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May 2008

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Download the April ASBMB AudioPhiles *MCP* News Podcast and hear summaries of some articles that appear in a special section of *MCP* highlighting some of the research presented this past August at the 8th International Symposium on Mass Spectrometry in the Health and Life Sciences.

This and other podcasts are available at: http://www.faseb.org/asbmb/media/media.asp

ASBMB today

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from the **editor**

A New Science Series

BY NICOLE KRESGE

This month, *ASBMB Today* is launching a new section to complement our Science Focus stories that profile exciting and innovative ASBMB researchers. Called ScienCentric, this new section will cover research centers and institutes in an effort to better spotlight some of the collaborative, multidisciplinary efforts helping answer fundamental questions in biology and pave the way for medical breakthroughs.

Perhaps fittingly, our first ScienCentric story looks at the Rutgers Center for Lipid Research (RCLR) in New Jersey, a new center that was just formed this past December following a grassroots initiative undertaken by several faculty members.

We hope to continue publishing ScienCentric pieces on a semi-regular basis, and although we have some future centers already in the works, we always welcome suggestions and nominations. It doesn't matter whether the center has 5 members or 50, if it's in New York City or New South Wales; if you're part of an academic or private institute that has an interesting history, is tackling an underappreciated area of research, or just has an amazing collection of talent that deserves recognition, feel free to email us at asbmbtoday@asbmb.org if you would like to be included in the series.

ASBMB Meetings

Many of you probably attended our Annual Meeting in San Diego this past April. In the next issue of the magazine we will have extensive coverage of the events, lectures, and symposia that were held at the meeting. But right now, it's not too early to begin thinking about the next meeting you'll be attending. This fall, ASBMB will be supporting the following three special symposia:

- **Cellular Lipid Transport: Connecting Fundamental Membrane Assembly Processes to Human Disease**, October 22-26 in Alberta, Canada
- **Post-translational Modifications: Detection and Physiological Evaluation,** October 23-26 in Lake Tahoe, CA
- **Transcriptional Regulation by Chromatin and RNA Polymerase II**, October 16-20, 2008 in Lake Tahoe, CA

This issue of *ASBMB Today* features overviews of the Cellular Lipid Transport and Post-translational Modification meetings. To register for the meetings go to www.asbmb.org/meetings. And don't forget to mark your calendars for the 2009 ASBMB Annual Meeting that will be held in New Orleans from April 18 to 22!

ASBMB Public Affairs—Two Years of Continued Progress

BY HEIDI HAMM

For almost 2 years now, I have used this space to express my concerns about the state of federally funded science and have implored our membership to take an active role in helping shape the policies that affect biomedical researchers. In fact, looking back at my first column, one finds a call for scientists to get involved and contact their legislators in response to the proposed flat funding of the National Institutes of Health (NIH).

Unfortunately, many of the pressing concerns we faced 2 years ago are just as relevant today—but this does not mean we have not made a difference. The last couple of years have seen a significant increase in the public affairs and advocacy activities of ASBMB, and I hope we will continue to build on this success in the future.

In 2007 we initiated a science policy fellowship program to bring recently graduated Ph.D.s into the public affairs office in Bethesda for a year to "learn the ropes" of federal science policy and advocacy. The goal of this program is to train young scientists to get involved in science policy issues and possibly even pursue future careers in policy. Several organizations have spoken up about the importance of bringing more scientists out of the lab and into the realm of public service, and we hope this fellowship will provide a mechanism for recruiting young civic-minded scientists into future political engagement.

Many of the pressing concerns we faced 2 years ago are just as relevant today and the last couple of years have seen a significant increase in the public affairs and advocacy activities of ASBMB.

We have been very fortunate in our selection for our first year's fellow. Angela Hvitved, a recent Ph.D. from Rice University, has taken the position by storm and is doing a terrific job for ASBMB since joining the staff last fall. She'll be with us until October, and I hope many of you will have the opportunity to meet her between now and then. If you know a newly minted Ph.D. not past the post-doctoral stage in his or her career who has shown an interest in public policy and is interested in applying for the fellowship at some point, please have that individual get in touch with Angela or Pete Farnham, our Director of Public Affairs, at the ASBMB office in Bethesda.

Regardless of whether our science policy fellows return to research careers or transition into the policy field, we should not underestimate the importance of having individuals who are well versed in the complexities of biomedical research as well as the processes by which policies affecting research are made, whether they be in the lab down the hall or in the halls of Congress.

In the area of grass roots advocacy, several efforts have been made to increase the activity and contact with our Local Advocates Network (LAN), a group comprised of ASBMB members that have volunteered to contact their legislators when critical policy decisions are being made. To keep our LAN involved and up-to-date, a monthly e-newsletter, *ASBMB Advocate,* was started and provides brief summaries of current "hot topics" along with links to more information. We have received several positive comments regarding this e-newsletter and believe it will be a valuable tool in keeping our members informed and engaged.

In addition to increasing contact and communications with our LAN participants, we have also expanded

the membership list to include any members that have participated in FASEB's e-action alerts. In doing so, the distribution list for the *ASBMB Advocate* has grown from approximately 300 members to 1800. This increase, in combination with the future option to join the network on line through our soon-to-be-debuted website, will hopefully increase the advocacy activity of our membership and subsequently our impact on important policy decisions.

ASBMB has also taken several public positions in recent months regarding policy changes important to our members. The NIH is undergoing an in-depth review of the peer review system, and we have carefully followed the progress of this process over the past year in an effort to keep our membership informed and encourage participation in a process with such significant and far-reaching impact on biomedical science.

In fact, ASBMB was one of the first societies to advocate a review of peer review. In 2005 we sent a letter to Toni Scarpa, Director of the NIH's Center for Scientific Review (CSR), making several suggestions on how to improve peer review. We also urged senior scientists to serve on study section (NIH was having a difficult time getting senior scientists to serve) and conducted a survey in which we put together a list of 700 ASBMB members who agreed to serve on study section if asked. This presaged an NIH-initiated effort to recruit candidates for study section through scientific societies by a full year!

During the CSR review of study section structure that went on last year, ASBMB worked with the American Society for Cell Biology to review membership on the study sections of most concern to us to see if the people selected were appropriate in terms of scientific expertise. We also surveyed individuals whose grants were reviewed in these sections to see what the level of satisfaction was. We provided these data to CSR and urged the Center to obtain additional feedback and advice from extramural scientists. We also actively participated in CSR's open houses, held last year, sending staff and members to almost all of them.

Additionally, we participated in the review of the peer review process conducted under the aegis of a Working Group of the NIH Director's Advisory Committee, attending all five of their regional meetings and providing comments. As well, ASBMB staff helped arrange a discussion session at the San Diego meeting with the co-chairs of the working group, Keith Yamamoto and Larry Tabak. It is hard to bring change to a large bureaucracy like NIH, but we are confident that our efforts in the area of peer review have had an impact, and we will continue to work hard on this for you, our members, but more importantly for the continued viability of biomedical science.

Another example of the power of speaking up was our response to the proposal by the National Board of Medical Examiners (NBME) to institute changes in the United States Medical Licensing Examination that would have had (in the view of many) the effect of downgrading the importance of basic science in the medical school curriculum. Many in the community were extremely concerned about the consequences of this change. NBME is actively addressing our concerns, and we continue to be in contact with NBME leadership regarding this issue, including a meeting at the ASBMB Annual Meeting between a senior NBME official and the ASBMB Council.

These examples demonstrate the importance of utilizing all available avenues of engagement, and in both cases the discussion has been richer for our involvement in addition to addressing the concerns of our members.

However, as always, it is dangerous to rest on our laurels. There are still many issues that require attention. One that I find most disturbing is the trend toward NIH funding of large research centers and program-initiated grants, which--in an era of flat funding--happens at the expense of investigator-initiated research dollars. Regular readers of this column will be familiar with this issue as it is one I have worked hard to highlight during my time as ASBMB President. Although I can draw attention to this and other important issues, it is up to you, our membership, to take an active role in reinforcing the importance of investigator-initiated science and the tremendous contributions that the R01 grant has made to our scientific achievements.

It is often said that policy makers interpret a lack of response from the public to mean that everything is fine. But we all know that often no response simply means people feel too frustrated or powerless to even bother. This is the most dangerous attitude we can have! It is absolutely critical that scientists speak up for themselves because the alternative is having others speak for you. Therefore, I urge you to get involved and stay involved—call your legislators, speak to community groups about your research and the importance of biomedical research in society, talk at your child's school about what it is like to be a scientist. It can be as simple as explaining your research at a neighborhood or church potluck supper, but it is our shared responsibility to continually remind the public of the importance of biomedical research and the benefits we all reap from it. If we, as scientists, aren't willing to speak up for our work, how can we expect any one else to speak?

FASEB Cosponsors Diversity Meeting

BY JENNIFER A. HOBIN

FASEB recently cosponsored a meeting to explore opportunities to increase the representation of minorities across the science and engineering pipelines. *Enhancing Diversity in Science: A Retreat to Discuss the Role of Professional Associations and Scientific Societies* brought together society executives from across the disciplinary spectrum—including FASEB and ASBMB executive directors Guy Fogelman and Barbara Gordon—with representatives of federal agencies and private foundations with an interest in diversity. In doing so, the meeting, which was sponsored by the National Institutes of Health (NIH) and National Science Foundation (NSF), forged opportunities for organizations that do not typically collaborate to learn from and work with each other on broadening participation in science.

The meeting's focus on the role of professional organizations distinguished it from other laudable efforts in this area. Although scientists change institutions several times over the course of their training and careers, they tend to remain connected to their professional associations. As a result, societies can provide targeted training and career support to investigators wherever their careers may take them. Professional organizations also amplify the voices of their members, enabling them to raise the profile of diversity issues within the academic, government, and industrial sectors.

In framing the issue, Shirley Malcom, Head of the Directorate for Education and Human Resources at the American Association for the Advancement of Science (AAAS), noted that in the future the United States may not be able to continue to rely on immigration to satisfy the increasing demand for scientists. Yet demographic trends indicate that a sizeable proportion of our college age population will come from groups that have not had a strong attachment to science and engineering fields. Professional societies can, however, encourage interest in science among these groups by providing training, mentoring, and career support, recognizing the efforts of individuals engaged in promoting diversity, and informing and affecting policy change.

Malcom's introduction was followed by a panel addressing the personal challenges facing under-represented minority scientists, as well as the institutional and legal impediments to enhancing diversity. Among these obstacles, Arthur Coleman, an attorney with Holland and Knight's educational policy team, cited the retreat from diversity programs by federal agencies, foundations, and associations in view of recent legal challenges. He provided perspective on the legal landscape in which these programs operate and emphasized that colleges and universities need to show that diverse educational systems serve clear, research-based educational goals in addition to social justice aims.

Following the keynote address by University of Maryland, Baltimore County, President Freeman Hrabowski, Jeremy Berg of the National Institute of General Medical Sciences (NIGMS), and Wanda Ward of NSF discussed the approaches their agencies are taking to increase minority participation in science. The last presenter in this panel, Ted Greenwood, noted that the Sloan Foundation is working toward its goal of increasing minority Ph.D.s by providing substantial scholarships to students to work in the labs of faculty who have been or have the potential to be champions of diversity.

These discussions provided a framework for five breakout sessions during which meeting participants rolled up their sleeves and set to work identifying opportunities for their organizations to work toward enhancing the participation of minorities in science. The breakout groups addressed topics such as how to evaluate the efficacy of diversity programs and how to generate public support for a diverse scientific workforce. Participants in each session developed a broad set of recommendations on each topic, ranging from improving the sharing of resources, data, and practices among societies, to building the infrastructure to support long term mentoring relationships, to advancing federal policies supporting diversity initiatives.

The planning committee hopes to catalyze the formation of working groups that can refine and, where appropriate, act upon the recommendations that emerged from the meeting. A detailed summary report is expected to be released in May 2008.

The recommendations from this meeting and other information can be found at: www.cossa.org/communication/diversity_workshop/upcomingmeetings.html.

Jennifer A. Hobin is a Science Policy Analyst for the Office of Public Affairs at the Federation of American Societies for Experimental Biology (FASEB). She can be reached at jhobin@faseb.org.

"Academic Freedom" Legislation under Discussion in Florida

BY PETER FARNHAM

Since a federal court ruled against the inclusion of intelligent design in biology education (Kitzmiller v. Dover decision in 2005), anti-evolution groups have adopted a new strategy to undermine the teaching of evolution in public classrooms—so-called "Academic Freedom" legislation. As the name suggests, these bills claim to protect the rights of teachers and students to examine the strengths and weaknesses of Darwinian evolution. However, it is difficult to read them as anything other than cover for the teaching of intelligent design and creationism. Over the past couple of years, attempts to pass this type of legislation have failed in several states, including Alabama, Oklahoma, and Maryland. But these failures do not seem to have deterred efforts elsewhere. The most recent example is in Florida, where such legislation has been introduced in both Houses of the legislature. Another bill has been has been prefiled with the Louisiana Senate.

The Florida legislation purports to protect the right of teachers to "objectively present scientific information relevant to the full range of scientific views regarding biological and chemical evolution in connection with teaching any prescribed curriculum regarding chemical or biological origins." They also state that a student should not to be "penalized in any way because he or she subscribes to a particular position or view regarding biological or chemical evolution." This legislation is widely viewed by the scientific community as an attempt to protect the teaching of "alternatives" to evolution in the science classroom and, if passed, will no doubt lead to a wave similar legislation in other states.

The legislation is apparently in response to the recently revised Florida science standards, which greatly improve how the subject of evolution is dealt with in biology curricula in the state public school system. The wording of the these bills is extremely similar to a draft piece of legislation provided by the Discovery Institute, a Seattle-based think tank known for its advocacy of intelligent design and their "Teach the Controversy" campaign.

