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June 2011

Gary Felsenfeld: Untangling Chromatin's Mysteries.

American Society for Biochemistry and Molecular Biology

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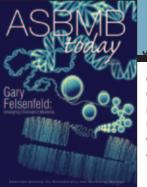
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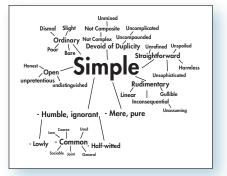
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asbmb today online

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June 2011



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

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Why the drop-out? A junior faculty perspective

To the editor:

I just came back from another invigorating American Society for Biochemistry and Molecular Biology annual meeting in Washington, D.C., packed with the usual cutting-edge scientific sessions as well as several exciting sessions on the future of life sciences education. However, what surprised me the most was the quantity and quality of sessions and workshops focused on providing substantive career support for current graduate students, postdoctoral fellows and junior faculty. When I first started coming to these meetings, the available career guidance was restricted to a few talks outlining standard career options followed by workshops on how to polish up your resume and what to say in an interview to convince employers that you are who they want you to be. While these services are still offered, it is great to see that the emphasis has shifted toward helping young scientists identify their own strengths and priorities early and providing practical advice on how to excel using their own potentials as scientists. There also is a clear growing interest in offering practical mentorship to help tackle the challenges of a scientific career, especially for young women scientists struggling to strike a balance between work and family life.

The women biochemists mixer on Tuesday evening certainly was one of those occasions. We heard and discussed several personal stories about a variety of challenges faced by women biochemists across the entire career spectrum in an informal and nonjudgmental setting. I have been to these mixers before, so I was not surprised when the conversation led to the familiar question: Why does the number of women scientists dwindle as they go up the scientific ranks? Despite the fact that about 45 percent of postdocs in the biomedical sciences are women, women hold only about 29 percent of tenure track positions and only about 19 percent of tenured faculty positions (1). However, what did surprise me was that there apparently are still many senior women scientists who believe that women are afraid to ask for what they need or are less willing to push their agenda forward compared to their male counterparts, resulting in their self-selection out of the system. Though this may still be true in some cases, many recent studies addressing the drop-off issue reveal the main reason to be the inability, especially for women scientists, to strike a reasonable work/life balance. Based on many discussions on this issue with female colleagues at different stages of their scientific careers, I am persuaded that our generation of junior faculty is much less fearful than our senior colleagues believe us to be. Thanks to all the doors they have cracked open for us, many of us know that if we push hard enough, we will get through. On the other hand, we also have witnessed the high price many of those women had to pay, and we realize that for many of us now, it is not only about making it through.

One of my favorite movies is "The Race for the Double Helix." Every semester I teach my biochemistry course, we have a movie night with popcorn and watch it, and then we spend significant class time comparing and contrasting the contributions of each of the players to this important discovery. Not surprisingly, at a women's liberal arts college whose mission is to "educate women who will make a difference in the world," the debate about Rosalind Franklin always becomes pretty heated. Every time we come to the scene where Rosalind is given a basement room to conduct her research and is not allowed into the men's lounge, I am reminded of how far we have come in ensuring equal opportunities for women scientists, and I am grateful to all our predecessors for making this happen. Yet I feel that this initial quest was relatively straightforward, because every woman had the same goal: to fight for the opportunity. The next pursuit



is more complex and therefore more challenging: to ensure sustainable opportunities that do not require women to make choices that men do not have to make. During our evening discussion, someone pointed out that things are much better now than they were before, since there are now several examples of women scientists with families in high ranks. Though I am sure this is true, most of the ones I see have yet to find some quality time they can spend with their families without feeling guilty.

It is curious to witness so many women junior faculty members pronounced inadequate or not a good fit for their jobs after a few years into their independent careers when they were found perfectly on a par with their male counterparts just a few years before. It makes you wonder if it really is the decline of an individual's performance or our inability to assess scientific worthiness appropriately. At the ASBMB meeting, I met many young women who are trying exciting new initiatives at the academic positions they have been offered, yet their performance still is being assessed by traditional standards. Perhaps it is time to be looking for some innovative ways to incorporate the values and expectations of today's global society into the scientific productivity analysis. Encouraging a system that focuses on honoring and rewarding diverse individual strengths and contributions would go a long way to ensuring a more balanced and sustainable scientific career model.

Our careers should not be battles to get from one point to the next and simply demonstrate it can be done. When we reach each of our milestones, we should still have the energy and passion to serve as role models for younger scientists with our enthusiasm, knowledge and experience through engagement in high quality science. At the time of tenure, we should have more than just our peer-reviewed journal articles to be proud of as personal accomplishments. We should not only be relying on our colleagues to pick our children up from school when we are running late because we have not had the time to get to know any other parents in our kids' classrooms. Hence, I would like to leave you with the idea that perhaps it is not the fear of failure at a specific career milestone that is causing the self-selection of women at higher ranks of the scientific career but rather the fear of an unsustainable life beyond that success and the awareness of all the life-long compromises they have to make during the long journey.

sincerely, Didem Vardar-Ulu

Assistant Professor of Chemistry SCI Science Center, Wellesley College

REFERENCE

 Martinez, E.D., Botos, J., Dohoney, K.M., Geiman, T.M., Kolla, S.S., Olivera, A., Qiu, Y., Rayasam, G.V., Stavreva, D.A., and Cohen-Fix, O. (2007) Falling off the academic bandwagon. Women are more likely to quit at the postdoc to principal investigator transition. *EMBO Rep.* 8, 977 – 981.



president's message

Roy Vagelos: forging links between academia and industry

BY SUZANNE PFEFFER

his month I write to honor Dr. Roy Vagelos, a long-term member of the American Society for Biochemistry and Molecular Biology who helped us create the ASBMB Earl and Thressa Stadtman Distinquished Scientist Award after Earl Stadtman died in 2008. The Stadtman Award recognizes a scientist for his or her outstanding achievement in basic research in the fields encompassed by ASBMB; it will be given annually and alternate between an established scientist and a young investigator with less than 10 years of experience as an independent investigator. Earl Stadtman helped elucidate the role of coenzyme A in fatty acid metabolism and made



Suzanne Pfeffer, Michael Brown, Joseph Goldstein and Roy Vagelos at the 2011 Earl and Thressa Stadtman Distinguished Scientist Award lecture.

major contributions to our understanding of reversible, interconvertible enzyme cascades in regulating glutamine synthetase (1). Thressa Stadtman made important contributions to vitamin B12 biochemistry, and her work included the first demonstration that selenium plays an essential role in the catalytic activity of many selenoenzymes (2, 3). Drs. Michael Brown and Joseph Goldstein from the University of Texas Southwestern Medical School were the first recipients of this award this year, which was especially gratifying for Mike Brown as a former Stadtman lab postdoctoral fellow.

Roy Vagelos presented the award to Brown and Goldstein at the 2011 annual meeting. Vagelos also was a Stadtman lab postdoctoral fellow. He earned his Bachelor of Science in chemistry from the University of Pennsylvania and his M.D. from Columbia University. After an internship and residency at Massachusetts General Hospital, he joined the National Institutes of Health and served as senior surgeon and then section head of comparative biochemistry. While at the NIH, Vagelos began his own pioneering research on lipid metabolism, which led to the discovery of acyl-carrier protein (4). Later, he became chairman of the department of biological chemistry at Washington University School of Medicine. In 1975, Vagelos joined Merck, first as president of Merck's research division and then as senior vice-president; he served as president and chief executive officer of the company from 1985, and chairman from 1986, until his retirement in 1994. Not only was he the lead scientist in Merck's development of the statin drugs Lovastatin and Zocor, he also was the key advocate in Merck's decision to make Ivermectin freely available to the people of Africa and Central America for the treatment of river blindness, a widespread, chronic and debilitating disease caused by the parasite Onchocerca volvulus and disseminated by black flies.

