooperate in lymphocyte homing and immune surveillance and provide a link between glycan structure and cell trafficking to secondary lymphoid organs. Considering the importance of glycan structures in other immune functions, the use of anticarbohydrate mAbs should become an increasingly important methodology.




Antiglycan mAbs S1 and S2 can inhibit the binding of labeled leukocytes to HEVs (outlined with dotted line) in peripheral lymph nodes.

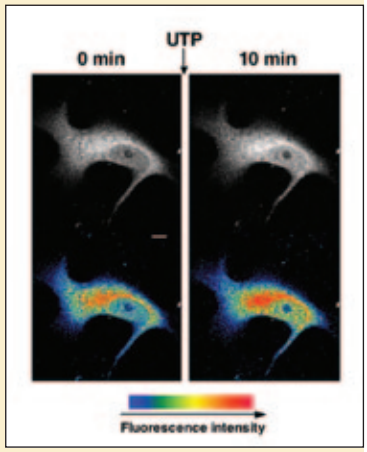
**Novel Anticarbohydrate Antibodies Reveal the Cooperative Function of Sulfated *N*- and *O*-Glycans in Lymphocyte Homing**

Jotaro Hirakawa, Koichiro Tsuboi, Kaori Sato, Motohiro Kobayashi, Sota Watanabe, Atsushi Takakura, Yasuyuki Imai, Yuki Ito, Minoru Fukuda and Hiroto Kawashima

J. Biol. Chem., published online Oct. 7, 2010

## Following PKCδ's Trail

The protein kinase C δ isoform promotes programmed cell death in response to apoptotic stimuli. Typically, PKCδ is activated indirectly through a tyrosine kinase cascade, and then it translocates to the nucleus to induce apoptosis; in some instances, though, PKCδ can be activated directly by phorbol esters, at which point it translocates to the plasma membrane to induce apoptosis. In this article, the researchers developed an approach to visualize the spatial and temporal properties of PKCδ activation using a genetically encoded Förster resonance energy transfer-based reporter specific for this isoform, known as the δ C kinase activity reporter. They observed both mechanisms of activation; phorbol esters triggered fluorescence at the plasma membrane (and also somewhat in the Golgi and mitochondria) in an Src-independent manner, whereas the G-protein-coupled receptor agonist UTP induced activity in the nucleus in an Src-dependent manner. This Src requirement was not solely for translocation but for PKCδ activation as well, as PKCδ pretagged to the nucleus did not activate in the presence of Src inhibitors. This study not only gives new insights into the regulation of PKCδ but also provides a new technological advance for the entire PKC signaling field.




The GPCR agonist UTP stimulates the nuclear translocation and activation of PKCδ.

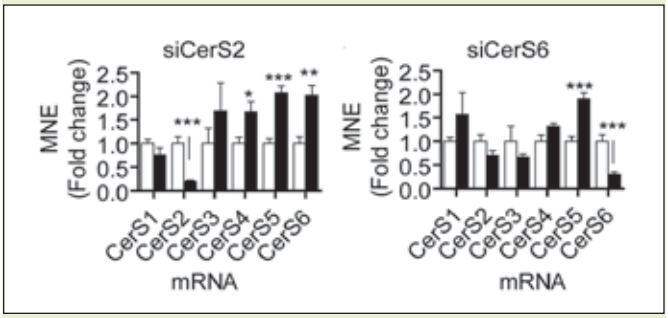
**Protein Kinase C δ-Specific Activity Reporter Reveals Agonist-evoked Nuclear Activity Controlled by Src Family of Kinases**

Taketoshi Kajimoto, Seishiro Sawamura, Yumi Tohyama, Yasuo Mori and Alexandra C. Newton