An organization called Florida Citizens for Science (www.flascience.org) has been tracking the progress of the House and Senate versions on their website. We encourage our members in Florida to get involved, either by participating in organized events or contacting Florida legislators directly. We will be following this legislation closely and will keep you informed as it progresses.

Peter Farnham, CAE, is public affairs officer of the Society, a position he has held since 1985. He can be reached at pfarnham@asbmb.org.

A Facelift for www.ASBMB.org

Over the past couple of months we have been working hard to combine some new technology and a fresh new face for the society's web page! The last redesign was about 3 years ago, and we thought it was time for an updated look and a revamp of the current functionality.

Coming this spring, ASBMB is proud to announce the unveiling of the brand new www.ASBMB.org. The entire site has been redesigned. Not only has site navigation been improved, we've added a few new sections to our site.

ASBMB has always posted society news, but the new version of the site will have a dedicated space for hot news stories, whether they be journal- or society-related. We also have enhanced search functionality and an archive for news stories with a powerful search engine allowing you to easily find that old article you read a while back, but can't remember exactly when.

The interactive area of the new site will include the ASBMB Audiophiles journal podcasts, a monthly summary of top research from each of the ASBMB Journals, including the *Journal of Biological Chemistry*, as well as video excerpts, members in the news, supplementary research footage, and other media of interest. This is also the place to come if you want to hear proprietary interviews with leading scientists and journal editors. We are also developing a concept for an "ASBMB On-line Lounge" that will include social networking functionality and provide a forum for knowledge sharing, whether through blogging or other Web 2.0 technology.

As an ASBMB member, you'll have access to restricted member-only areas of the website. Your unique member-only space will include personal profile information, the ability to update your contact information on line, and to monitor event registration, exclusive access to the digital edition of our monthly member magazine *ASBMB Today*, and a number of other member-only privileges.

We're excited about the new design look and functionality, and we hope you enjoy the fresh new face of www.ASBMB.org! If you have comments or feedback as we proceed through the website launch, please feel free to email Jessica Homa, Marketing Manager at ASBMB at jhoma@asbmb.org.

asbmb member spotlight

Brenner Honored with Cancer Lectureship

Sydney Brenner, Senior Fellow of both the Crick-Jacobs Center of the Salk Institute and the Janelia Farm Research Campus of Howard Hughes Medical Institute, was recently honored with the Fourth Annual American Association for Cancer Research (AACR)-Irving Weinstein Foundation Distinguished Lectureship.

The lectureship was established to recognize outstanding science that inspires new thinking and perspectives on the etiology, diagnosis, treatment, or prevention of cancer. Brenner presented his lecture at the AACR annual meeting this past April.

Brenner is one of the leading researchers in genetics and molecular biology. Among his many notable contributions to the field of molecular biology are his demonstration of the existence of messenger RNA and his work in aiding with the elucidation of the triplet nature of the code of protein translation. Brenner also contributed to establishing *Caenorhabditis elegans* as a model organism for the investigation of animal development, including neural development. This work clarified the fundamental nature of our genetic code and opened the fields of developmental biology and programmed cell death.

Gilmer Selected as AWIS Fellow

Penny Gilmer, Professor in the Department of Chemistry and Biochemistry at Florida State University, was recently selected to be an Association for Women in Science (AWIS) 2008 Fellow. She was given this honor for her outstanding commitment and dedication in support of women in science and engineering.

Gilmer was formally recognized at an awards ceremony and reception held in conjunction with the annual meeting of the American Association for the Advancement of Science (AAAS) this past February.

Criteria for selection as an AWIS Fellow include a demonstrated exemplary commitment to the achievement of equity for women in science, technology, engineering, and mathematics (STEM). The first AWIS Fellows were named in 1996 as part of AWIS' 25th anniversary celebration. The 2008 Class brings, to date, 129 AWIS Fellows so honored by the organization.

Gilmer's research focus is in science education, including chemical and biochemical education. She is particularly interested in teacher change, both at the K–12 level and the university/community college level. In the past, she studied cell-cell recognition events between immune T cells and their tumor target cells.

Gutierrez-Hartmann Awarded AACR Lectureship

Arthur Gutierrez-Hartmann, Professor in the Departments of Medicine and Biochemistry & Molecular Genetics and Director of the Medical Scientist Training Program at the University of Colorado Denver/Anschutz Medical Center, received the Third Annual Minorities in Cancer Research Jane Cooke Wright Lectureship from the American Association for Cancer Research (AACR).

The Lectureship was established in 2006 to give recognition to an outstanding scientist who has made meritorious contributions to the field of cancer research and who has, through leadership or by example, furthered the advancement of minority investigators in cancer research. Gutierrez-Hartmann presented his award lecture at the AACR annual meeting this past April. He was selected for his outstanding laboratory work studying transcription factors and gene expression and for his active role in recruiting minority physician-scientists to cancer research.

Gutierrez-Hartmann is noted for defining RNA polymerase II and polymerase III promoters found in several members of the growth hormone gene family, including growth hormone and prolactin (PRL). He also defined the molecular mechanisms that restrict PRL gene expression to pituitary lactotroph cells, determined the role of the Ets transcription factor ESE-1 in breast tumorigenesis, and defined a novel mechanism whereby ESE-1 transforms normal human mammary epithelial cells through a cytoplasmic mechanism.

Eisenberg Receives Emily Gray and Graduate Education Awards

This past February, David S. Eisenberg of UCLA received the Emily M. Gray award from the Biophysical Society. The award is for significant contributions to education in biophysics either by teaching, developing novel educational methods or materials, promoting scientific outreach efforts to the public or to youth, generating a track record of attracting new students to the field of biophysics, or by otherwise fostering an environment exceptionally conducive to education in biophysics. Eisenberg, who shared the award with Donald M. Crothers of Yale University, presented the Emily M. Gray lecture at the society's Annual Meeting.

Eisenberg has also been selected to receive the Nobel Laureate Signature Award for Graduate Education in Chemistry from the American Chemical Society (ACS). The award, which recognizes an outstanding graduate student and her or his preceptor in the field of chemistry, will be presented to Eisenberg and his graduate student Rebecca Anne Nelson at the ACS meeting in August.

Seeman Honored with Nicholas Medal

Nadrian Seeman, the Margaret and Herman Sokol Professor of Chemistry at New York University, was awarded the American Chemical Society's Nicholas Medal for his work in founding and establishing the field of structural DNA nanotechnology. Created in 1902, the Nichols Medal annually recognizes outstanding contributions in the field of chemistry and is given by the society's New York section.

The Nichols Medal, the first award created by the American Chemical Society, includes a cash prize of $5,000. Seeman received the award this past March at a ceremony in White Plains New York.

Seeman's work over the past 25 years has aided in founding and developing the field of DNA nanotechnology. The systems he and his colleagues have produced enable the specific organization of a variety of other chemical species, relevant to nanoelectronics, photonics, and drug design. They have also built machines that work on the nano-scale, such as a device that allows for the translation of DNA sequences, thereby serving as a factory for assembling the building blocks of new materials. The invention has the potential to develop new synthetic fibers, advance the encryption of information, and improve DNA-based computation.

Nagy Receives Award for Excellence in Biomedical Investigation

László Nagy, Professor of Biochemistry and Molecular Biology at the Medical and Health Science Center of the University of Debrecen and Head of the Debrecen Clinical Genomics Center, has received the 2008 European Society for Clinical Investigation (ESCI) Award for Outstanding Achievement in Biomedical Science. The award was presented to Nagy at the ESCI's annual meeting this past March.

Since 1976 the ESCI has awarded its annual prize for biomedical science to young biomedical investigators. Nagy was selected for the award because of his "groundbreaking contributions to the understanding of the physiology of nuclear hormone receptors and the molecular pathomechanism of atherosclerosis, as well as for his active leadership role in biomedical sciences in Europe."

During his scientific career, Nagy's research has focused on the role of nuclear hormone receptors in basic biological processes, including the molecular details of how nuclear hormone receptors fulfill their physiological function, and the role of these receptors in nonmetabolic processes such as inflammation or the development and function of the innate immune system. Nagy has also looked at the pathogenesis of major human diseases and has managed to elucidate some of the molecules involved in the early events of atherosclerotic plaque formation.

Silhavy Awarded Novitski Prize

Thomas J. Silhavy of Princeton University has been awarded the first Novitski Prize from the Genetics Society of America. Named for Edward Novitski (1918-2006), a noted geneticist, the prize is awarded in recognition of innovative experimental approaches and extraordinary creativity in solving a significant problem in genetics research.

Silhavy is a bacterial geneticist who has made fundamental contributions to the field of cell biology. His work, using *Escherichia coli* as a model system, led to his isolation of signal sequence mutations and the mechanisms for sensing extracellular conditions and stimuli. His lab is now researching the regulatory systems that allow cells to survive starvation as well as the cellular machinery that assembles the outer membrane, a barrier against antibiotics and other toxic molecules.

IN MEMORIAM:
Ann Ginsburg

R. Ann Ginsburg passed away this past February in Bethesda, Maryland.

Ginsburg received both her B.A. and M.A. from the University of California, Berkeley. Her Ph.D. studies were cut short when her husband, Victor Ginsburg, accepted a postdoctoral position to work with Herman Kalckar at the National Institutes of Health (NIH). After moving to Bethesda in 1956, Ann Ginsburg spent 2 years at the NIH as a chemist in Bernard L. Horecker's laboratory at the National Institute of Arthritis and Metabolic Diseases. She then obtained her Ph.D. from George Washington University in 1964, under the direction of William R. Carroll. Her Ph.D. research focused on the thermally induced unfolding of ribonuclease. Results of these studies have been reproduced in textbooks published in the United States and overseas.

Ginsburg then did a postdoctoral fellowship with Alan Mehler at the Dental Institute at NIH before joining the NIH's National Heart Institute. Between 1966 and 1988, she published over 50 papers on research aimed at the elucidation of the kinetics of ligand interactions with glutamine synthetase and the structural perturbations that occur in response to the binding of substrates, metal ions, and inhibitors of the enzyme, and also to the adenylyltransferase and uridylyltransferase that control the sensitivity of glutamine synthetase to feedback inhibition.

In recognition of her achievements, Ginsburg was promoted to chief of the Section on Protein Chemistry in the Laboratory of Biochemistry, National Heart, Lung, and Blood Institute at NIH in 1974.

ASBMB 2008 Election Results

The results of the 2008 ASBMB elections are in. Ann Stock and Dafna Bar-Sagi will become members of the ASBMB council, Ken Blumer and Lucy Waskell will join the Publications Committee, and Tony Hunter and Judith Klinman will become members of the Nominating Committee. All newly elected members will begin serving their terms on July 1, 2008.

COUNCIL MEMBER

Dafna Bar-Sagi

is Professor and Chair of the Department of Biochemistry at the New York University Medical Center's School of Medicine and Hospitals Center. She received her B.Sc. from Bar-Ilan University in Israel and her Ph.D. from the State University of New York. Her research focuses on the molecular dissection of signal transduction pathways involved in growth control.

COUNCIL MEMBER

Ann M. Stock

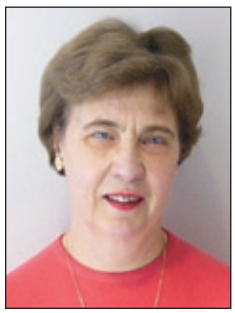
is Professor of Biochemistry at the University of Medicine and Dentistry of New Jersey–Robert Wood Johnson Medical School, a resident faculty member at the Center for Advanced Biotechnology and Medicine, and a member of the Cancer Institute of New Jersey. She is also a Howard Hughes Medical Institute investigator. Stock received her A.B. and Ph.D. from the University of California, Berkeley. Her research is directed toward understanding the molecular mechanisms of receptor-mediated signal transduction. She has been a member of ASBMB since 1991.

PUBLICATIONS COMMITTEE

Kendall J. Blumer

is currently a Professor in the Department of Cell Biology and Physiology at Washington University in St. Louis. He received his B.A. from Rice University and his Ph.D. from Duke University. His research looks at G protein signaling mechanisms in the cardiovascular and nervous systems. Blumer has been an ASBMB member since 2001 and was Chair of the ASBMB Annual Meeting in 2008.

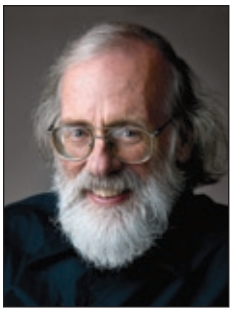
PUBLICATIONS COMMITTEE



Lucy Waskell

is a Professor in the Anesthesiology Department at the University of Michigan. She received her B.S. from Pennsylvania State University, her M.D. from Columbia University, and her Ph.D. from the University of California, Berkeley. Her research program is concerned with the interaction of cytochrome P450 with its redox partners, cytochrome b_5 and cytochrome P450 reductase. Waskell has been a member of ASBMB since 1989.

NOMINATING COMMITTEE



Tony Hunter

is a Professor in the Molecular and Cell Biology Laboratory at the Salk Institute. He received both his B.A. and Ph.D. from the University of Cambridge in England. Hunter studies how cells regulate their growth and division and how mutations in genes that regulate growth lead to cancer.

NOMINATING COMMITTEE

Judith P. Klinman

is a Professor of Chemistry and Professor of Molecular and Cell Biology in the Chemistry Department at the University of California, Berkeley. She received both her B.A. and her Ph.D. from the University of Pennsylvania. Her research looks at the relationship of enzyme structure and dynamics to catalysis. Klinman has been a member of ASBMB since 1974.