Roy's son Randall Vagelos, an outstanding cardiologist at the Stanford School of Medicine, adds, "My father treats the development and evaluation of every new and potential drug as critically as if he were assessing and treating a patient. This strong association is what drives him to push to deliver new therapies to patients and can be seen in the novel approach he took in his leadership style at Merck and afterward in his career. He is patient-centered."

Having worked in academia and the pharmaceutical

industry for more than 40 years, Vagelos has long been an advocate of the importance of interactions between these two arenas (5). He points out that these interactions are essential for the discovery and development of new drugs and for providing scientific and educational information about new products to physicians for use in patient care. Drug discovery usually takes place in industry, but it is absolutely dependent upon knowledge that is generated at universities. Once a drug is developed (usually in industry), testing often involves close collaboration with university physicians to design and analyze data from clinical trials and to help formulate a strategy for U.S. Food and Drug Administration review of the findings.

During our annual meeting in March, Vagelos took time to talk with ASBMB leadership about the continued importance of links between academia and industry. He noted that some companies now are turning to academic institutions to help discover new targets and new drugs. According to Vagelos, Pfizer is cutting back intramural research and is providing academic researchers with access to chemical libraries and antibodies and preliminary toxicology results in exchange for rights to develop future discoveries. Merck, on the other hand, is one of the large pharmaceutical companies that is not cutting back basic research activities.

Vagelos noted that the medicinal chemistry needed to develop effective drugs is not an academic activity; rather, it is an area in which industry excels. He feels strongly that translational research is best tackled in partnership with industry – and that it would be foolish not to take advantage of the vast expertise and resources that industry can provide. Vagelos added, "Universities are best at obtaining new knowledge. Industry needs that new knowledge, and if the U.S. National Institutes of Health wants to best support new drug discovery, pursuit of fundamental knowledge should be the focus of its limited resources."

Vagelos, and recently Johnston et al. (6), summarized a number of cases where a drug could not have been developed without productive interactions between academia and industry. For example, Imatinib (Gleevec) is used as a first-line therapy for patients with chronic myelogenous leukemia. Nicholas Lydon, an industrial scientist, partnered with an academic investigator, Brian Druker, to identify novel tyrosine kinase inhibitors for the Bcr-Abl kinase implicated in this disease. As noted by Johnston et al. (6), "Academia is not charged or organized to bring therapies to the public... With rare exception, the public benefits of discoveries made in academia are realized only when they have been translated into use through industry. Unlike academia, industry is designed to effectively and efficiently produce and distribute therapies. Thus, academia and industry each have an essential role in improving health through biomedical discoveries."

The reputation of collaborations between industry and academia has suffered in recent years from undisclosed financial ties and perceived conflicts of interest (5, 6). These must be dealt with explicitly and with maximal transparency to ensure the reliability of research findings, proper design of clinical trials and avoidance of corruption of the prescribing behavior of physicians. But all of us must work together to promote strategic research interactions between academia and industry.

As the NIH prepares to establish a National Center for Advancing Translational Sciences, ASBMB urges NIH to leverage what industry brings to the table rather than trying to reinvent the wheel. Congress and the public are justified in wanting cures, but they will not be there if we stop supporting basic research. Drug company breakthroughs are few and far between, and when existing drugs stop working, it is only the basic science that can help industry determine what tack to take next. There was no Gleevec before we knew about tyrosine kinases. And given that we have no idea what a large proportion of human genes do, there is plenty of fundamental research that still needs to be done.

Thank you, Roy Vagelos, for your outstanding contributions, your advocacy for basic research, and your continued support of ASBMB. VXX



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

REFERENCES

- Kresge, N., Simoni, R.D., and Hill, R.L. (2005) Fatty acid synthesis and glutamine synthetase: the work of Earl Stadtman. J. Biol. Chem. 280, e23.
- Park, B. S. Thressa Stadtman: how does vitamin B12 function? http://history. nih.gov/exhibits/stadtman/nose_VB12.htm
- Park, B. S. Thressa Stadtman: pioneer of selenium biochemistry http://history. nih.gov/exhibits/stadtman/nose_selenium.htm
- Kresge, N., Simoni, R.D., and Hill, R.L. (2005) The role of the acyl carrier protein in fatty acid synthesis: the work of P. Roy Vagelos. J. Biol. Chem. 280, e32.
- Vagelos, P. R. (2007) Innovation and industry-academia interactions: where conflicts arise and measures to avoid them. *Cleve. Clin. J. Med.* 74, Suppl. 2:S12-3.
- Johnston, S. C., Hauser, S. L., and Desmond-Hellmann, S. (2011) Enhancing ties between academia and industry to improve health. *Nat. Med.* 17, 434–436.

news from the hill



Alternative energy nation?

Congress considering legislation to promote and develop *laboratory-based biofuel production.*

BY BENJAMIN CORB AND GEOFFREY HUNT

The establishment of Advanced Research Projects Agency-Energy was one of the major accomplishments of the America COMPETES Act. ARPA-E is intended to "bridge the gap between basic energy research and development/industrial innovation," incorporating tools across the life sciences spectrum to facilitate high-risk, high-reward projects that, according to the agency's mission statement, promise "genuine transformation in the ways we generate, store and utilize energy." The primary focus at ARPA-E is on developing alternative energy sources while improving the efficiency of energy usage and storage. The agency funds 121 groundbreaking projects divided among 10 overarching categories; tellingly, the Conventional Energy category contains but a single project.

Within this broad agenda there are several niches into which biochemistry fits. The Direct Solar Fuels program funds projects that use genetically modified bacteria to harness solar energy to drive the production of fuel sources from natural products such as carbon dioxide. Alternative fuel sources also are at the heart of the Biomass Energy program, which is aimed at improving the conversion of plant material into fuel by means of biochemical modifications, including enhanced enzymatic activity.

The types of projects funded by ARPA-E are considered by private industry to be too risky to warrant significant investment. To help spur development of these alternative energy sources, Congress is reviewing and considering several legislative courses of action. Numerous bills have been introduced during the 112th Congress that would greatly expand existing programs focused on alternative fuel production while also providing tax incentives for producers. Historically, most bills aimed at alternative energy sources and biofuels focused on alcohol-based ones such as ethanol or an ethanol/gasoline blend; however, the recently introduced legislation calls for expansion of current guidelines to include the newer forms of biodiesels, notably cellulosic and algae-based fuels.

House of Representatives bills

H.R. 1149 (sponsored by U.S. Rep. Brian Bilbray, R-Calif.) would update existing legislation to include algae-based biofuel in the renewable fuel program, thus making tax benefits that had previously only been available to producers of plant-based biofuel available to producers of renewable algae-based biofuel.
H.R. 851, the Clean Energy Jobs Act of 2011 (sponsored by U.S. Rep. Bruce Braley, D-lowa), would extend tax credits for algal fuel development and repeal some fossil fuel subsidies.

Senate bills

S. 187, the Biofuels Market Expansion Act of 2011 (sponsored by U.S. Sen. Tom Harkin, D-Iowa), would amend the Energy Policy Act of 2005 to make renewable fuel pipelines eligible for loan guarantees for projects that avoid, reduce or sequester air pollutants or anthropogenic emissions of greenhouse gases and employ new or significantly improved technologies.
S. 748, the Algae-Based Renewable Fuel Promotion Act of 2011 (sponsored by U.S. Sen. Bill Nelson, D-Fla.), would update existing legislation to include algae-based biofuel in the renewable fuel program, thus making available to producers of renewable algabased biofuel tax benefits that had previously only been available to producers of plant-based biofuel.

These bills represent clear opportunities for politicians to make good on their repeated calls for energy independence. In addition, they will help propel innovative laboratory discoveries across the "valley of death" that so often is an impediment to commercial development of basic research. XXX



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washington update

Engaging basic scientists in translational research

Symposium explores ways to facilitate and encourage translational research.