J. Biol. Chem., published online Oct. 19, 2010

# Complex Inter-regulation of the Cers

Although several types of sphingolipids exist within a cell, they all share a common backbone — ceramide. To date, six enzymes, named ceramide synthases, have been identified as responsible for producing Cer. In this study, researchers examined how individual CerS proteins maintain and regulate the cellular pool of Cer species and other sphingolipids, using small interfering RNAs to decrease the expression of CerS1-6 in a human adenocarcinoma cell line, MCF-7. The knockdown of individual CerS proteins resulted in increased expression of nontargeted CerS proteins and shifted the profile of Cer and other sphingolipid species but did not decrease the total level of sphingolipids. When multiple CerS proteins were knocked down simultaneously, the total level of Cer did not change but caused upregulation of other sphingolipids that are associated with other sphingolipid metabolism pathways as well as increased ER stress responses. Together, these data suggest that Cer synthesis is regulated highly and maintained through the redundant and counter-regulatory network of CerS-mediated synthesis — a finding that provides more insight into the complexities of lipid biosynthesis.




Small interfering RNA-mediated knockdown of CerS2 (left) and CerS6 (right) cause a shift in the expression of nontargeted CerS proteins.

**Selective Knockdown of Ceramide Synthases Reveals Complex Inter-regulation of Sphingolipid Metabolism**

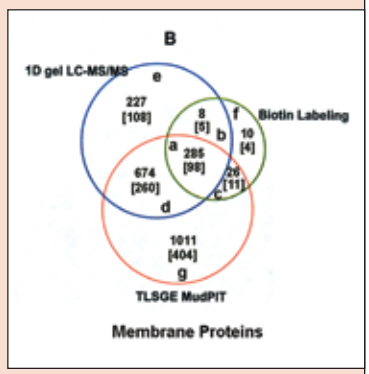
Thomas D. Mullen, Stefka Spassieva, Russell W. Jenkinds, Kazuyuki Kitatani, Jacek Bielawski, Yusuf A. Hannun and Lina M. Obeid

J. Lipid. Res., published online Oct. 11, 2010

JLR

# Gondii's Membrane Revealed

Toxoplasma gondii, an obligate intracellular parasitic protozoan that normally causes self-limiting infections in cats, also can infect humans. Toxoplasmosis, the acute illness caused by this intracellular parasite, often manifests itself as encephalitis, causing miscarriages in pregnant women and death in immunocompromised patients. In this study, the researchers employed three proteomic techniques to generate a comprehensive catalogue of the membrane proteins in T. gondii. Two of the techniques — 1D gel liquid chromatography-tandem mass spectrometry and TLSGE MudPIT — targeted the entire membrane proteome, whereas the third — BDAP LC-MS/MS — specifically targeted integral plasma membrane proteins. When the researchers combined the results from each technique, they identified 2,241 membrane protein sequences with at least one predicted transmembrane motif — a number that translates to 841 nonredundant proteins or protein clusters. Based on annotation of the T. gondii genome, a large portion of the proteins identified are membrane proteins; however, 42 percent are hypothetical proteins, half of which appear unique to T. gondii. The unique and novel membrane proteins identified in this study likely represent new drug targets and will inform the pathophysiology of T. gondii.




A Venn diagram showing the membrane proteins in Toxoplasma gondii identified using three different proteomic approaches.

**Comprehensive Proteomic Analysis of Membrane Proteins in Toxoplasma gondii**

Fa-Yun Che, Carlos Madrid-Aliste, Berta Burd, Hongshan Zhang, Edward Nieves, Kami Kim, Andras Fiser, Ruth Hogue Angeletti and Louis M. Weiss

Mol. Cell. Proteomics, published online Oct. 10, 2010

MCP

# Remembering Richard E. Pagano

BY MICHAEL KOVAL

Richard E. "Dick" Pagano, a pioneer scientist in lipid cell biology, recently died at the age of 66. At the time, he was the head of a vibrant and productive laboratory in the department of biochemistry and molecular biology at the Mayo Clinic College of Medicine in Rochester, Minn. An overarching theme of Dick's research for the past 45 years was the innovative application of lipid biophysics and imaging technology to understanding the molecular organization of cell membrane lipids.