We thank the following outgoing Council and committee members for their service to the Society:

K-T Jeang
Council Member

Suzanne Pfeffer
Council Member

Linda Pike
Council Member

Robert Rhoads
Publications Committee Chair

Ruma V. Banerjee
Publications Committee

Margaret A. Phillips
Publications Committee

Susan Taylor
Nominating Committee Chair

Bruce M. Alberts
Nominating Committee

Special ASBMB-Sponsored Symposium: Post-translational Modifications

BY KATALIN F. MEDZIHRADSZKY AND RALPH A. BRADSHAW

The post-genomic era has generated a series of buzzwords such as "proteomics," "metabolomics," and "glycomics," as well as large amounts of evaluation and prediction software. Both advances reflect the important changes in biological research that have characterized the last decade and strongly underscore the central importance of proteins in understanding cellular processes. Key to that understanding is the elucidation and functional evaluation of the wide spectrum of post-translational modifications (PTMs).

Unimod (www.unimod.org), a popular catalogue of protein modifications, features 549 entries, a significant portion of which represents post-translational modifications, and most likely this is only the tip of the iceberg. As mass spectrometry has become the method of choice for PTM analyses, reports of novel modifications have significantly multiplied. For example, the widely studied "histone code," which is formed in part by acetylation and methylation of lysine residues, has now been enriched by the addition of propionyl, butyryl, and formyl groups on these residues as well.

However, the wide variety of possible modifications and their very different physical properties prevent the use of any single approach for their complete determination and characterization. Indeed, PTMs can be present at any amino acid (if we consider proteolytic processing), and they can be stable or dynamic, low level or complete, and may significantly alter the physical characteristics of a protein, its immunogenicity, and its biological activity.

Most protein modifications have to be studied by targeted approaches. Enrichment strategies have been worked out for phosphopeptides, some glycopeptides, and ubiquitinated proteins, to name a few, but many remain elusive and hard to detect. Studying the biological significance of PTMs is also difficult in many instances because of our often limited understanding of their formation and regulation. Both situations are made considerably more complex by the commonly encountered situation of multiple modifications on the same protein.

In the ASBMB-sponsored symposium, "Post-translational Modifications: Detection and Physiological Evaluation," we plan to welcome biochemists, who are trying to decipher the biological significance of such modifications; analytical chemists, who are developing methods for large scale PTM analysis or the comprehensive characterization of a single, multiply modified protein; separation scientists, who are trying to find new ways to isolate different protein populations or modified molecules; and bioinformaticians, who are using mathematical and programming tools to interpret, catalogue, sort, and analyze all this experimental information. It is our intention to bring together researchers from these very diverse fields, with a common interest in post-translational modifications, in order to look at this essential biological problem in new ways.

Speakers representing each field listed above have been invited. The opening lecture, which will outline the broad scope of the meeting, will be presented by Matthias Mann (Max-Planck-Institut of Biochemistry, Martinsried, Germany). Other invited speakers are Jeffrey J. Gorman (The Queensland Institute of Medical Research, Brisbane, Australia), Frank Eisenhaber (Bioinformatics Institute, Singapore), Gerald W. Hart (The Johns Hopkins University, Baltimore), James Paulson (The Scripps Research Institute, San Diego), Andrew Alpert (PolyLC Inc., Columbia, Maryland), Joshua J. Coon (University of Wisconsin, Madison), Pavel Pevzner (University of California, San Diego), Yingming Zhao (University of Texas Southwestern Medical Center), Catherine E. Costello (Boston University School of Medicine), and Judith Klinman (University of California, Berkeley). Approximately

Biological Evaluation

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Meeting registration and abstract submissions will begin in May.

Abstract deadline: September 15th, 2008.

half the program will be in the form of oral presentations selected from the submitted abstracts. Two evening poster sessions are also scheduled.

The meeting will be held at Granlibakken, a small lodge/conference center located close to Lake Tahoe in the beautiful Sierra Nevada Mountains. Rooms and all meals are included in the registration fee. Following lunch, there will be an afternoon break each day offering an opportunity for networking with fellow attendees or simply discovering the natural beauty of the area.

ASBMB Small Meeting on Cellular Lipid Transport and Human Disease

BY DENNIS R. VOELKER

Cellular lipid transport constitutes one of the most fundamental aspects of membrane biogenesis. Lipid transport at the cellular level is also central to metabolic energy generation. In metazoan systems, cellular regulation of lipid transport plays a critical role in both the assimilation and partitioning of essential components for membrane synthesis and energy generation at the tissue and organ level.

Within the last 5 years we have dramatically expanded our knowledge of basic lipid transport processes within cells. The information has grown from a handful of known genes to well over 100. The simple application of genomic information is now fueling more rapid expansion of this field. Although progress in the field of lipid transport has long been difficult because of the paucity of genetic information, the recent advances have abruptly ended this stage and provided new tools for rapid expansion of knowledge.

The new ASBMB Meeting, *Cellular Lipid Transport: Connecting Fundamental Membrane Assembly Processes to Human Disease*, will be the first international meeting focused solely on cellular lipid transport and its relationship to human genetic diseases. The meeting will provide a forum for the latest research in this discipline, which is now rapidly expanding as a consequence of advances in the biochemistry, genetics, and genomics of lipid transport in multiple eukaryotes.

The meeting will convene from October 22 to 26, 2008, in Canmore, Alberta, Canada. The participants in the meeting will be leading scientists whose focus is on lipid transport processes within cells and the relationship of these processes to cellular pathology and human diseases. In addition to invited speakers, attendees will include senior scientists with active research programs in the topic areas of the conference and graduate students and postdoctoral fellows from these laboratories. Women and minority scientists are encouraged to participate in this meeting, and 25% of the invited speakers are women.

There will be ample opportunities for presentation of work by attendees who are not invited speakers during poster sessions and short oral presentations, which are mixed with invited speaker presentations.

The objectives of the meeting are to publicize the latest advances in the topics of cellular lipid transport and critically discuss how disease processes result from molecular defects. The topics to be addressed include: 1) ABC transporters and their roles in eye, lung, and liver disease in humans and mice, and the biosynthesis of endotoxins in prokaryotes; 2) P-type ATPases and their role in fundamental membrane assembly processes of eukaryotes, and the development of intrahepatic cholestasis in humans; 3) the importance of lipid recognition proteins in cell growth and development and production of steroid hormones; and 4) the role of Niemann-Pick C family proteins in controlling lipid transport processes in the intestine and brain and their relationship to specific disease processes.

Cellular Lipid Transport: Connecting Fundamental Membrane Assembly Processes to Human Disease

OCTOBER 22-26, 2008 • RADISSON HOTEL & CONFERENCE CENTER, CANMORE, ALBERTA, CANADA

Organizers:
Dennis R. Voelker, National Jewish Medical Research Center; Jean Vance, University of Alberta, Edmonton; and Todd Graham, Vanderbilt University

For further information visit www.asbmb.org.

Meeting registration and abstract submissions will begin in May.

A New Sphingolipids Review Series in *JLR*

BY MARY L. CHANG

The May issue of the *Journal of Lipid Research* marks the start of a new Thematic Review Series on sphingolipids. Three of the series' reviews appear in the May issue of the journal, along with an editorial by John H. Law, Regents Professor Emeritus, University of Arizona, and Robert K. Yu of the Medical College of Georgia. Yu is an associate editor of *JLR* and is also the coordinator of the series.

What is unique about this series is that most of the contributing authors of this series were guest speakers at a fall 2007 seminar in Tucson, Arizona, honoring the life and work of Herbert E. Carter. The editorial by Law and Yu provides insight into Carter's many contributions to biochemistry research and the scientific community.

In the May issue of the journal, Robert C. Dickson of the University of Kentucky College of Medicine explains how much research over the last 2 years in the bakers' yeast *Saccharomyces cerevisiae* has furthered understanding of yeast sphingolipid metabolism and function.

Although yeast do not contain sphingomyelin, they do have inositol phosphosphingolipids. One type of mammalian sphingomyelinase, neutral sphingomyelinase, is a homologue of inositol phosphosphingolipase C (coded by *ISC1*) in *S. cerevisiae*. Nabil Matmati and Yusuf A. Hannun of the Medical College of South Carolina discuss *ISC1*'s function in their May review, as well as its localization, its mechanisms, and its roles in cell responses to stress. They will also suggest what implications these findings have for mammalian research.

Gangliosides are glycosphingolipids with one or more sialic acids attached to the sugar chain and have been linked to tumor growth and metastasis. Vascular endothelial growth factor (VEGF) promotes angiogenesis, which is a key step in the transition of tumors from dormancy to malignancy. In the May issue of *JLR*, Thomas N. Seyfried and colleagues at Boston College review the therapeutic potential of monosialoganglioside GM3 in reducing tumor angiogenesis by countering the activity of VEGF and disialoganglioside GD1a.

In the June issue of *JLR*, Robert Yu and colleagues will look at the role of gangliosides in the pathogenesis of Alzheimer disease (AD). Aggregates of GM1 ganglioside and amyloid β-protein have been observed in brain tissue affected by AD. However, *in vitro* and *in vivo* models of neuronal injury and related neurodegenerative diseases indicate that gangliosides may also provide neuroprotective and/or neurorestorative effects.

The importance of sphingolipids in the nucleus is explored in a review by Robert W. Ledeen and Gusheng Wu of the New Jersey Medical School, University of Medicine & Dentistry of New Jersey, which will also appear in the June issue. The activities of sphingomyelin (the most common sphingolipid found in cell nuclei) and gangliosides indicate their significance in signaling leading to the initiation of and regulating metabolic and functional processes in the nucleus.

Sphingosine 1-phosphate (S1P) plays a major role in the activity of G-protein-coupled receptors. Cytokines and growth factors are involved with S1P synthesis and degradation. In the July *JLR*, Deborah A. Lebman and Sarah Spiegel of the Virginia Commonwealth University School of Medicine will review the coordination of activities and cross-talk between S1P, cytokines, and growth factors and what effects this cross-talk has on cell signaling and cell biology.

And finally, in the July *JLR*, Alfred H. Merrill, Jr., and colleagues from the Georgia Institute of Technology and Emory University will discuss the biodiversity of sphingolipids. Sphingolipids have sphingosine backbones. Over the years, the incredible structural diversity and unusual features of sphingolipids and sphingo base-like compounds in nature have gone beyond simply differences in chain length and branching and the number and position of double bonds. The review will provide an overview on both types of compounds in their naturally occurring and synthetic forms.

Mary L. Chang is the Managing Editor of the *Journal of Lipid Research*. She can be reached at mchang@asbmb.org.

Presenting... PowerPoint 2007

This article is third in a series on publishing your research in the *Journal of Biological Chemistry*. The series will address a variety of issues that authors may have when writing and submitting articles to the *JBC*. The articles are written by Cadmus Professional Communications, a Cenveo Company, who are responsible for the editing, production, and printing of *JBC* articles.

If you've familiarized yourself with Word 2007 and Excel 2007, take a look at PowerPoint. Microsoft's Office 2007 suite includes a new PowerPoint program as well as Word and Excel. Remember that PowerPoint was designed to be a presentation program, and PowerPoint 2007 provides even greater display features.

Where, Oh, Where Are My Favorite Commands?

As with other 2007 Office programs, PowerPoint has the new interface; the ribbon and commands are not in the customary menu locations. The ribbon that was the main functional site for Word and Excel is the primary visual cue for PowerPoint 2007 as well. Menus, tabs, and commands are there, but finding them is a challenge. Learning where your favorite commands are lurking in this new version can be a struggle. However, you can use this link to identify the location of PowerPoint 2003 commands in the 2007 version: http://office.microsoft.com/en-us/powerpoint/HA100666231033.aspx.

Saving in XML

The XML file format in PowerPoint 2007 provides advantages over earlier versions of PowerPoint. The new XML formats provide for compact, more compressed documents. In fact, some documents are up to 75% smaller. Another advantage is the ability to recover damaged files. Even if a chart or table within the PowerPoint presentation is damaged, you can still open and retrieve the presentation. If you are part of a network administered by an IT department, that department will likely prefer PowerPoint presentations prepared in 2007. IT administrators can block documents with unwanted macros or controls.

Looking Smart

SmartArt, design templates, and graphical previews are more lively and dynamic than in older versions of PowerPoint. If you want to create a slide show or sales pitch, this is the program for you (Fig. 1). Lively, colorful templates are a great new feature in PowerPoint 2007. If you can't

Fig. 1. Themes in PowerPoint 2007.

find a tab, try clicking on the item on the page. Want to display the Picture Tools formatting tab? Try clicking on the picture to trigger it. Text effects and outline text are new features in PowerPoint 2007. Shape effects, theme templates, and custom colors add pizzazz to the slides (Fig. 2). Images, sounds, clip art, drawing tools, and charts are handled the same way. Pulling in a chart from Excel is easier than ever in PowerPoint 2007. And, if you edit the chart in Excel, you can see the dynamic changes in PowerPoint preview.

Not happy with the display within a slide? Hover over the text with your cursor and right click to pull up a formatting toolbar. Now you can change the font, size, or style of the text in the slide. Three-dimensional styles are visible with a click and available in a dynamic gallery of images. But if you want to add sound, PowerPoint 2007 offers little in managing multimedia content.