BY JENNIFER A. HOBIN

Translational research has gone from a buzzword to a focal point in biomedical research policy. Currently, the National Institutes of Health is in the midst of implementing a fast-moving plan to create a new center dedicated to translational science. A major goal of the proposed National Center for Advancing Translational Sciences is to accelerate the pace at which basic research discoveries are developed into new and improved drugs and devices for patients. While NIH leadership has affirmed its commitment to supporting the fundamental research that is the foundation for clinical applications, the agency's move toward therapeutics development has left some basic investigators wondering how their research programs will be affected and what role they can play in this emerging field.

To address these issues, the Federation of American Societies for Experimental Biology launched an initiative to examine how research institutions, funding organizations, professional societies and scientific publishers can facilitate basic scientists' participation in translational research. Led by Richard Galbraith, associate dean and director of the Center for Clinical and Translational Science at the University of Vermont College of Medicine, the project kicked off with a two-day symposium in March to discuss both the opportunities and challenges for basic investigators interested in pursuing translational science projects. The meeting brought together more than 150 basic, clinical and translational scientists; scientific journal editors; and leaders from private and public research funding organizations, research institutions and professional societies.

Francis Collins, director of the NIH, delivered the opening address. He discussed the reasons that fundamental knowledge does not get translated into clinical applications, the role that the NIH, particularly through NCATS, will play in knocking down those barriers and promoting the development of novel diagnostics and therapeutics, and the critical contributions that basic investigators make to translational research. These contributions also were highlighted in the keynote address by Mary Hendrix, president and scientific director of the Children's Memorial Research Center, Robert H. Lurie Comprehensive Cancer Center at Northwestern University Feinberg School of Medicine. Hendrix, a former FASEB president, shared insights she gleaned from establishing a translational research program focused on the genetics of cancer metastasis.

The meeting also featured a panel discussion on the benefits that both basic scientists and their institutions derive from participation in translational research.

The second day of the symposium began with a discussion of the challenges of engaging basic researchers in translational work. These discussions set the stage for the main thrust of the meeting: four breakout sessions during which participants were asked to provide recommendations for building and capitalizing on the interest of basic investigators to develop translational research programs. The breakout groups focused on translational research training; providing appropriate recognition and rewards, including tenure and promotions, to basic scientists working in the translational space; facilitating productive research collaborations; and the role of private and public funding organizations in providing basic researchers with incentives to consider or conduct translational research.

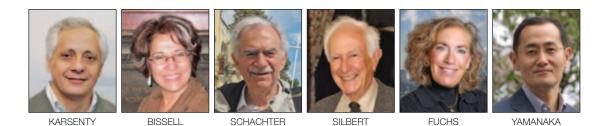
FASEB's steering committee now is focused on developing a white paper articulating the major recommendations that emerged from the meeting.

For more information on the symposium, go to http:// bit.ly/FASEBTransResearch.



Jennifer A. Hobin (jhobin@faseb.org) is director of science policy in FASEB's office of public affairs.

asomb member update



Karsenty garners inaugural Herbert A. Fleisch Medal

The European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis and the International Osteoporosis Foundation recently announced that Gerard Karsenty of the Columbia University Medical Center has been awarded the first Herbert A. Fleisch ESCEO-IOF Medal. Herbert Fleisch was a renowned researcher whose groundbreaking work contributed to the development of the field of scientific knowledge about metabolic bone diseases and their treatment.

The newly created award, valued at 20,000 euros, recognizes a researcher who has made outstanding and groundbreaking achievements in basic bone science.

Karsenty is professor and chair in the department of genetics and development at the Columbia University Medical Center. He is known for his many fundamental contributions to understanding skeletal development and skeletal physiology. Karsenty's laboratory has been instrumental in identifying Runx2 as the master gene of osteoblast differentiation and in deciphering the genetic cascade of osteoblast differentiation. He also has contributed to the molecular elucidation of bone mineralization and has made significant advances in the study of bone physiology. Lastly, Karsenty's lab has shown that gutderived serotonin is a powerful inhibitor of bone formation. \mathbf{X}

Bissell wins Jill Rose Award

Mina Bissell, a distinguished scientist in the life sciences division at Lawrence Berkeley National Laboratory, has been named the recipient of the 2011 Jill Rose Award by the Breast Cancer Research Foundation. The award, named for the late New York philanthropist and founding BCRF board member, comes with a gift of \$25,000.

Bissell is being recognized for her "pioneering work in the field of tumor microenvironment and singular contributions to our understanding of the importance of the extracellular matrix and its impact on gene expression in cancer biology, particularly breast cancer."

Bissell's current research focuses on the role of extracellular matrix, its receptors and its degrading enzymes as central modulators of tissuespecific gene expression, signal transduction, apoptosis and cancer. Using mammary glands from mice and humans, she and her colleagues study the above processes in breasts and breast cancer. VXX

Schachter and Silbert receive award for lifetime achievement in glycobiology

The Society for Glycobiology recently awarded the 2009 Rosalind Kornfeld Award Lifetime Achievement in Glycobiology to Harry Schachter and Jeremiah Silbert.

The Kornfeld award was estab-

lished in 2008 to honor Kornfeld's distinguished scientific career and service to the Society for Glycobiology. The award is given to scientists who have, over their professional lifetimes, made significant contributions to glycobiology.

Schachter is professor emeritus of biochemistry at the University of Toronto and senior scientist emeritus at the Research Institute at the Hospital for Sick Children in Toronto. He has made many seminal contributions to glycobiology and the biochemistry of glycan synthesis.

Silbert is a professor of medicine at Harvard Medical School and Brigham and Women's Hospital and senior medical investigator emeritus at the Veterans Affairs Medical Center. He has pioneered studies on glycosaminoglycan biosynthesis, structure, function, degradation, localization, and description in cells and tissues. XXX

Fuchs and Yamanaka share prize in medicine and biomedical research

ASBMB members Elaine Fuchs and Shinya Yamanaka are two of the three recipients of the 11th annual Albany Medical Center Prize in Medicine and Biomedical Research. Fuchs, Yamanaka and James A. Thomson of the University of Wisconsin-Madison were honored for pioneering work in isolating human stem cells.

Yamanaka is director and professor of the Center for iPS Cell Research and Applications at Kyoto University in Japan and senior investigator at the Gladstone Institute of Cardiovascular Disease in San Francisco.

Fuchs is the Rebecca C. Lancefield professor, head of the Laboratory of Mammalian Cell Biology and Development, and a Howard Hughes Medical Institute investigator at The Rockefeller University in New York City.

The Albany Prize, which is awarded annually, recognizes extraordinary and sustained contributions to improving health care and promoting biomedical research with translational benefits applied to improved patient care. Fuchs, Thomson and Yamanaka are being recognized for work that has moved scientists closer to realizing the regenerative and potentially healing properties of stem cells as well as helping illuminate how human tissues develop and function. The \$500,000 prize is the largest award in medicine and science in the U.S.

Yamanaka and Thomson are credited with discovering how to genetically reprogram adult human cells back to an embryonic state. The production of these induced pluripotent stem cells, made independently in each researcher's lab and reported in 2007, was hailed as a major scientific breakthrough. Fuchs is known for developing reverse genetics techniques that have made stem cell and genetic research easier for all scientists. VXX

ASBMB members receive academy honors

This past spring, seven American Society for Biochemistry and Molecular Biology members were elected to the National Academy of Sciences, and 11 were elected to the American Academy of Arts and Sciences.

Arthur L. Beaudet, Brian K. Kobilka, Lynne E. Maquat, Carl F. Nathan, Athanasios Theologis and Stephen T. Warren were honored with election to the NAS, and Alberto R. Kornblihtt and Shinya Yamanaka were named foreign associates. They are among the Academy's 72 new members and 18 foreign associates from 15 countries in recognition of their distinguished and continuing achievements in original research.