PHOTO CREDIT: DAVID MARKS.

Dick trained with Thomas E. Thompson at the University of Virginia, where he received his doctoral degree in biophysics, studying ion permeability in model membranes. He continued to work with model membrane systems during his postdoctoral work with Norman L. Gershfeld at the National Institutes of Health and then with Israel R. Miller at the Weizmann Institute. During a brief fellowship in Dennis Chapman's lab at the University of Sheffield, Dick performed some of the first direct measurements confirming that gel and liquid phases could coexist in the same membrane.

Dick started his own lab in 1972 at the Carnegie Institution department of embryology in Baltimore, Md., where he worked for more than two decades before moving to the Mayo Clinic. It was at Carnegie that Dick first applied his experience using model membranes to addressing the central and largely unanswered questions in the cell biology of membrane lipids. The combination of lipid biophysical and cell biological approaches proved extremely fruitful. Dick's initial work elucidated mechanisms of interaction between artificial membrane vesicles and cells, which has relevance to the pharmacologic use of liposomes. His work also provided an early method of introducing labeled lipids into the outer leaflet of the plasma membrane. Ultimately, the creative use of lipid probes incorporated into cell membranes to study lipid metabolism and trafficking would become the signature of Dick's scientific career.

Dick pioneered the use of lipids in which a native acyl chain was replaced with a short chain fluorescent analogue that readily incorporated into cell membranes and faithfully mimicked the behavior of the natural lipid equivalent. The Pagano lab created dozens of fluorescent lipid probes, which enabled several key advances, including tracking membrane lipid transport, labeling the Golgi apparatus of living cells, identifying intracellular compartments involved in sphingolipid metabolism, measuring transbilayer movement of aminophospholipids and demonstrating that sphingolipids regulate several membrane transport pathways.

Among these milestones, a fluorescent lactosylceramide analogue enabled the Pagano lab to discover a common mechanism of action that underlies sphingolipid storage diseases, namely, that cholesterol accumulation diverts internalized sphingolipids from the Golgi recycling pathway to lysosomes where they accumulate. This allows fluorescent lactosylceramide to be used as a sensitive diagnostic tool to identify patients with defects in sphingolipid metabolism. Dick's work in this area also led to the identification of several potential therapeutic options for treatment of sphingolipidoses, which have been verified to reverse the trafficking defect in vitro and in animal models of Niemann-Pick disease, type C.

During his career, Dick trained more than 50 students and postdoctoral fellows, many of whom are current leaders in the field of lipids that he pioneered. He successfully trained scientists largely by example since, in demeanor and practice, Dick was first and foremost a bench scientist. The environment in the Pagano laboratory was one where spirited discussion was encouraged, where everyone's opinion was considered and each piece of data scrutinized. Discussions occasionally became heated, but this was tempered by Dick's dry humor and desire to get the story right. Dick appreciated the joy of discovery, including the rigor and creativity that are needed to be an outstanding scientist. He is deeply missed by colleagues, friends and family. XOXO

Michael Koval (mhkoval@emory.edu) is an associate professor of medicine and cell biology at the Emory University School of Medicine.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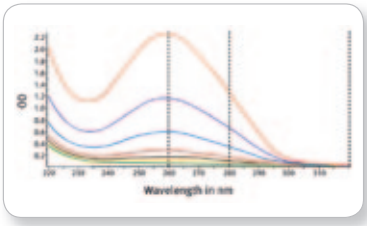


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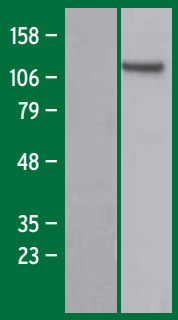


HEK293 were transfected with L) empty vector R) TrueORF for Myc/DDK-tagged hTERT(Cat# RC217436). The lysates were analyzed using anti-DDK antibody to show over-expression of hTERT. *DDK is the same as FLAG.

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