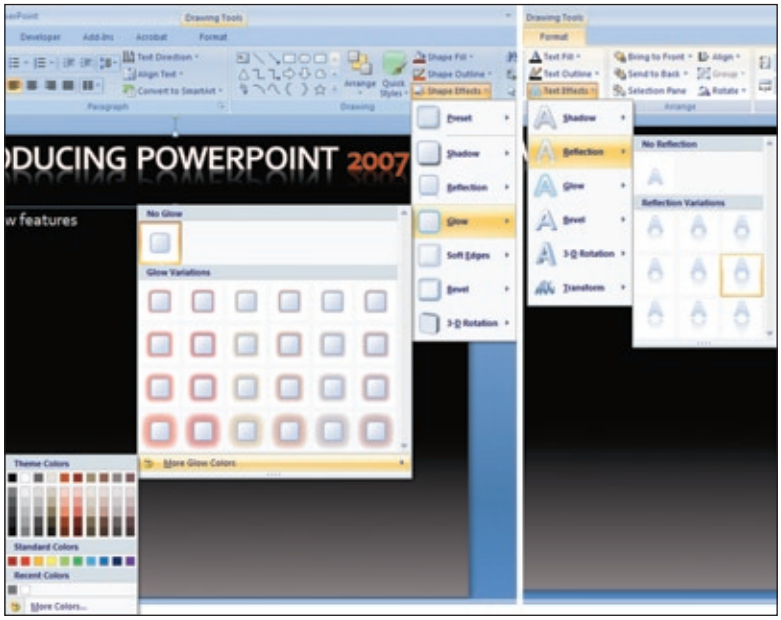

Fig. 2. Shape and text effects.

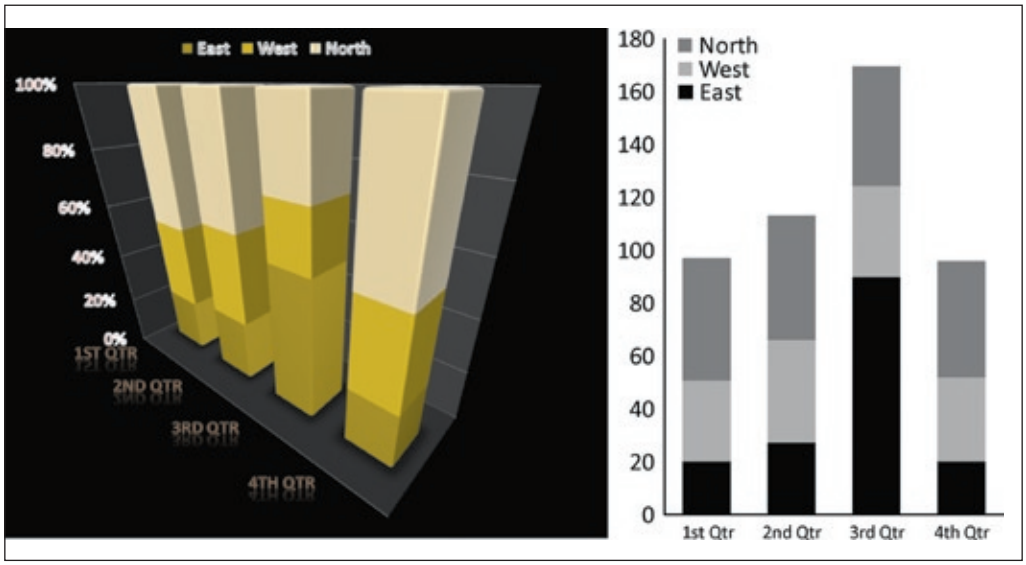

Fig. 3. A PowerPoint figure saved for print submission.

PowerPoint Figures

PowerPoint 2007 is designed to help you present your ideas with images. That eye-catching image, however, may be problematic for inclusion in your manuscript submission for print publication (Fig. 3). Graphics or images that are submitted as part of an article to be published in the journal should be in .TIF or .EPS formats. They should be at least 300 dpi for best quality in print. The PowerPoint 2007 program is made for on-line presentations and displays–great for conferences or projecting your information before a large group, but if you plan to present your report in print, and to submit it to an academic journal, the figures need to be acceptable for print publication.

To Buy or Not to Buy

We've only highlighted the new features in Office 2007 in the last three issues of *ASBMB Today*, covering Word 2007 in the March issue, Excel 2007 in the April issue, and now PowerPoint 2007 in the May issue. Now it's time to determine whether an upgrade is best for you. If you're happy with your current Office suite of programs and can readily produce the documents you need with the current functions and commands, you may want to wait. If, however, the new features are more beneficial to you than the issues of file sharing and learning the new interface, it's time to take the plunge. Whatever your decision, we hope these overviews have helped you determine whether Office 2007 will be your Friend or Foe.

Removing the Barrier between Teaching in the Classroom and Research in the Laboratory

BY CARLA MATTOS

Faculty Who Make a Difference—Part II

This article is the second in our series about faculty who make a difference. Carla Mattos, an Associate Professor at North Carolina State University, teaches a very unique class where undergraduates participate fully in her research. She and Lisa Gentile, who was featured in last month's column, are not only outstanding role models and mentors for the students they teach, but they are also excellent examples of innovative teaching to which rest of us can aspire if we are to be faculty who make a difference in the lives and aspirations of our students.

When I first came to North Carolina State University as an Assistant Professor in Biochemistry, I encountered an environment of change that filled me with energy and the belief that I could contribute in very significant ways to the undergraduate experience in our department and to our students' long term commitment to science. From my own experience I know that this commitment comes from a deep personal involvement and that it simply cannot be achieved from a detached attendance of classes that culminates in a degree. For me as a student, the most exhilarating times were those when I was learning through research, driven by curiosity and the expectation of a leap in understanding. At those moments I would devour information, read papers, go to the textbooks, and talk to other scientists, all while synthesizing information in a way that made sense to what I wanted to understand.

Fig. 1. Undergraduates involved in the MSCS project.

As a teacher, I wanted to avoid the danger of giving lectures detached from the students and running classes that did not provide the venue for personal engagement. I did not want the students to take my classes just "because it is part of their major" or "because it is the easy class where they have the best chance of getting an A." These are reasons that are detached

Fig. 2. Mychal Smith, an undergraduate student who worked on the MSCS of chymotrypsin, RNase A, and lysozyme over 2 years, presenting a poster.

from the subject and so can lead to students being passive, uninterested, overwhelmed, and simply wanting to be spoon-fed the material that will be on the test. I wanted students to take my classes because they would lead to something meaningful. Although there are many ways to engage students in class, I wanted to do that through research. Research is the root of discovery and knowledge. It is what drives me to continuously learn. In many ways it is what we are trying to prepare our students for as we lecture about the many facts they must know in order to function at a high level in science.

If research can be a powerful driving force for learning, why not use it for teaching? Is it possible to merge teaching and research within our current academic setting? There I was with a vibrant research group and charged with the task of teaching undergraduates about protein structure, chemistry, and function. My research is on protein-binding sites, based primarily on x-ray crystallography. Why not use this to get students to see with their own eyes the beauty of a protein model at atomic resolution, to refine that model themselves, to see its strength and weaknesses? The protein model could then be used to illustrate material that we discuss in the course, such as secondary structure, the active site of an enzyme, the hydrogen bonding networks that are so prominent in proteins, and the packing of hydrophobic residues at the core, so important in attaining the folded state in an aqueous environment. The amino acid residues would cease to be only drawings in a textbook and would come alive in the protein, with their physicochemical interactions, in a context that gave meaning to their structure.

At the same time, by refining the structures, these students would be contributing to research in our group, under my supervision and that of graduate students and postdocs for whom the outcome of the work is critically important. The students would be part of the research discussions and would understand the reason for solving the structures. They would be involved, engaged. They would experience first hand the passion that goes into research, and they would want to continue beyond this course.

This dream, though seemingly unrealistic, did not leave me. I had to try it out. The vision that I had a project amenable to this experiment consumed my thoughts. I began to devise my experiments in this context. I wrote a grant that the National Science Foundation funded. I had the support, I had the go ahead, I had the research team, I had the students, and so I had to try it.

The project, which is now in the beginning of its 5th year, aims to probe binding surfaces on proteins using the Multiple Solvent Crystal Structure (MSCS) method (1). For this, the crystal structure of a protein is solved in about 10 organic solvent environments. To get at the general properties of binding sites, such as plasticity and anchor points for ligand binding and hydration patterns, we work with some of the very well known classic proteins such as serine proteases, RNase A, and hen egg white lysozyme. Solving these structures is essentially equivalent to the last stages of structure refinement, where the protein structure is already known and where the solvent structure is the focus. The final structures are superimposed to reveal characteristic patterns of bound organic solvents for analysis.

At the beginning of the course, each of about 10 students is given an x-ray diffraction data set and a starting model for refinement. Members of our research team work individually with the students to ensure that they under-

stand how to do the structure refinement. In addition to overseeing the laboratory sections, I have designed discussions around the properties of protein structure, chemistry, and function that take place during the scheduled lecture hours and that relate back to the structures being refined by the students. We have developed a series of modules to simultaneously guide the students through the protein refinement process and to point out properties of protein structure and chemistry being discussed in class. Graduate students, postdocs, and I work individually with the undergraduates in a coordinated fashion, and at the end all students will be either authors or acknowledged for their work in the publications.

The project brings together various groups that are often separated in the traditional academic setting to accomplish common goals in a situation that 1) decreases the gap between teaching and research, 2) exposes students to topics discussed in traditional classrooms in the context of the pressing questions guiding cutting edge research, and 3) motivates graduate students and postdocs to be excellent teachers because the results provided by the undergraduates feed into their research and publications.

The project brings together various groups that are often separated in the traditional academic setting

My experience has been that this connection between teaching, learning, and research is effective in keeping students interested in science. To date we have had four groups of about 10 students. They include both undergraduate and graduate students interested in learning about proteins and their properties. Twenty undergraduate students have been through what we originally called the "O" group and later changed to "Coot" group, *named after the software packages that we use for electron density visualization during x-ray structure refinement.* Eight of the students are currently in graduate programs in universities throughout the United States, two are in pharmacy school, and one is in medical school. Additionally, one of the students is teaching science at a local private high school, and four are applying to graduate school this year.

It is remarkable what undergraduates can do. Through this project I have seen my students learn at a level of sophistication that I have never observed in my more traditional classroom settings. When teaching I try to convey my enthusiasm for protein structure and for the problems in biology that it can help solve. I believe that I can do this in both in the classroom and in the lab. The difference is that in the traditional lecture class the students are intrigued but detached. They see that this topic can be very exciting, but they cannot experience the source. With research I can try to get my students "hooked" by the intellectual rewards that come with their own discovery and understanding. It is the difference between being told how things are and experiencing how things are.

This kind of teaching research requires a great deal of individual attention, of working one on one with the students. This is a huge commitment, even for the small classes of 10 students, and it works primarily because it is a two-way street. The investment that I and members of my lab put into this project is rewarded not only by the way students learn, but also by the structures we get at the end, by advancement of our research in a way that outpaces what could be done by our graduate students and postdocs alone. Thus, one of the key factors in this project responsible for decreasing the barrier between teaching and research was to have real productivity on the part of the students and real gains in the part of the laboratory. This takes teaching from the altruistic or duty-related realm and puts it into a productive and dynamic interconnection with research. It is a win-win situation for the students and the mentors. Students and mentors at all levels of the academic ladder become part of a common goal, driven by common interests.

Although it has come with many challenges along the way, I do feel like I have succeeded in accomplishing my "seemingly unrealistic dream" to a great extent. For students, having ownership of their projects and knowing that the product of their work contributes to a bigger picture in understanding protein-protein and protein-ligand interactions is important in keeping them engaged. They understand the questions, and they understand how we planned to answer them. They understand how they can contribute. Many stay on after the semester is over. Most want to stay in science.

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Flight-or-Flight Response to Cultural Isolation

BY JEROME C. NWACHUKWU

As more under-represented minorities are being recruited to careers in biomedical science, the extent of cultural isolation experienced in graduate studies continues to pose a significant threat—one that can undermine the recruitment and retention of minorities in the field. If unaddressed, this threat may eventually feedback and hinder the progress being made in diversifying the field, and thereby compromise the problem-solving potential and successful implementation of key biomedical research findings nationally and globally.

The Outlook for Minority Success in Academia

The basic principles of fight-or-flight response are hard-wired to the core of life. Each species is well equipped to sense potentially hazardous environments, and to decide with an effective degree of accuracy whether to make a stand or flee. In the convoluted field of biochemistry and molecular biology, most graduate students, especially those of under-represented minority ethnic background, have already sensed the potential apocalypse looming over their chances of success in academia.

Several issues that could have severe impacts on the future of the field have developed, including the rapidly receding economy, the ballooning national debt, and the decline in federal research funding. In fact, the National Science Foundation (NSF) Science and Engineering (S&E) Indicators (2008) report shows a decrease in the academic share of all doctoral S&E employment from 55% in 1973 to 45% in 2006. Additionally, the share of tenured/tenure-track full time faculty appointments fell from 88% in the early 1970s to 72% in 2006. The report also shows a general increase in unemployment rates in S&E occupations. Interestingly, from 1993 to 2006, the unemployment rates for females doubled from 2.1 to 4.2%, whereas that for blacks increased from 2.8 to 5.3%; however, the unemployment rates for Hispanics fell from 3.5 to 2.7% (1).

Cultural Isolation

This sense of impending doom is amplified by the blatant racial discrimination and cultural isolation to which minority scientists are often subjected. Although racial discrimination is a civil rights violation prohibited by law and largely addressed, albeit to widely variable extents, by research and teaching institutions, cultural isolation is not. For minority graduate students, the sense of cultural isolation includes the academic and social aspects of life that makes recent recruits feel like they are participating in a study-abroad program, without actually going abroad, and with no end in sight. Cultural isolation can affect academic performance, depending on the student. Moreover, although academic performance may affect retention rates, the decision to explore or remain in academia is rarely based on academic performance but is often influenced by personal and communicated experiences. For some aspiring students, a single summer research internship in a culturally isolating setting has proved sufficient to turn them away from biomedical research and often toward medicine, which I have to concede is currently more ethnically diverse and therefore less culturally isolating than biomedical research.