Chi Dang, Raymond Deshaies, Vishva Dixit, Maxwell Gottesman, Richard Morimoto, Martine Roussel, David Russell, Eric Selker, Kevan Shokat, Wesley Sundquist and Marvin Wickens were among the 212 new members who joined the American Academy of Arts and Sciences.

Arthur L. Beaudet is the Henry and Emma Meyer professor and chair in the department of molecular and human genetics at Baylor College of Medicine.

Chi Dang is the Johns Hopkins family professor in oncology research as well as a professor of medicine, cell biology, oncology and pathology and vice dean for research at the Johns Hopkins University School of Medicine.

Raymond Deshaies is a Howard Hughes Medical Institute investigator and a professor of biology at the California Institute of Technology.

Vishva Dixit is vice president of physiological chemistry at Genentech.

Maxwell Gottesman is the Revson professor of biochemistry and molecular biophysics and microbiology and immunology at the Columbia University College of Physicians and Surgeons.

Brian K. Kobilka is a professor in the departments of molecular and cellular physiology and medicine at the Stanford University School of Medicine.

Alberto R. Kornblihtt is a professor of

molecular and cell biology at the University of Buenos Aires.

Lynne E. Maquat is the J. Lowell Orbison chair and professor in the department of biochemistry and biophysics at the University of Rochester School of Medicine and Dentistry.

Richard Morimoto is a professor in the department of molecular biosciences at Northwestern University.

Carl F. Nathan is chairman of the department of microbiology and immunology at Weill Cornell Medical College.

Martine Roussel holds an endowed chair in molecular oncogenesis. She also is co-chair of the Cancer Center Signal Transduction Program at St. Jude Children's Research Hospital and full professor in the department of molecular sciences at The University of Tennessee.

David Russell is the Eugene McDermott distinguished chair in molecular genetics at the University of Texas Southwestern Medical Center.

Eric Selker is a professor of biology at the University of Oregon Institute of Molecular Biology.

Kevan Shokat is a Howard Hughes Medical Institute investigator and professor and chair in the department of cellular and molecular pharmacology at University of California, San Francisco, as well as a professor in the department of chemistry at the University of California, Berkeley.

Wesley Sundquist is a professor of biochemistry at the University of Utah.

Athanasios Theologis is an emeritus adjunct professor at the University of California, Berkeley.

Stephen T. Warren is the William Patterson Timmie professor and chair in the department of human genetics at the Emory University School of Medicine.

Marvin Wickens is the Max Perutz professor of molecular biology and biochemistry at the University of Wisconsin-Madison.

Shinya Yamanaka is a senior investigator and L.K. Whittier Foundation investigator in stem cell biology at the Gladstone Institute of Cardiovascular Disease, University of California, San Francisco.



Retrospective: Quentin H. Gibson (1918–2011)

BY JOHN OLSON AND WILLIAM ROYER

Quentin H. Gibson, who is best known for his pioneering work on the kinetics of ligand binding to hemoglobins and the development of stopped-flow and flash photolysis instruments, passed away in March at the age of 92.

Gibson was born in 1918 in Aberdeen, Scotland, He attended Queen's University Belfast, receiving an M.D. in 1944 and a Ph.D. in 1946. From 1947 to1956, Gibson was successively appointed a lecturer, senior lecturer, and reader in the school of medicine at the University of Sheffield. During this time, he began close collaborations with F. J. W. Roughton and built a stopped-flow, rapid mixing spectrometer and a flash photolysis apparatus to examine O₂ and CO binding to hemoglobin and red cells. The stopped-flow spectrometer was later commercialized by Durrum (later Dionex) Instruments, Inc. and sold as the "Durrum-Gibson" instrument.

In 1957, Gibson was awarded a professorship and the chair of the department of biochemistry at the University of Sheffield. In 1963, he moved to the U.S. to take a joint professorship of biophysics and physical biochemistry at the Johnson Research Foundation and of physiology in the graduate school of medicine at the University of Pennsylvania. There, Gibson expanded his work to studies of a variety of enzymes and, with Colin Greenwood, made the first measurements of bimolecular O_2 binding to cytochrome c oxidase using a new flow flash apparatus, which set the standard for these types of measurements for more than 30 years.

In 1965, Gibson became the Greater Philadelphia Professor in the Section of Biochemistry, Molecular and Cell Biology at Cornell University. During his early years at Cornell, Gibson and Richard DeSa automated the collection of data from all his rapid kinetic instruments, using minicomputers to provide the first millisecond digital readouts of kinetic data in enzymology. This technology then was applied to a complete analysis of O_2 binding. Next, Gibson turned to the problems associated with naturally occurring hemoglobin-opathies, the properties of globins from plant and animal species, the differences between the α and β subunits of human hemoglobin, and the rate of the R to T quaternary transition.

In the 1980s, Gibson's group constructed laser photolysis systems to examine internal (geminate) rebinding within globin molecules at room temperature. In the 1990s, Ron Elber helped Gibson implement the use of molecular dynamics simulations for interpreting the ultrafast picosecond and nanosecond recombination processes that were being measured in his laboratory with mutant and wild-type globins. While at Cornell, Gibson served as an associate editor for the Journal of Biological Chemistry.

In 1996, Gibson retired and moved to Etna, N.H., but spent the winter months in Houston, Texas. There, he worked in a kinetics laboratory set up for him with John Olson at Rice University. This time period was highly productive and led to a detailed map of the pathway for O_2 migration into and out of Mb. In 2002, Gibson decided to stay year-round in New Hampshire, but again a small kinetics laboratory in William Royer's laboratory at the University of Massachusetts Medical School allowed him to keep doing experiments on hemoglobins until 2009, the year his last research article appeared in print.

To read more about Gibson or to add your comments, go to http://bit.ly/ATodayGibson. XXX

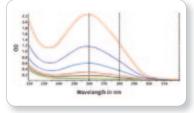
John Olson (olson@rice.edu) is the Ralph and Dorothy Looney professor of biochemistry and cell biology at Rice University. William Royer (William.Royer@umassmed.edu) is a professor of Biochemistry and Molecular Pharmacology at the University of Massachusetts Medical School.



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feature story

Got grants?

Foundation promotes the integration of teaching and research by funding early-career science faculty.

BY KATHLEEN PARSON AND JAMES M. GENTILE

Since 1912, the Research Corporation for Science Advancement, a foundation dedicated to the advancement of science, has been funding grants, conferences and advocacy. RCSA supports faculty members who have innovative ideas for transformative research as well as projects that have the potential to integrate research and science teaching. The foundation's programs specifically target early-career faculty members at both research universities and primarily undergraduate institutions.

The Cottrell Scholar Award program

One of RCSA's initiatives is the Cottrell Scholar Award program, which originated in the foundation's concern about the separation of teaching and research in universities. The program seeks to reinforce the growing awareness that these two functions are complementary rather than wholly or partially exclusive. This convergence is essential for increasing the fraction of students attracted to and retained in science as well as for increasing science literacy in all students.

The CSA program supports early-career science faculty members engaged in both outstanding research and undergraduate teaching practices at doctoral degree-granting institutions. The ability of applicants to mount a strong research program and their commitment to teaching excellence at the undergraduate level are primary criteria in the selection of awards.

RCSA also holds an annual conference to convene Cottrell Scholars. There, they are encouraged to share best practices and to build a community of exemplary scholareducators dedicated to leadership in both research and teaching. Collectively, the scholars have the potential to change the way science is taught nationally. One of the program's long-term goals is to build a Cottrell Scholar community that will contribute to the development of leaders who catalyze departmental change to enhance science education in research universities.

The Cottrell College Science Award program

The Cottrell College Science Award program is RCSA's oldest initiative, created in the early 1970s to provide funding for research that enhances the professional and scholarly development of early-career faculty working with their students at primarily undergraduate institutions. Disciplines traditionally funded included astronomy, chemistry and physics. In recent years, the CCSA program has expanded to include research in other disciplines including biochemistry, biophysics and molecular biology.