Because biomedical research in the United States is largely supported by public funds and is driven to enhance the well being of a multicultural populace, it seems logical that the public, including biomedical scientists, should continue to initiate, support, acknowledge, and appreciate efforts directed against cultural isolation of minorities in biomedical research. Yet paradoxically, many successful initiatives or programs (often referred to as "Affirmative Action programs"), which had the potential to effectively address cultural isolation of minorities in academia and were initially supported by state governments and universities to increase diversity, are persecuted nationally and have continued to suffer severe and damaging invectives, especially from organizations that attack the legal basis of such initiatives.

Must minority scientists continue to view cultural isolation as more of an "occupational hazard" than an inconvenience? Must aspiring minority scientists nullify any cultural philosophies in order to have a successful career? Must culture and science exist in mutually exclusive realms of reality? If this was the case, how attractive would a career in biomedical science seem to the bulk of exceptionally intelligent and intuitive minority college and graduate students aspiring to become biomedical researchers?

Although these questions may not have definitive answers, it is clear that cultural diversity in biomedical research has potential ethical benefits that are relevant, particularly in basic, translational, and clinical aspects of the field, including drug development and testing. We should acknowledge that many research institutions now realize the importance of diversity and express their desire and commitment toward addressing it. However, we should also note that only a handful of institutions currently have successful support systems in place to effectively offset the level of cultural isolation facing recently recruited minority students.

> "The basic principles of fight-or-flight response are hardwired to the core of life."

Addressing the Issue

However, it is not too late for steps to be taken to address this issue. Perhaps if academic institutions and professional societies were to collaborate and essentially pool some of their resources to promote networking among minority graduate students and postdocs, significant progress could be made. As an example, a handful of minority graduate students successfully founded the New York City Minority Graduate Student Network (NYCMGSN, http://nycmgsn.com/) in 2006. Recognition, participation, and support from the parent institutions will be essential to the long term success of such organizations. In addition, the minority affairs committees (MAC) at professional and scientific societies such as ASBMB should also consider supporting such organizations, in their quest to increase the visibility of minority scientists at the national level.

Addressing cultural isolation via increasing visibility and networking at the national level could also be an effective piston to drive minority recruitment and retention through the pipeline. However, networking and mentoring to encourage minority graduate students to compete for funding on a national level and publish and pursue careers in biomedical research is severely lacking. While in college, several minority graduate students, now at research institutions across the nation, participated in the Annual Biomedical Research Conference for Minority Students (ABRCMS, www.abrcms.org) and the Society for Advancement of Chicanos and Native Americans in Science (SACNAS, www.sacnas.org) national conferences. These conferences have been extremely successful at reducing cultural isolation by encouraging networking and mentoring, and as a result have played pivotal roles in increasing the nationwide retention and recruitment of minority undergraduates in colleges and to graduate programs, respectively. Therefore, ASBMB through its MAC should continue to prioritize support and outreach at such undergraduate conferences. Moreover, with public interest in mind, it is worth noting that although increasing recruitment is very important, enhancing retention rates is equally important and eventually feeds forward to fuel and sustain diversity in the field.

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Taking Chances When They Come Your Way

BY FAIZ KERMANI

There are times when I think that the route to my current career in medical communications can only be described as surreal! I started off in a research lab in London, United Kingdom, and never envisaged that my career would go through so many changes and then finally bring me to the United States.

Although I had found my Ph.D. in immunopharmacology very fulfilling, as I had worked on a project that had a direct relevance to the treatment of patients in our hospital clinic, the subsequent postdoc positions made me yearn to do something different. Most postdoc positions seemed geared to producing yet another iterative academic paper, and although that might have satisfied some people, it was not enough for me. I wanted to know more about how research translated into a real medicine that was used by real people, and I knew that meant learning some new skills. By chance I saw an advertisement for a consulting company that was looking for a scientifically qualified person to write a reference publication on the activities of the international pharmaceutical industry. The idea was that it would be used by the management of companies to gauge how they were performing. The interview process was very demanding, and after being called back three times and having to present to the senior management, I somehow managed to get the job.

The reference publication I worked on was divided into several volumes that tackled everything from the drug discovery process for molecules in different therapeutic areas to the regulatory procedures in every major global region. This meant doing hours of background reading to pull out relevant details from scientific and commercial reports, sifting through data bases of drug development data to create summarized analyses, and obtaining information from official organizations that represented the pharmaceutical industry from as far away as Japan! The effort to create this publication was mentally draining, but it gave me an excellent insight into many of the major issues in drug development.

My next job took me into the clinical trials sector, which had always fascinated me, as clinical trials reveal whether a new compound actually has the potential to become a useful drug. My initial job was to develop the budgets for potential trials and write up the proposals that documented how the company proposed to conduct them. Fortunately, I had to interact with every department in our international offices, and this gave me a great insight into how clinical trials were run in different countries.

During my 1st year, the company's marketing manager suddenly decided to leave. At the time, because the company only had around 250 people, not all the company's senior management had bought into the idea of having a full-time marketing manager. They were more interested in hiring staff in other specialist fields, and so the marketing position remained vacant. I was interested in the marketing job and because no one else apparently wanted to get involved, I persuaded my boss to let me try it.

At first the marketing role was pretty thankless as it had no identifiable budget and resources associated with it. However, I was fortunate in that I had contacts in most departments of the company, and so various colleagues

Kermani

Faiz Kermani received his B.Sc. in Pharmacology with Toxicology and his Ph.D. in Immunopharmacology from the University of London. He subsequently worked at CMR International on international research and development productivity analyses for pharmaceutical industry clients. He then moved into the clinical trials sector, working for the CRO Chiltern International. He then worked as a medical writer for Euro RSCG Life UK before joining Health Interactions as an account manager. In November 2007, he was transferred from the company's London office to join its office in Princeton, New Jersey. He recently finished co-editing a textbook entitled "A Quick Guide to Clinical Trials" published by BioPlan Associates.

attempted to help me. Also, thanks to my previous writing and organizational skills, I was able to devise a few low cost ways to get our company publicity externally and to improve communication internally. My first initiative was to launch a press release campaign based on news from around the company. We were lucky in that the company was expanding rapidly internationally, and so there was plenty of useful material. I then found out that a number of industry publications, both in Europe and the United States, wanted not only press releases but also articles on clinical trials tackling both scientific and commercial issues. These articles proved to be a surprisingly effective means for publicizing the company to clients; the basic idea was that if you were knowledgeable enough to write an in-depth article on a subject then the chances were that you knew something about it! Feedback on some of these articles also led to other interesting opportunities. For example, I was invited by the UK government's Trade and Industry Department to attend an official fact-finding mission to China and contribute to a report on the healthcare industries emerging in that country. Another project was co-editing a book to serve as a beginner's guide to clinical trials (after a lot of time spent in chasing contributing authors, the book should finally come out in 2008!).

Once it was possible to prove to my senior managers that our unusual marketing campaign was having a perceptible effect with clients, I was given more resources. Over the next few years, this allowed us to rebrand our company logo and its publicity material, attend major industry conferences, launch a new website, and hire a PR company to distribute our press releases and articles to a wider audience. By this time, the company had tripled in size and expanded across four continents. Strangely enough, now that we had a more mainstream marketing campaign, it was not as much fun as in the early "pioneer" days, and so I looked for a new opportunity.

I decided to venture into medical communications, as it made use of both my scientific background and some of the marketing skills I had picked up along the way. Pharmaceutical companies look for medical communications agencies to develop an appropriate strategy to ensure a favorable launch environment for their products. So far, what I have enjoyed most about medical communications is that every project is truly different. Although some projects will have a very academic "feel" to them and will be aimed at a scientific/medical audience, others may have a more commercial slant for a broader audience. To date, I have been involved in preparing abstracts, manuscripts, and reviews for medical journals, medical textbook chapters, slide sets for investigators to use at conferences, scientific material to be incorporated into publications used by marketing departments, physician product guides, and even some patient-focused materials. Recently, I was offered the opportunity to transfer from the London office of my company to Princeton, New Jersey. After observing the United States pharmaceutical market from the outside for so long, it is really fascinating to finally be working in it!

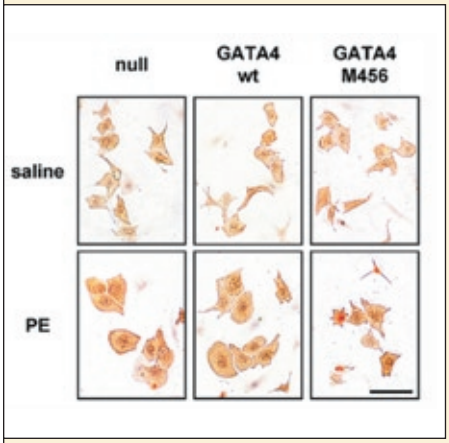
Outside my day job I have also found my assorted skills to have come in handy. In 2005, I had a fun idea for a children's science fiction book called *My Alien Penfriend* (www.myalienpenfriend.co.uk), and I thought up most of the plot while being stuck in traffic while commuting to my previous jobs! Although the process for producing a fiction book might seem different to publishing scientific or business-related material, it actually has a lot in common. Both require organizational and project management skills and a lot of persistence. Funnily enough, a lot of people I have met through work have been interested in the book and provided me with useful advice and encouragement. In one case, staff from a local pharmaceutical company were rebuilding a school library for a literacy campaign and got in touch with me because they were looking for an author to talk to the children at the official opening.

One thing that you will notice from the media is a very negative portrayal of the pharmaceutical industry, because it continues to make substantial profits while there is huge disparity in healthcare access across the world. However, there are people in the industry who feel very frustrated at this state of affairs, and I have come across a number of them who are individually trying to change this situation. At the moment I am working with a few friends to set up a charity that provides educational and training initiatives for healthcare professionals in developing countries. There are some very talented local healthcare professionals in these countries with whom we hope to work. From our point of view, each of us has picked up various skill sets through our scientific careers, and we want to combine these to get the project off the ground.

My scientific background has been more valuable than I ever imagined, and I have found that if you have other skills to combine with the science then some interesting opportunities will come your way—and not just for your day job! It is very important to keep challenging yourself and not be afraid to take on new opportunities, even if not everyone backs your decision. If you have a genuine interest in a particular field, and you feel that you have the drive to succeed, then my advice is that you should go for it!

GATA Have Acetylation

In response to cardiac hypertrophy, or a thickening of heart muscle, transcription factors like GATA-4 induce the expression of proteins that increase cell size, contractile strength, and vasoconstriction. GATA-4 is in part turned on through acetylation by its coactivator p300. However, the exact residues that receive these acetyl tags were unknown, until this paper. The researchers performed mutational analysis on two lysine-rich motifs in GATA-4 and identified four closely spaced lysine residues as critical for GATA-4 hypertrophy activation; a GATA-4 tetra-mutant still managed to localize to the nucleus and interact with its cofactors but could not bind DNA and induce transcription. In addition, the mutant protein could inhibit normal GATA-4 activity and suppress the hypertrophy response when coexpressed in rat heart cells, indicating it possesses dominant-negative properties.



Expressing a GATA-4 tetralysine mutant in rat myocytes suppresses cell hypertrophy in response to chemical stimulus.

Given the importance of understanding the molecular mechanisms underlying heart failure, these studies may prove pivotal in the design of potential heart failure therapies.

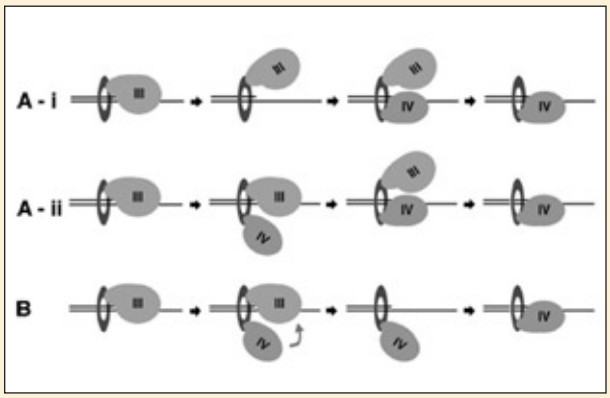
Identification of p300-targeted Acetylated Residues in GATA-4 during Hypertrophic Responses in Cardiac Myocytes

Tomohide Takaya, Teruhisa Kawamura, Tatsuya Morimoto, Koh Ono, Toru Kita, Akira Shimatsu, and Koji Hasegawa

J. Biol. Chem. 2008 **283**, 9828-9835

jbc

The Polymerase Exchange



Three proposed models for pol III*-pol IV dynamic exchange.

During DNA replication in *Escherichia coli*, the DNA polymerase (pol) III holoenzyme will stall upon encountering a lesion. At this point, special translesion synthesis (TLS) polymerases like polymerase IV take over and bypass the bad site, allowing normal replication to continue. It remains unclear how TLS polymerases gain access to the primer site whereas the stalled pol III sits there. In this paper, the authors propose a model where pol IV displaces pol III. Using an assay measuring the DNA synthesis burst of primed pol III following the addition of dTTP, they found that adding pol IV before or after the nucleotide inhibited the synthesis burst. During this slow down, the pol III* complex (two core units and the DnaX protein) no longer fractionated with the template DNA, instead being replaced by pol IV. The researchers propose a dynamic exchange model, where a stalled pol III complex enables pol IV to replace the stuck enzyme, and following lesion bypass, free pol III exchanges back in through mass action.

A Dynamic Polymerase Exchange with *Escherichia coli* Pol IV Replacing Pol III on the Sliding Clamp

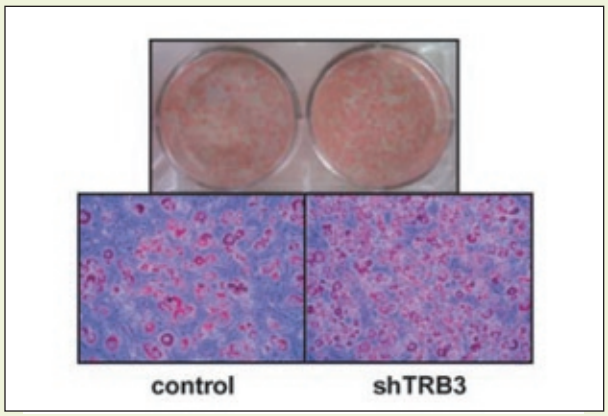
Asako Furukohri, Myron F. Goodman, and Hisaji Maki

J. Biol. Chem. 2008 **283**, 11260–11269

jbc

Regulating Adipogenesis

Adipose tissue, which specializes in storing energy as fat, is made up of adipocytes. These cells are formed from preadipocytes in a process that is regulated by an elaborate network of transcription factors, including peroxisome proliferator-activated receptor γ (PPARγ). In an attempt to discover the proteins that regulate PPARγ, the authors of this paper found that a protein called Tribbles homolog 3 (TRB3) reduces PPARγ transcriptional activity. They showed that *TRB3* gene and protein expression increased during adipocyte differentiation, and that forcing the expression of TRB3 decreased the mRNA levels of PPARγ target genes. Conversely, knockdown of TRB3 expression increased the expression of these genes. The team also proved that TRB3 and PPARγ interact with each other directly. These results indicate that TRB3 plays a critical role in adipogenesis and could potentially be a novel therapeutic target for preventing the abnormal adipocity that is involved in metabolic disorders.



Knockdown of TRB3 expression increases the expression of PPARγ target genes.

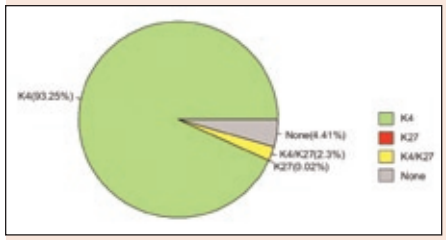
TRB3 Suppresses Adipocyte Differentiation by Negatively Regulating PPARγ Transcriptional Activity

Yu Takahashi, Nobumichi Ohoka, Hidetoshi Hayashi, and Ryuichiro Sato

J. Lipid Res. 2008 **49**, 880-892

The Embryonic Stem Cell Proteome

Embryonic stem (ES) cells are pluripotent cells isolated from mammalian preimplantation embryos. They are capable of differentiating into all cell types and therefore hold great promise in regenerative medicine. In this *MCP* paper, the authors identify and quantify over 5,000 distinct proteins from ES cells. This is the largest quantified proteome reported to date. Using a technique called SILAC (stable isotope labeling with amino acids in cell culture), the team labeled the cells and then fractionated them by one-dimensional gel electrophoresis and by isoelectric focusing of peptides. They then used mass spectrometry to perform a high resolution analysis of the proteins. The researchers also quantified the proportion of the ES cell proteome present in cytosolic, nucleoplasmic, and membrane/chromatin fractions and showed that proteins involved in proliferation are overrepresented in the stem cells. The authors also observed an excellent correlation between protein expression and active *versus* repressive chromatin marks, lending strong credence to chromatin structure as an important influence in protein expression.



Distribution of activating (K4), repressing (K27), and bivalent markers (K4/K27) in the ES proteome dataset.

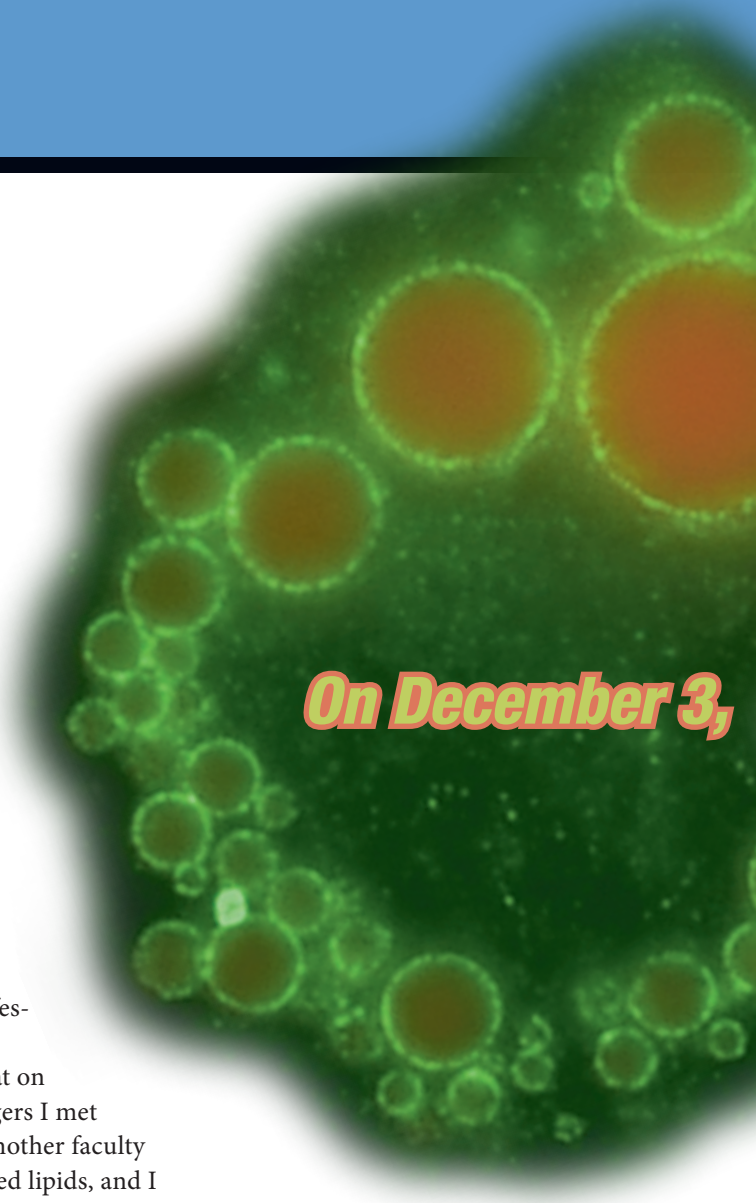
SILAC Labeling and Proteome Quantitation of Mouse Embryonic Stem Cells to a Depth of 5111 Proteins

Johannes Graumann, Nina C. Hubner, Jeong Beom Kim, Kinarm Ko, Markus Moser, Chanchal Kumar, Juergen Cox, Hans Schoeler, and Matthias Mann

Mol. Cell. Proteomics 2008 **7**, 672-683

The Rutgers Center for Lipid Research

BY NICK ZAGORSKI



The lipid droplets (*red*) of cultured 3T3-L1 adipocytes are coated with CGI-58 (*green*), a protein of unknown function that participates in metabolism of triglyceride.

Driving through Rutgers University's School of Environmental and Biological Sciences (SEBS) (formerly known as Cook College), one might get a sense of being in a different time or place. Just a few miles north and south the strip malls, diners, and jug-handle turns that make New Jersey notorious are in full bloom; but here on this campus that hosts the agricultural, environmental, and food and nutritional science programs, the hustle of suburban life is replaced with rolling pastures, grazing livestock, and a sprawling botanical garden.

But although this bucolic setting evokes memories of times past–like the museum within Martin Hall that honors Selman Waksman's pioneering research with antibiotics–there are also those within this campus who are quite forward thinking. Among those are George Carman*, a professor of Food Science and the Director of the recently formed Rutgers Center for Lipid Research (RCLR), one of the first such dedicated lipid groups in the United States.

"There are a few well known lipid-focused institutes around the world," says Carman, noting the Biomembranes Institute at Utrecht University in the Netherlands and the Molecular and Cellular Biology of Lipids (MCBL) group at the University of Alberta as two examples. "And I believe Rutgers has a core group of lipid researchers that's just as strong as those places, so we decided to get ourselves added to that small but distinguished list."

The Birth of a Dream

As an entity, the RCLR may be fairly new, but as a concept, it has been coalescing for many years. In fact, the first seeds may have been planted right after Carman arrived at Rutgers as a fresh-faced assistant professor back in 1978.

"I remember that on my 2nd day at Rutgers I met Charles Martin*, another faculty member who studied lipids, and I found out that we had been hired only 1 day apart." The pair, in fact, had fairly similar research goals: using yeast as a model to understand lipid metabolism. Carman is interested in how the synthesis of phospholipids, the structural components of cell membranes as well as important signaling molecules, is regulated, whereas Martin's interests lie in the enzymes responsible for elongating and desaturating fatty acids, the precursors of many lipids.

Yet despite this connection, Carman notes that since that first encounter, the two of them would only cross paths at conferences. "I could usually count on seeing Chuck twice a year," he says. "At the Gordon Conference on Lipid Metabolism and the ASBMB annual meeting. And it wasn't just him; as the years went by I met many other scientists who either worked at or eventually ended up getting jobs at Rutgers."

These lipid researchers came together via many different routes. In 1992 Carman himself helped recruit conference colleague and Judith Storch*, who studies the transport of fatty acids inside of cells, whereas others arrived for slightly different reasons. Lipoprotein expert Joseph Dixon, for example, relocated in 2004 from his position at the University of Missouri where he had moved 12 years earlier

for his son's asthma, thus bringing the Brooklyn native back home.

Dawn Brasaemle*, who's deciphering the composition and function of lipid droplets–a cell's major energy silo–also found herself at Rutgers through a bit of happenstance. In 1997 she started her first faculty position at the Allegheny University of the Health Sciences in Philadelphia, which had recently formed from a merger of two local medical schools. As luck (and a bit of top-level corruption) would have it, the University was forced to declare bankruptcy just 1 year later.

"I called Judy [Storch], who I knew from all the meetings, the next day and told her I was scared that I would show up to work and there would be chains on all the doors and I couldn't access my own lab," she recalls. "And then I said "What the heck am I going to do now?""

To which Storch quickly replied: "You send me your resume, because we have a spot here!"

Considering this convergence of talent, it seemed odd that these researchers would meet so infrequently. However, such is the nature of Rutgers, which encompasses three different campuses across New Jersey. Even the "main campus," which houses most of the lipid team, is actually a conglomeration of five sub-campuses that sprawls across six townships. "Many of us are only separated by a river and a highway," says Dixon, "but it might as well be another state."

In 2005, Carman decided that it was about time these strangers became friends. "I got in touch with my colleagues and mentioned that we never see each other on campus, so why don't we get together once a month and present our work at a joint meeting. That wouldn't be too burdensome." Naturally, these meetings brought the group closer together, revealing even more shared interests–"As a mammalian cell researcher, I never thought I'd have so much in common with a yeast guy like George," Brasaemle says–and opportunities for collaboration.

In their first major group effort, several of the lipid clan wrote up a joint grant to purchase a new state of the art liquid chromatography mass spectrometer (LCMS), which they could use to analyze the lipid and protein content of various samples. It's a machine many of them needed to take their research to the next level, but none could afford by themselves.

"The LCMS definitely helped bring us together even more," Brasaemle says. "Of course our real thanks should go to Joe who set aside some of his personal research on the components of lipoproteins to teach the rest of us how to use this instrument." Dixon, though, was more than glad to do it. "At Missouri, I was *the* lipid guy, which on one hand was satisfying, but on the other meant I had no one with whom to collaborate. That's definitely not a problem here."

This past summer Carman felt this lipid group was ready for a true "identity" and decided to make a pitch to the Dean of SEBS, Robert Goodman. "I told him we have this outstanding group of lipid people and we would like to form a center," he says. "Our needs were minimal; we just wanted an official designation and website so we could publish collaborative papers and apply for National Institutes of Health training grants and program project grants, as well as a little seed money to start a seminar program."

"It was a brilliant idea," agrees Goodman. So on December 3, 2007, with a speech by Phil Yeagle* (a lipid biophysicist and founding member of the RCLR who had recently been appointed as Dean of the Faculty of Arts and Sciences at Rutgers Newark), a round of applause, and a popping of corks, the Rutgers Center for Lipid Research–conceived and nurtured by the work of just a few dedicated faculty–was officially born.

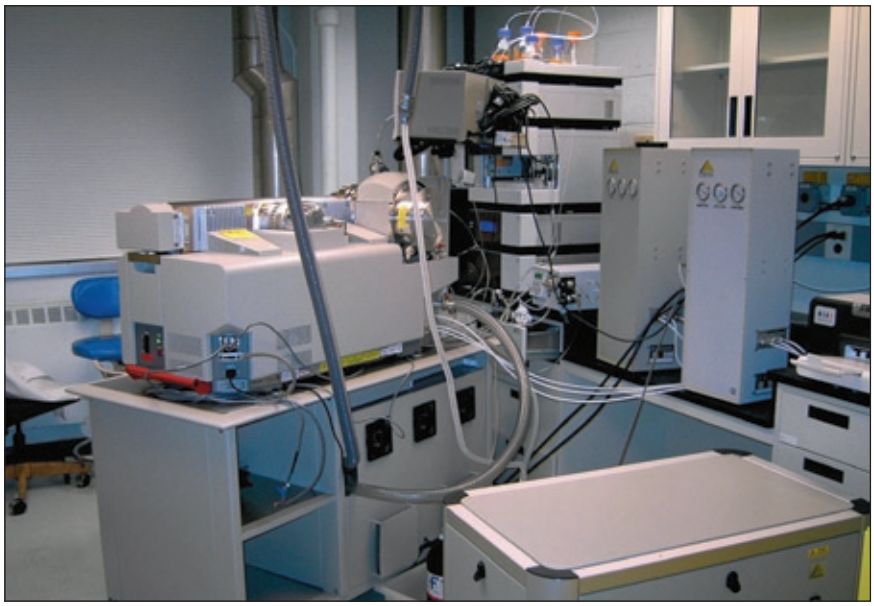
2007 the Rutgers Center for Lipid Research was officially born.