Grants are available for single investigators as well as for multidisciplinary teams in a pilot program for targeted institutions. The potential of a proposed research project to add to fundamental scientific knowledge is a prime criterion in its evaluation, as is its likelihood for developing into a viable research program capable of attracting support from other agencies.

The Scialog[®] program

The RCSA's Scialog^{*} program supports research, intensive dialogue and community building. Scialog was conceived as a research grant program emphasizing annual meetings and the opportunity, encouragement and expectation to form cross-disciplinary teams.

The initial Scialog program in 2009 focused on funding recently tenured scientists and building research teams to undertake groundbreaking studies in solar energy conversion. Funded projects included Boston University associate professor Sean Elliott's "Transforming heme proteins into solar driven redox catalysts by site-directed zinc porphy-

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For more information

For more information on all the awards, go to www.rescorp.org.



feature story

A major step forward, with many more ahead

While women in STEM disciplines have made progress, there still is much work to be done.

BY JOAN M. HERBERS

s president of the Association for Women in Science, I was very pleased to read the recent report from the Massachusetts Institute of Technology that documented dramatic progress in the status of women faculty members. The science and engineering faculties there include nearly twice as many women as they had when their first report was released in 1999. This increased representation of women has been the result of sustained, concerted effort to diversify the faculties, and we applaud MIT for taking a leadership role in this important arena.

The report, which generated substantial coverage in the press, emphasizes that the impressive demographic gains for women faculty do not necessarily imply gender equity. I especially appreciate this cautionary note in the report, because at AWIS, we know that the work is not done!

Faculty diversity at leading research institutions tells only part of the story about how women fare in science, technology, engineering and mathematics (the STEM disciplines). Such institutions play a lead role in training future STEM professionals, and the educational environments for undergraduates, graduate students and postdoctoral fellows are known to be influenced by faculty diversity. As students proceed through their training, they can experience both subtle and overt sexism from some faculty and fellow students, as detailed in the MIT report. Furthermore, access to positions of authority and power within academic institutions are not as readily available to women as they are to men.

We now know a fair amount about the status of women faculty at research institutions, thanks in part to grants funded for that purpose by the National Science Foundation's ADVANCE program; we also understand the pivotal role that small liberal arts colleges play in promoting women's full participation in STEM. We know far less about the environment for women at under-studied institutions, such as smaller regional campuses and community colleges. Our members who work and study in these institutions are passionate about tackling issues of gender equity but have few studies to guide their efforts.

We applaud MIT for the courage it has shown by examining its data, and AWIS certainly hopes additional academic institutions will follow MIT's lead. Even more, we encourage other kinds of institutions to think about their own environments and cultures. Because AWIS is a national organization that supports women working in all STEM disciplines and all work sectors, we know that the progress toward gender equity in academic environments like MIT simply is not paralleled in government labs, industry and other work sectors. Our members tell us that after leaving college and grad school, they are shocked to find workplaces structured to disadvantage women.

The Athena Project afforded a glimpse into the world of STEM industries, and additional research in these sectors is urgently needed. Data collection and reporting by industry tends to pool technical with clerical and management employees, although their responsibilities and working environments clearly are different. Similarly, government agencies that work in STEM areas (e.g., the National Institutes of Health, the U.S. Department of Energy, state wildlife agencies) do not routinely report data on their employees by gender and job classification. AWIS has found that women STEM professionals in these work sectors are highly active and vocal about their needs, yet the institutions that employ them are just beginning to collect data to assess their own cultures.

Similarly, important organizations such as scientific societies have not necessarily absorbed lessons learned from decades of research on gender in science. AWIS currently is working with a number of such societies to help them examine their procedures for identifying recipients of awards so that women are given the recognition they deserve.

Finally, women STEM entrepreneurs who enter into the world of business find many doors closed to them. Not sur-

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science focus

Gary Felsenfeld: untangling chromatin's mysteries

From DNA structure to gene expression, Felsenfeld has done a lot during his five decades at the NIH.

BY ANGELA HVITVED

t would be understandable if someone as accomplished as Gary Felsenfeld decided to take it easy and enjoy all his past successes, but this distinguished 81-year-old investigator is not one to rest on his laurels.

Sitting at his desk, which like most surfaces in his office is covered with stacks of papers, Felsenfeld recounts his group's most recent results with the enthusiasm of a graduate student who has just published his first article and not a scientific elder statesman with more than five decades of influential discoveries under his belt.

It's easy to understand his eagerness to discuss the findings though. Felsenfeld, currently chief of the section on physical chemistry in the Laboratory of Molecular Biology at the National Institute of Diabetes and Digestive and Kidney

Diseases at the National Institutes of Health, describes an intriguing mechanism by which the insulin gene can stimulate the expression of a far distant gene, sequentially speaking. This is accomplished by having insulin and the target gene brought into close physical proximity by external factors.

This long-distance regulation offers just one example of how researchers like Felsenfeld are changing the way we view the relationship between chromatin structure and gene expression. This sort of right-place-at-the-right-time understanding of gene regulation also may be an apt analogy for appreciating Felsenfeld's own scientific story.

Which kind of doctor?

While Felsenfeld's mentors during his training read like a "Who's Who" of 20th-century biochemists, his progression along the research path was not immediately obvious. His fascination with the natural world was cemented by the time he was eight, but his family interpreted his early interests as a sign that he would be a physician.

"At that time, if you were interested in biology, you had to be a doctor," he recalls. "I even remember my father, an attorney, telling me that science was just a hobby."

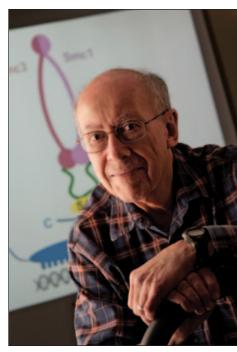
"He was right," Felsenfeld adds with a laugh. "Science is a fun hobby for me— one I'm paid to do!"

As a teenager, Felsenfeld was accepted to the renowned Stuyvesant High School, one of three specialized science high schools in New York City, and was a Westinghouse Science Talent Search finalist (now the Intel Science Talent Search). The finalists traveled to Washington, D.C., and toured the NIH, which Felsenfeld remembers being rather bleak and

> imposing. But he met young scientists who encouraged him to pursue his scientific interests.

Felsenfeld went on to attend Harvard University with the intent of becoming a physician and studied with John Edsall, the famous protein chemist and former Journal of Biological Chemistry editor. Edsall, who had gone to medical school but found it disappointing and instead became one of the earliest biophysical chemists, encouraged his scientifically inclined students to forgo medical training and get a doctorate instead.

Edsall's encouragement and a lackluster freshman biology course pushed Felsenfeld toward a more chemistryoriented curriculum. In his last three years at Harvard, during weekly meetings, he and Edsall read and discussed influential scientific literature of the time including Pauling's "The



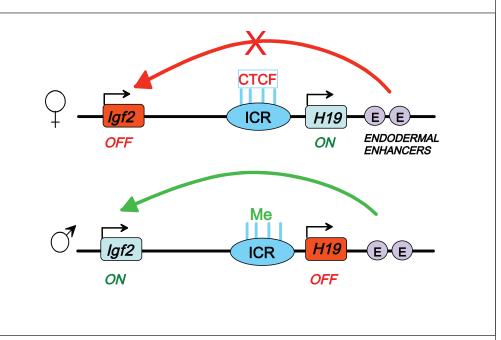
This year marks Gary Felsenfeld's 50th at the NIH, an institution he credits with much of his success.



Nature of the Chemical Bond" and Eyring, Walter and Kimball's "Quantum Chemistry."

"It made an enormous difference in my life," he says of those meetings, and the influence on his future career is evident.