George Carman

The Little Center That Could

Joe Dixon knows that a little notice can go a long way. Years back, the biotech company Parke-Davis brought him in to evaluate some promising research on a next-generation cholesterol-lowering drug, atorvastatin. "This drug was originally developed by Parke-Davis," he says, "and then Warner-Lambert realized this new drug might be pretty big, so they bought Parke-Davis. Well, some time later, Pfizer caught wind of this drug and realized that it might be *really* big, so they bought Warner-Lambert. Today, Pfizer makes around $12 billion per year off of Lipitor, and most doctors don't know that they had nothing to do with its development."

Dixon and rest of the RCLR hope that their own little center might someday reach such a lofty status. Similar to how Alberta's MCBL receives generous support from Canada's canola oil industry, Carman envisions that his group will catch the eye of New Jersey's substantial pharmaceutical presence. After all, numerous lipid research discoveries in the 30 years since Carman came to Rutgers, from the strong link between fat metabolism and diabetes to the role of lipid messengers in cancer development, have illuminated the central contribution of lipids in disease.



This new LCMS will enable RCLR scientists to identify the many components of lipoproteins and tackle other complex questions.

Another future partership for the RCLR with be with Rutgers newly planned Institute for Food, Nutrition, and Health (FNH), one of three University-wide initiatives aimed at promoting more cross-disciplinary and translational research in areas of high public interest. "I see the Lipid Center becoming a core element of this initiative," Goodman says."

RCLR Mini-Bio: *Dawn Brasaemle*

While leafing through the back of a journal in 1992, Brasaemle came across an intriguing job opening. "This lab mentioned they had just identified perilipin, the first lipid droplet protein, and were looking for a lipid specialist to help out. I thought, this is a gold mine!" Lipid droplets, the cell structures that store lipids for energy, had long been thought to be inert structures. But Brasaemle, who applied for and got that staff scientist position in Constantine (Dean) Londos' lab at the NIH, is helping change that view. "Of course, when I first told Dean how excited I was to look for more lipid droplet proteins, he said "Oh no, this is the only one." Well, sure enough I soon found numbers two and three."

Since starting her own lab at Rutgers, Brasaemle has continued her characterization of lipid droplets (now properly known as dynamic organelles), particularly how these three surface proteins (perilipin, adipophilin, and TIP47) regulate the access of metabolic enzymes to the energy-rich lipids stored inside.

RCLR Mini-Bio: *Judy Storch*

"It's an unresolved issue as to whether or not cholesterol can just zip through membranes," says Storch, who's long been interested in lipid traffic inside and across cells. She points out that if a cell is defective in a cholesterol-binding protein called NPC2, then the cholesterol accumulates in the cell's degradation center, the lysosome. "It makes you wonder, because if cholesterol could just move out through mass action, then why doesn't it?" Using both biochemical and biophysical approaches, Storch is unraveling how NPC2 controls cholesterol transport, and has recently found that a lipid found only in lysosome membranes, LBPA, might also be involved.

Channeling her previous career as a nutritionist, Storch emphasizes that this mystery is important at the individual and not just cellular level; defects in NPC2 and its phenotypic cousin NPC1 lead to Niemann-Pick disease, a terrible and fatal metabolic disorder. "And unfortunately one that's overlooked because it's so rare," she says. "Of course, it's only rare when it's not your child."

At present, however, this little group has more modest ambitions. The first order of business is completing the coalescence of the RCLR and getting more of the team under one roof. Fortunately, space has opened up in the Food Science building where Carman works, providing enough room for all the members at the SEBS campus, who can hopefully complete the move by the end of the year.

The Food Science building may not be the fanciest digs (although the 10-year plan of the FNH Institute calls for a new building, perhaps housing a Lipid Center wing?) but it will let the researchers acquire more shared lab equipment and build the kind of relationships needed for success. As Brasaemle notes, "Bumping into people in the hall, that's where most great science gets done."

Beyond packing up lab equipment, the RCLR members are busy trying to increase their visibility at their own university and external scientific circles. If assistant professor Ariel Igal, one of the newest members of the RCLR, is any indication, then they've been doing a great job.

Igal, a promising young Argentine who studies the enzyme stearoyl-CoA desaturase and how it connects lipid metabolism and cancer, had been offered a great position with the latest and greatest amenities at a highly regarded biomedical research center, but instead chose Rutgers because of the people with whom he would work.

And with Igal's addition, Carman believes the 10 scientists comprising the RCLR are an exceptional group, with each one adding their own wrinkle to the diverse field of lipid research–whether it involves cell membranes, fat metabolism, energy storage, cholesterol, or even fat-soluble molecules like vitamin A and its derivatives, the area of expertise of another new addition, nutritional scientist Loredana Quadro*. The studies also range in scope from Carman's fundamental yeast biochemistry to Rich Mendelsohn's biophysical analysis of lipid membranes to clinical work examining how fat cells contribute to insulin resistance being carried out by Hong Ruan at the Robert Wood Johnson Medical Center.

"I may have made some sacrifices in terms of lab space and facilities," Igal says of his quaint lab in the Thompson Nutrition Building, "But you can't beat the people here; they're top-notch."

Nick Zagorski, Ph.D., a graduate of Johns Hopkins and Cornell Universities, is a science writer for ASBMB. He can be reached at nzagorski@asbmb.org.

Ohara Augusto: Detecting Free Radicals in Biology

BY NICK ZAGORSKI

Ohara Augusto

Researchers in the United States certainly have to face their share of difficulties, be it trying to secure highly competitive funding or place their results in highly competitive journals. Of course, other researchers like Ohara Augusto, Professor in the Department of Biochemistry at the Universidade de São Paulo in Brazil, wish they had such problems. Although Brazil has made great strides in improving its scientific enterprise, it still cannot match—as Augusto puts it—"the scientific machine" running in the U.S.

"It can be difficult here" she says. "Unlike America it's hard to get good post-doctoral candidates to come work here, so I've always had to work with young students. And that requires more effort to train them and go over their work." With more financial constraints as well, Augusto notes Brazilian researchers have to be more selective in the projects they pursue, and generally shy away from highly competitive areas of research.

But as Augusto also adds, "Just because our research is not competitive does not mean it's not interesting." This axiom holds true for Augusto, who for over 30 years has been studying the formation and metabolism of free radicals, molecules harboring an unpaired electron and thus highly reactive. Her studies have helped solidify free radicals as physiologically prevalent, and relevant, biomolecules in both health and disease.

Her biggest contributions, however, have been bringing into focus species that previously had not been really considered in the literature. Whereas reactive oxygen species like superoxide ($O_2^{\bullet -}$) and hydroxyl radicals ($HO^{\bullet}$) have historically been front and center in the free radical arena, Augusto's work has helped usher in new species like peroxynitrite ($ONOO^-$) and carbonate radicals ($CO_3^{\bullet -}$) into the discussion. And considering how many different diseases have oxidative stress as a component, it's becoming an important discussion indeed.

Radical Fascination

Growing up in a lower middle class family in São Paulo, only two generations removed from illiterate immigrants who arrived from Portugal and Austria, Augusto never envisioned a future career as a distinguished researcher. She didn't even like science, until one particular moment when she was 13. "One of my secondary school teachers was explaining the concept of electrons to me," she says, "and I remember that talk just fired up my imagination."

> **"I became fascinated by the connections**

From that point forward, Augusto became heavily interested in chemistry, and decided to attend a technical school instead of regular high school, which did hinder her general education, but provided good training in chemistry and laboratory techniques. She then continued on to the University of São Paulo in 1967 to get her undergraduate degree in chemistry, while also working as a high school chemistry teacher at night.

While an undergraduate, Augusto befriended Francisco Nóbrega, a biochemist who had just returned from his doctoral studies in the United States. "I knew nothing about biochemistry, but listening to him I became fascinated by the connections between biology and chemistry, and how these basic chemical processes would relate to how organisms function and dysfunction," she says. To help Augusto learn more, Nórbrega

also lent her his copy of the recently published biochemistry textbook by Albert Lehninger, which she studied intensely. She then made the choice to continue her education in this field, and stayed on at São Paulo to get her biochemistry Ph.D.

Her decision was fortunately well timed; following the 1964 coup d'état that ushered in a military dictatorship and subsequent radical student movements, the latter 1960s were not especially kind to the Brazilian education system. By the early 1970s, however, things had begun to turn around, and in fact government funding agencies were aiming to strengthen biochemistry-related research in the country. "As a result the university had just created its first biochemistry department," she says. "They joined scientists together from the schools of medicine, chemistry, and pharmacy, and it made for a stimulating environment."

Augusto's thesis supervisor was Giuseppe Cilento, an Italian émigré who had become one of Brazil's most eminent chemists. Cilento worked on biological oxidation, with particular emphasis on oxidation reactions that generated excited chemical states, and he gave Augusto a project looking at how catecholamines, ringed chemicals that include natural compounds like adrenaline and dopamine, affected oxidations mediated by microsomal oxidases and hemoglobin.

"I think as a result of my project we may have been one of the first labs to propose that oxyhemoglobin exists as an iron(III) superoxide," she says, adding that unfortunately she and Cilento never pursued her initial studies so their work became lost in the literature. Nevertheless, she persisted in the emerging field of free radical biology. "It was right around this time that Irwin Fridovich discovered the antioxidant enzyme superoxide dismutase, and from his work and others, it was becoming clear that free radicals were continually being produced in organisms," Augusto says. "I became fascinated with free radicals and ever since then I wanted to understand their role in biology."

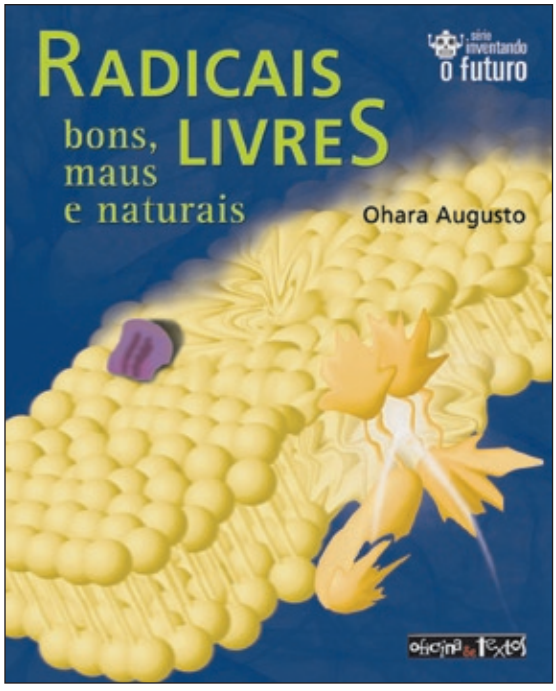
To America…

After receiving her Ph.D. in 1975, Augusto began a professorship at the University of São Paulo. In order to develop her own research, though, she still needed to learn more about free radical biology and needed to go abroad to do it. "Detecting free radicals, back then and even still today, is difficult," she says. "The only technique to detect radicals directly is electron paramagnetic resonance (EPR) spectroscopy." As Augusto wanted to learn more about EPR, she was granted a leave of absence to the U.S., obtaining a post-doc in 1980 with Lester Packer at the University of California, Berkeley.

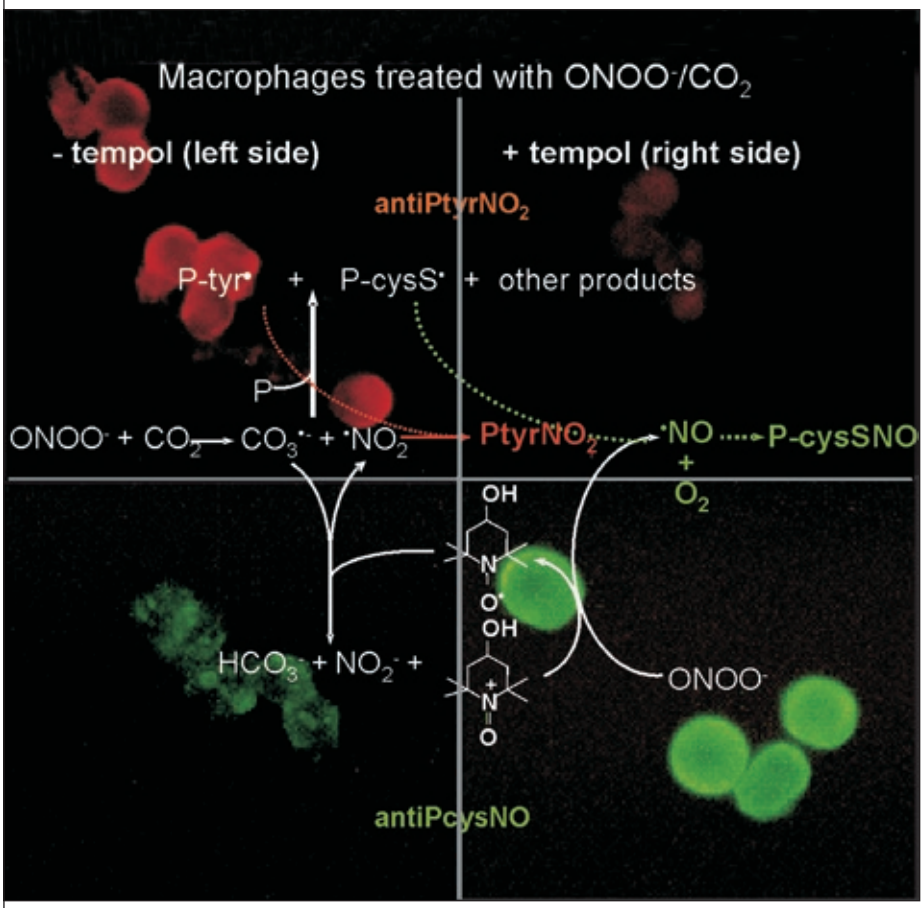
between biology and chemistry"

In her 1st year with Packer, Augusto had a great experience and learned a lot of basic knowledge about EPR techniques, but she also wanted to steer her studies in a different direction than Packer's research, which was concentrated in photobiology. "I wanted to focus more on drug metabolism," she says, "because this was relevant to the chemicals used to treat infectious diseases like malaria. As I came from Brazil, I was of course interested in these 'neglected diseases'; but Packer was not."