During Felsenfeld's senior year, Linus Pauling gave a speech in which he said that anyone who chose chemistry as a career should take vows of poverty, an acknowledgement of the limited amount of funding and jobs for research scientists in those days. Interestingly, that only emboldened Felsenfeld. "I thought that forgoing monetary gain was wonderful, it was noble. And I committed myself to it."



Imprinting at the IGF2/H19 locus: presence of a CTCF-dependent insulator.

Perhaps it was a bit of youthful naïveté on the part of a 20-year

old student, but Felsenfeld, with Edsall's support, followed through and applied to graduate school at the California Institute of Technology to study physical chemistry. Edsall had told him that the future of biology was in chemistry, so Felsenfeld went to Caltech to learn theoretical chemistry and prepare himself for the new biology to come.

Out of respect for his parents, he also applied to Harvard Medical School, but did so having already made up his mind to get a doctorate degree. In an act that reveals his mischievous side, he sent Harvard a rejection letter to let them know of his decision.

During his second year at Caltech, Felsenfeld started working with Pauling, who had an interesting approach to helping students develop projects. "He'd leave notes in your mailbox with different ideas, and you'd find one that appealed to you." What appealed to Felsenfeld, and what would become the topic of his thesis, was the theory of ferromagnetism, although he readily admits, "I'm not sure I would understand it at this point!"

He completed his graduate work in three years and told Pauling he would like to move into biology. He wanted a position in Copenhagen with Kaj Linderstrøm-Lang, a prominent protein chemist, but Pauling said he needed more chemistry training and refused to write a recommendation. Instead, he wrote a recommendation for Felsenfeld to go to Oxford University to work with noted mathematician and theoretical chemist C.A. Coulson. Although it sounds odd today, young scientists expected this level of guidance back then. "The idea that graduate students were people with rights had not yet really emerged," Felsenfeld says with a quiet laugh. All joking aside, he has no doubt about the wisdom of Pauling's decision.

"I was grateful. Pauling said 'I think this is what's right for you,' and I appreciated his guidance."

Returning stateside

Felsenfeld had a productive year with Coulson, predicting one of the earliest molecular structures using crystal field theory (the chlorocuprate anion CuCl_4^{-2}) and completing what would be his last purely theoretical work.

He returned to the U.S. in 1956 and took up a post at the NIH, following an arrangement he had made prior to departing for Oxford. His draft board (the Korean War was over, but the draft was still active) had told Felsenfeld to obtain an officer's commission while in England or he would be serving in the infantry when he returned. Fortunately, Alexander Rich, whom Felsenfeld had befriended at Caltech, invited him to join the NIH as an officer in the Public Health Service.

Together with Rich and David Davies, another former Caltech colleague, Felsenfeld began working with synthetic polynucleotides, in vitro synthesized RNA segments of defined sequence, that in a few years would prove instrumental in cracking the genetic code. Felsenfeld, Davies and Rich, though, were using these building blocks to understand how nucleic acids formed stable ordered structures like the recently solved DNA double helix. This was his first project with nucleic acids — and it proved to be an auspicious start.

While analyzing the salt requirements for double helix formation using complementary strands of poly-adenine and poly-uracil, Felsenfeld noticed that his spectrophotometer readings displayed some unusual absorption data at certain salt concentrations. Initially he tried to ignore it — perhaps he had made some experimental errors — but eventually he accepted that the data, which suggested a helix with twice as many U's as A's, was real. He remembers asking Davies, "Is there any way to fit a second poly-U into the structure?"

What they had uncovered was the formation of a triple nucleotide helix. "It was a wonderful, wonderful moment, exhilarating. You're so lucky to have something like that when you're just starting out."

To be young and in science

After three years at the NIH, Felsenfeld was offered a faculty position in the biophysics department at the University of Pittsburgh. Biophysics was still emerging as a distinct field, and it was an unusual opportunity to join a discrete biophysics department. Recently married and ready to set out on a new endeavor, he accepted their offer. While continuing his biochemical characterizations of synthetic polynucleotides, Felsenfeld also was given leeway to start working on the copper protein hemocyanin, which he felt would be an ideal project to weave together his scientific interests in quantum chemistry and biology.

However, only two years later, the NIH brought Felsenfeld back to Bethesda with an offer he couldn't refuse. The intramural research director of the Institute of Arthritis and Metabolic Diseases (now NIDDK), DeWitt Stetten, had been persuaded to form a new laboratory of molecular biology. In a twist from the norm, this new group would be composed entirely of young, rising investigators rather than established scientists.

Felsenfeld recalls those early years as a marvelous time, and the lab was full of energy and enthusiasm. The only downside was that Felsenfeld quickly realized that his studies with nucleic acids would be all-consuming; after a few years, the work with hemocyanin fell by the wayside.

He continued investigating the stabilization of multistranded nucleic acid structures by counter ions; this soon led to studies using polylysine and polyarginine as models to examine the interaction of DNA with basic proteins in the nucleus. Eventually, though, he got tired of saying they were good models, "because they weren't good models!"

So he decided to work directly with chromatin. The move

resulted in a big change for the longtime chemist. "The thing with chromatin," he says, "is that I got sucked into the biology and trying to figure out what is the biological function of this DNA-protein packaging."

Insulated activity

Felsenfeld's early work in chromatin biology was aimed at understanding how a gene is controlled through a combination of histone interactions and transcription factors. He used the four-gene chicken beta-globin gene locus for his studies, which was an ideal system for his work, because chicken blood cells have stable chromatin that can be isolated easily in large quantities. Using the beta-globin model, his group contributed numerous findings regarding the role of structural and biochemical changes in chromatin in regulating globin gene expression.

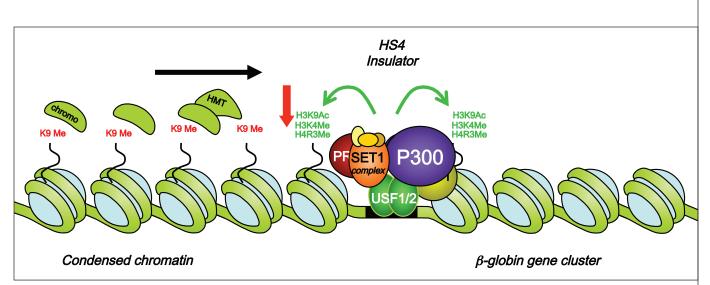
Later, Felsenfeld became more intrigued at what lay at the edges of the beta-globin locus. In blood cells, the globin locus is an open and accessible chromatin domain; at the terminus, where the locus borders a stretch of condensed chromatin, there is a DNase hypersensitive site that appears to mark the boundary. (HS sites are short regions of chromatin distinguished by their extreme sensitivity to nuclease cleavage.)

Felsenfeld proposed testing this region to determine if it did, in fact, constitute a boundary between the open and closed domains. At the time, there was only one published example of such an insulator element, the gypsy element in Drosophila. Victor Corces and Dale Dorsett had shown that gypsy could block an enhancer's ability to increase gene promoter activity if positioned between the two, effectively insulating the promoter from enhancer influence. Felsenfeld's group tested the HS site and found that it behaved similarly.

They commenced studying the insulator region in detail and discovered several protein binding sites, one of which, they showed, bound a protein that was necessary and sufficient for enhancer blocking. The protein, CTCF, had been known for some time to regulate gene activity; however, this new discovery suggested it might also be involved in higher order chromatin organization.

They looked for other locations where CTCF might function and found that it played a critical role in the control of the Igf2/H19 imprinted locus. This two-gene region is special in that individuals only express the paternal copy of Igf2.

Felsenfeld's group described a regulatory mechanism in which the H19 and Igf2 genes are separated by an imprinted control region containing CTCF-binding sites. The ICR on the paternal allele is methylated, preventing CTCF from binding and allowing a downstream enhancer to promote expression of both genes. The maternal allele, however, remains unmethylated and capable of binding CTCF, thus blocking enhancer activity and preventing it from driving expression of Igf2. Sim-



A possible mechanism by which an insulator element could protect against the propagation of a silencing histone modification into a transcriptionally active chromatin domain.

ilar results were obtained independently in the laboratories of Shirley M. Tilghman at Princeton University and Rolf Ohlsson at the Karolinska Institutet in Sweden.

The role of CTCF now is well established, and it's been shown to function by promoting the formation of DNA loops that bring distant genetic elements physically closer. "CTCF is part of a regulatory network that's three dimensional and physical, long-range physical," Felsenfeld says enthusiastically. "We just keep going up in scale."

Here and Now

Felsenfeld is continuing his own upward trajectory, and recently his group began working on human pancreatic cells. Given that the insulin gene is close to the imprinted Igf2/H19 locus, Felsenfeld has become interested in potential longrange contacts between insulin and other genes mediated by CTCF, and that has led to his most recent findings that the insulin gene's physical proximity with a distant gene's regulatory elements affects that target gene's expression.

Despite the rapidly changing nature of his work, Felsenfeld has managed to keep a proper focus on the "big picture," an ability that arises from a keen intellectual discipline honed over many years and mentors. "Always keep in mind what you are trying to answer," he says. "Something may seem interesting, but if it's not directly relevant, note it and hope to remember that it exists, but you have to move on.

"Edsall once said, 'I stop outside the atomic nucleus; I've got enough to think about," Felsenfeld recalls. "And it's true. You can only do so much!"

In Felsenfeld's case, though, only so much seems to be a lot. This year marks the 50th year of his lab at the NIH, an institution he credits with much of his success. "The NIH Intramural program is one of the few places in the world where I could do science the way I wanted to."

Along the way, Felsenfeld has had the fortune to have great people around him. Foremost would be his family (including three children and eight grandchildren), which has long been a pillar of support. And of course, all the work carried out over those 50 years would not have been possible without a remarkable group of postdocs and grad students. Many of his former protégés now are distinguished researchers in their own right, which provides great pride for Felsenfeld, who considers training young scientists to be one of his most important responsibilities.

And he shows no signs of slowing down.

"Whenever someone asks, 'What's the most exciting thing you've done?' I say, 'What we're doing right now,' because that's all that counts." XXXX



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REFERENCES

- Xu, Z., Wei, G., Chepelev, I, Zhao, K., and Felsenfeld, G. (2011) Mapping of INS promoter interactions reveals its role in long-range regulation of SYT8 transcription. *Nat. Struct. Mol. Biol.* **18**, 372 – 378.
- Wallace, J. A. and Felsenfeld, G. (2007) We gather together: insulators and genome organization. *Curr. Opin. Genet. Dev.* 17, 400 – 407.
- Gaszner, M. and Felsenfeld, G. (2006) Insulators: exploiting transcriptional and epigenetic mechanisms. *Nat. Rev. Genet.* **7**, 703 713.
- West, A. G., Gaszner, M., and Felsenfeld G. (2002) Insulators: many functions, many mechanisms. *Gene. Dev.* 16, 271 – 288.
- Bell, A. C. and Felsenfeld, G. (2000) Methylation of a CTCF-dependent boundary controls imprinted expression of the lgf2 gene. *Nature* 405, 482 – 485.
- Felsenfeld, G. and Rich, A. (1957) Studies on the formation of two- and threestranded polyribonucleotides. *Biochim. Biophys. Acta.* 26, 457 – 468.

feature story

How to write top-flight manuscript titles

BY ANGELA HOPP

Pick up any newspaper or magazine, and one of the first things you'll notice are the headlines. Copy editors put a great deal of time and care into developing just the right combination of words to synthesize the facts of stories, to echo the tones of the writers and to entice readers to immerse themselves in the tales that are about to unfold on the page. In scientific publications, titles carry the same importance, only the manuscript author must act as both article composer and title writer extraordinaire. That's a pretty big undertaking, given that scientists aren't likely to frequent workshops on topnotch title writing or masterful wordsmithing.

Whether you're a born poet or still a relatively clunky scribe, crafting a compelling title for an article takes creativity and concentration. I should know: I'm a recovering newspaper copy editor and have written more headlines than I can count. So when it was suggested that I provide some tips on how to write slam-dunk titles for scientific papers, I huddled with the editors of the American Society for Biochemistry and Molecular Biology's journals and the society's chief multimedia communicator to come up with some general advice and specific pointers for authors submitting to the Journal of Biological Chemistry, Molecular and Cellular Proteomics, and the Journal of Lipid Research.

Alphabet soup

"Clarity trumps just about everything else," says Ralph A. Bradshaw, co-editor of MCP. Indeed, the consensus is that the greatest challenge authors face when crafting titles is communicating complex ideas clearly in a small space.

Perhaps feeling constrained by mandated word or character limits, many well-meaning but misguided authors resort to loading titles with acronyms, which can result in what editors of all walks have dubbed derisively "alphabet soup." Here's a somewhat soupy example: "ABC activates DEFG1 channels via HI2K-LMN-OPQ-RST3/4 signaling pathway." (Note: The acronyms in this story have been changed to protect the innocent.) "The simple rule is this: Don't use them," Bradshaw says.

But he and the others acknowledge that even best practices are contingent upon multiple variables. JBC Editorin-Chief Marty Fedor says she agrees that use of acronyms should be minimized, but she adds, "There are good arguments for not banning them completely, including their usefulness as indexing and search terms."

If you simply must use an acronym in a manuscript title, make sure that it is one that has been deemed acceptable by the publication to which you are submitting. The JBC, for example, has a list of approved acronyms on its website for this very purpose; a panel of editors has determined that those on the list are understandable for researchers across the discipline.

"A major advantage of publishing in the JBC is that our articles attract scientists from a broad range of fields. What we want to avoid are titles that wouldn't mean anything to a reader who is not familiar with field-specific nomenclature or jargon," Fedor says. Also, Fedor adds, some acronyms are not all that meaningful even when they are spelled out: "When this is the case, modifiers can help to clarify the meaning of the acronym, as in 'membrane receptor,' 'cytokine,' 'regulatory RNA,' and so forth."

Working with words

The nuts and bolts of good writing also apply to titles, of course. That means authors should employ active voice rather than passive voice. Take this title, for instance: "The DNAdamage-response kinases DNA-UV and XYZ are stimulated by bulky adduct-containing DNA." Putting that idea in active voice, which means putting the object of the action last, simply requires switching the structure around to say "Bulky adductcontaining DNA stimulates the DNA-damage-response kinases DNA-UV and XYZ." An easy fix.

Another tenet of effective composition is to use lively, descriptive verbs. Rather than reporting that something "affects" something else, for example, try to come up with a word that means "affects" but also tells readers how it affects whatever it is. To unearth verbs with depth, don't be afraid to consult a thesaurus. You don't have to have all the right words in your head; you just have to have all the right words in your title.

But, Bradshaw warns, "Don't get cute." You should be in tune with the audience you are trying to engage. Wordplay, according to Bradshaw, "is OK for editorials, news articles or other sorts of opinion pieces, but I think that research articles shouldn't have such. Many of the witticisms you see are based on cultural references, and they are likely lost on or not understood by many readers in different countries."

Meanwhile, authors often avoid using precise language in titles because the results they are reporting are not completely conclusive. Yet, says Fedor, "A direct assertion of the major finding is likely to capture more interest than a vague, descriptive title."

Label titles usually don't have the aforementioned weak verb problem: They simply abandon verbs altogether. Here's an example of a verbless label title: "Hydrolysis of O-Acetyl-ADPribose isomers by ADP-ribosylhydrolase 3 (ARH3)." The label title is a safe route to take under certain circumstances, but at least consider whether a more straightforward approach will be more strategic.

"When I write a manuscript, I spend a lot of time designing the title, as it is the single most important line in an article," says JLR Editor-in-Chief Edward Dennis. "Titles should be assertive and relay the conclusion. 'Studies on ...' doesn't do it, whereas 'Demonstration of ...' does. Even better is to say 'X causes Y.""