While attending a meeting in Mexico, however, Augusto heard a lecture by Paul Ortiz de Montellano, who was studying the activation of cytochrome P450 enzymes, a diverse family of heme-containing oxidases, by various drugs. His work fit Augusto's interests very well, and even better, he was literally next door at the University of California, San Francisco. "To think



Free Radicals: Good, Bad, and Natural is a book by Augusto published in 2006 (Oficina de textos, São Paulo, SP, pp. 115), and belongs to a series of books aimed to encourage high school and undergraduate students to pursue scientific careers.



Schematic representation of the mechanism by which tempol diverts the reactivity of peroxynitrite/carbon dioxide in cells from protein nitration to protein nitrosation (structures). The background show cells treated under different conditions, responding to antibodies that detect either protein nitration or protein nitrosation.

he was so close and I had to go all the way to Mexico to find him," she says with a laugh. And although Packer was reluctant to let a quality trainee like Augusto go, he remained quite supportive and allowed her to use his EPR machine anytime she wanted.

Augusto spent 2 years in Montellano's lab, using a method known as electron spin trapping to 'trap' and thus detect elusive radicals, unstable molecules with extremely short half-lives. She produced some important findings during this period, such as uncovering that some drugs metabolized by P450 produced carbon radicals that attacked the heme group and irreversibly inactivated the enzyme. This work was some of the first describing radical formation by hemoproteins other than peroxidases (enzymes that use hydrogen peroxide or similar compounds in their catalytic cycles).

Augusto notes her findings had an important implication for drug developers as well. "Many chemical drugs have a narrow therapeutic window," she says, "and if they can inactivate the enzymes that react with them, it would alter the cell's metabolism and lead to toxicity."

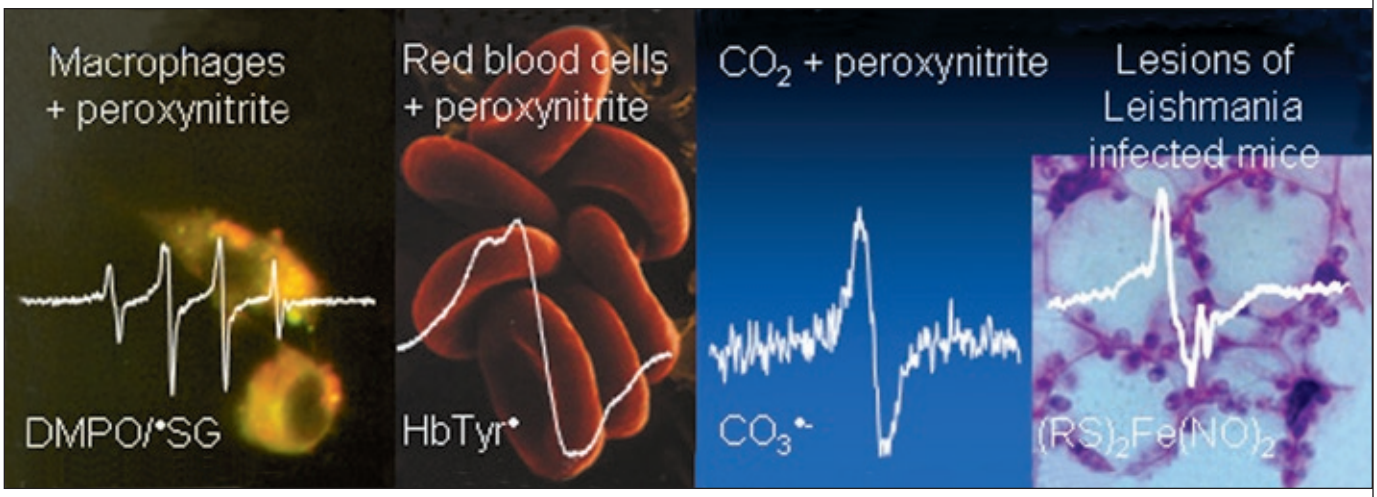
… And Back

All good things come to an end, and in 1983 Augusto's leave of absence expired and she had to return to Brazil. It was a bit rough coming back home, as Brazil was going through an economic depression, and laboratory resources were difficult to come by. She insisted that an EPR machine would be critical, and joined with fellow faculty member Shirley Schreierto, she helped establish an EPR facility at São Paulo. With this new facility in place, Augusto was able to continue her work with carbon radicals, and she also began examining the metabolism of primaquine, a common malaria treatment.

Although certainly a necessity for her own research, Augusto points out that the São Paulo EPR facility has been valuable in fostering science communication by bringing in researchers from across Brazil and all of Latin America. In the early 1990s Augusto herself became a part of the multinational connection, as she began a long collaboration with Rafael Radi from the Universidad de la República in Uruguay. Radi introduced Augusto to peroxynitrite, a molecule produced by the reaction of superoxide anions with nitric oxide.

"The discovery of peroxynitrite was an immediate hit," she says, "because of its association with inflammation and vascular damage (NO and superoxide are both up-regulated during inflammation). At the same time, a lot of the early literature was controversial, especially whether or not this peroxide produced free radical intermediates."

Augusto demonstrated that this molecule did indeed manufacture free radicals, several different types, in fact, depending on the conditions. When protonated at acidic pH, it produced nitrogen dioxide and hydroxyl radicals, and in the presence of bicarbonate buffer, it produced carbonate radicals. Having proven radical formation in test tubes, Augusto then proceeded to show that



Augusto's lab logo.

adding peroxynitrite to cells could 'radically' alter susceptible biomolecules like glutathione and tyrosine, and also proposed that macrophages used peroxynitrite to kill *Leishmania* parasites by nitrifying them.

More than Just Oxygen

Her research into peroxynitrite, and even her earlier post-doc work with cytochrome P450s, has led Augusto to champion an overlooked set of compounds known as cyclic nitroxides, ringed molecules that can scavenge nitric oxide-derived oxidants. "I am among those who think cyclic nitroxides might offer new windows for antioxidant therapies," she says. "Antioxidants are a frustration right now; many large scale intervention trials with classical antioxidants like vitamin C have been recently carried out, and they've failed to have a significant effect."

Of all her work, however, Augusto stresses her direct EPR evidence of carbonate radicals forming at physiological pH as the most important. "It was a critical discovery because investigators did not consider the oxidative potential of bicarbonate, which is the principal buffer in biological systems," she says. "This affects not only how we view peroxynitrite damage but other oxidizing agents as well."

Currently, Augusto has undertaken an ambitious project exploring the possible role of bicarbonate in amyotrophic lateral sclerosis (ALS or Lou Gehrig disease). Whereas mutations in superoxide dismutase are known to be responsible for some ALS cases, she thinks carbonate radicals may also contribute to protein aggregation and the degeneration of motor neurons. She has developed a hypothesis combining mechanisms proposed by different investigators and is in the process of collecting the evidence for her idea.

She's not sure how the results will turn out but is bolstered by the support of some other free radical researchers like Irwin Fridovich. "That is one good thing about having competitors," she says. "They can also become your allies."

Out of Focus: GOAL!

Many PIs here might experience a brief drop in productivity during the period known as "March Madness," although it probably pales in comparison with the empty labs in São Paulo whenever the Brazilian soccer team has an important match. "It's impossible to get any work done," she says, but without complaint. After all, Augusto, who enjoys reading books on sociology and listening to classical music, is also a big soccer fan. "I'm usually watching the game next to my students."

Nick Zagorski, Ph.D., a graduate of Johns Hopkins and Cornell Universities, is a science writer for ASBMB. He can be reached at nzagorski@asbmb.org.

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www.proteomecenter.org/nav.course.05.08.php
Email: info@proteomecenter.org

2008 ATS International Conference
MAY 16–21, 2008
TORONTO, CANADA
www.thoracic.org/

Keystone Symposium—G-Protein Coupled Receptors
MAY 18–23, 2008
KILLARNEY, IRELAND
www.keystonesymposia.org/Meetings/ViewMeetings.cfm?MeetingID=908

Gordon Research Conference on Thiol-based Redox Regulation and Signaling
MAY 25–30, 2008
IL CIOCCO, ITALY
Chair: Ruma Banerjee.
Vice Chair: Roberto Sitia
www.grc.org
E-mail: rbanerje@umich.edu

JUNE 2008

Immunobiology and Pathogenesis of Influenza Infection
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ATLANTA, GEORGIA
http://web.mac.com/tcassin/iWeb/IPIRC/HOME.html

FASEB Summer Research Conferences
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VARIOUS LOCATIONS
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American Diabetes Association 68th Scientific Sessions
JUNE 6–10, 2008
SAN FRANCISCO, CA
http://scientificsessions.diabetes.org

90th Annual Meeting of the Endocrine Society
JUNE 15–18, 2008
SAN FRANCISCO, CA
www.endo-society.org/apps/Events/Event.cfm?EventID=1253

Understanding Aging: Biomedical and Bioengineering Approaches
JUNE 27–29, 2008
LOS ANGELES, CA
www.mfoundation.org/UABBA

33rd FEBS Congress & 11th IUBMB Conference
JUNE 28–JULY 3, 2008
ATHENS, GREECE
www.febs-iubmb-2008.org

JULY 2008

Trends in Enzymology 2008
JULY 2–5, 2008
ST MALO, FRANCE
Organizers: Susan Miller and Bernard Badet
http://TinE2008.org
E-mail: TinE2008@icsn.cnrs-gif.fr

Natural Genetic Engineering and Natural Genome Editing
JULY 3–6, 2008
SALZBURG, AUSTRIA
www.naturalgenome.at

17th International Symposium on Microsomes and Drug Oxidations
JULY 6–10, 2008
SARATOGA SPRINGS, NY
http://mdo2008.org

Second Warren Workshop on Glycoconjugate Analysis
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http://glycomics.unh.edu/WarrenWorkshop/index.htm

The XXth International Fibrinogen Workshop
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Contact: Dr. Mattia Rocco (mattia.rocco@istge.it)
http://alisf1.univpm.it/XXifw/

FASEB Summer Conference: Molecular Mechanisms Involved in the Nutrient Control of Cellular Function and Metabolism
JULY 20–25, 2008
CAREFREE, AZ
https://secure.faseb.org/faseb/meetings/Summrconf/Programs/11715.pdf

Society for Developmental Biology 67th Annual Meeting
JULY 26–30, 2008
PHILADELPHIA, PA
www.sdbonline.org/2008Mtg/webpage.htm

AUGUST 2008

HUPO 7th Annual World Congress
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AUGUST 24–28, 2008
BREGENZ, AUSTRIA
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Glutathione and Related Thiols in Microorganisms
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https://matar.ciril.fr/THIOL/homephar.php

30th European Peptide Society Symposium
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www.kuleuven.ac.be/aidslab/veme.htm

Workshop: *Biology of Signaling in the Cardiovascular System*
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HYANNIS, MA
www.navbo.org/BSCS08Workshop.html

Symposium on Extracellular and Membrane Proteases in Cell Signaling
SEPTEMBER 18–21, 2008
AMES, IA
www.bb.iastate.edu/~gfst/homepg.html

International Conference on Structural Genomics
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OXFORD, UK
www.spine2.eu/ISGO

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www.insulinresistance.us

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OCTOBER 2008

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www.glycobiology.org

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SAN DIEGO, CALIFORNIA
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The 48th American Society for Cell Biology Annual Meeting
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http://ascb.org/meetings/

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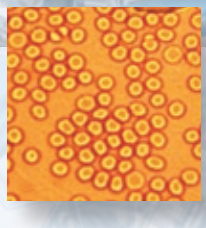
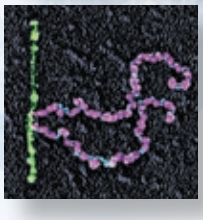
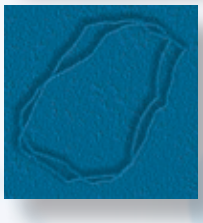
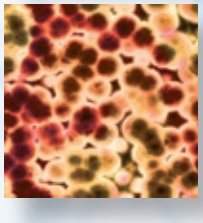
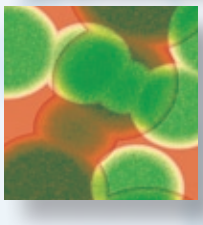
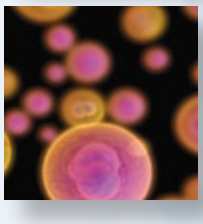
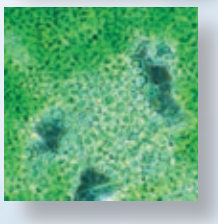

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