Keep it simple

Also problematic are lengthy, often convoluted word combinations meant to operate in unison to describe a single concept. Here's a fabricated example: "The β -arrestin pathway-selective angiotensin AB1C receptor agonist Def2Igh3Ijk." And here's another: "A novel XIM (XYZ-9 interacting mediator of cell death) D8-ligase, tripartite motif containing protein 57 (TRIM57)." In isolation, those word combinations aren't impossible to navigate. But if you insert them into a title and read it as a whole, the cadence of the language can drag. The root of this problem, of course, is that sometimes there is no single word that conveys such a complex idea. It is up to the writer, then, to take a step back and make sure the title doesn't trip up readers. Rule of thumb: Rewrite so that your reader doesn't have to reread.

"You don't have to explain everything in the paper in the title," adds Bradshaw. "Long, long titles usually are more confusing than helpful, particularly because readers will find the papers they are looking for by keyword or even whole-text searches, so run-on titles aren't needed and basically aren't helpful."

Mediums matter

With texting, RSS feeds and social media sites like Twitter driving communication today, the pressure is on authors to write titles that are brief and that resonate across multiple technological platforms. Everything communicated on Twitter, for instance, must be done in 140 characters or fewer. Talk about making every word count! Think back upon the title of the last manuscript you submitted for publication. Could it have been tweeted?

"Shorter titles are not only less intimidating for readers, but they also are easier to read on mobile devices such as iPhones," emphasizes Sarah Crespi, who heads up ASBMB's online communication efforts. The JBC has an iPhone app and can be read on the Kindle, and all three of the journals have mobile sites that streamline content for handheld devices. Also, ASBMB has Twitter and Facebook streams that are updated throughout the day. The content you create should fit on all the lanes of the information highway, or it will get left behind.

All of the journal editors recommended that authors make crafting a strong title a priority during the manuscript composition process, and they emphasized that the title, abstract and figures work together to tell your whole scientific story. If those elements are not deliberately and skillfully crafted, all the other important prose that you placed in the body of the manuscript may not get the attention it deserves.



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feature story

Fostering creativity in science

Unique undergraduate course shows how imagination informs scientific discovery.

BY NICK ZAGORSKI

ow to describe Stephen Ragsdale's Creativity in Science class in one word?

Cupcakes, perhaps?

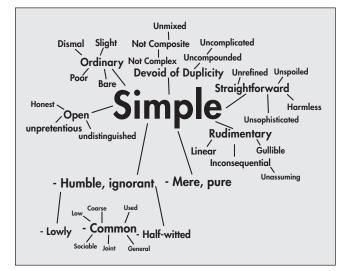
At least one student thought that developing a novel recipe for these tasty treats serves as a fine example of how science and art act in harmony. The science involved testing hypotheses about the proper blending of various ingredients (fats, sweeteners, flour, eggs, leaveners, flavorings, etc.) that react upon heating to create an edible piece of art with the proper shape, texture and taste. The art came from the personal touches, such as the special mix of spices and decorative icing, which provide the cupcake with a unique taste and appearance. It became a perfect example of hypothesis-driven art/science.

A discussion on the chemistry of baking may not be on the syllabus in a typical biology class, but it's exactly the outsidethe-box discussion that makes Ragsdale's class, part of the honors program at the University of Michigan, so unique.

Ragsdale's seminar-style class, which he teaches every fall, features guest lecturers who come in and, through an energetic talk and Q&A session, discuss their work and how creativity influences it.

In some cases, like when music instructor and jazz musician Geri Allen talked about the importance of improvisation in both jazz and in her life, the connection between work and creativity seemed obvious.

However, as the students (and sometimes even Ragsdale) surprisingly learn throughout the semester, creativity permeates all manner of academic pursuits, as demonstrated by faculty, from departments like chemistry, physics, history and dance, who have graced the class over the years. In his class, students learn quickly how greatly imagination informs scientific discovery. Atmospheric scientist Sushil Atreya described his work on a NASA mission to send a probe into Jupiter to detect the elements in its core and learn about the nature and origins of the universe. Physicist Mark Newman, author of "The Atlas of the Real World," discussed how he uses statistics and cartography to examine how we perceive our world. Students also begin to recognize how much planning and pre-



Part of student Julien Lafortune's "A Manifesto of Simplicity," exploring the connotations of the word "simple."

cision is required in a work of art, as when poet A. van Jordan revealed his difficulties in developing the right voice for his award-winning book "M-A-C-N-O-L-I-A" and the importance of following an impulse to tell the story in reverse for eventual acceptance of this work by the publisher.

"Science, whether it's biological, physical or social, is fundamentally a creative process," says Ragsdale, a professor of biological chemistry. "Why can't we engage students and teach them that fact?"

The impetus for Ragsdale's efforts can be traced back to his youth, when he sat through many prepackaged science lectures that seemed to lack passion and energy. "I remember one instance where the topic was the Krebs cycle," he notes, "and the lecturer made it seem so very cut and dry, like there was nothing left to discover.

"And I was thinking, what are the lingering controversies with this pathway? What are the boundaries that scientists today are exploring? That's what I wanted to hear."

Years later, when he was a biochemistry professor at the University of Nebraska-Lincoln, Ragsdale read a National

Science Foundation report that bemoaned the percentage of students that were leaving science and moving to other disciplines because they felt their science courses were not engaging enough, that courses felt geared too much toward vocation as opposed to education.

"The other problem is that many of our brightest students sell themselves short by choosing a major and eventually a career that does not foster their creativity — that, in the words of Carlos Castaneda, lacks a heart."

Ragsdale teamed up with a like-minded colleague in Nebraska's history department, Patrice Berger, who headed the honors program, and developed his idea for a class aimed at studying the role of creativity across the disciplines of science and art. An accomplished musician as well as a scientist, Ragsdale knew a lot of individuals in the science and arts departments who could come in as guest speakers, and the class became a big hit.

In fact, the class was one of the harder items to leave behind when Ragsdale moved to Michigan with his wife, Ruma Banerjee, in 2007 to take on a new position, though he is happy to hear that Berger and NAS member Jim Van Etten have continued running the Nebraska course to great acclaim.

"But after just one year, I missed teaching the class so much I had to bring it back," he says. When he presented the idea to Tim McKay, head of the honors program at Michigan, he realized that he had found a new home for the course.

Given Michigan's strong academic reputation in both arts and sciences, he figured rounding up potential speakers wouldn't be a problem. "And at the least, I figured as a new member of the Michigan faculty it would be a good way to meet some of my colleagues."

In the years since the course's revival, Ragsdale has tweaked the original guest speaker format to provide a further sense of engagement with the students.

For example, after each lecture series, the students choose a specific topic from the discussion and write a reflection about that class. "It's not just a recap or a response paper," Ragsdale explains. "I want the students to come up with something different and original, such as relating the lecture to something personal in their own life or following up on an argument raised in the talk and either defend it or defeat it."

Then, in alternate weeks between the guest speakers, Ragsdale teams up with instructors from Michigan's Sweetland Writing Center and divides the class into small workshop groups that collectively discuss and edit their reflections.

The editorial back and forth provides a great opportunity for the students, who, like the speakers, come from a wide range of academic departments, to interact with their peers and learn more about other disciplines. It also prepares them for their culminating course project, in which they creatively expand on a concept presented during the course. Projects have included statistical surveys assessing the role of intuition in a creative work, multimedia investigations of the importance of uncertainty in the creative process, drawings illustrating simplicity or attention, musical compositions exploring the nature of listening, platonic dialogues on the nature of creativity and films depicting giving. Basically, students may develop their projects and reflections in any genre that seems appropriate, including visualizing the concept of harmony through cupcakes.

Though Ragsdale initially was unsure if the course in Michigan could match the success it had in Nebraska, he holds no such doubts today. At the beginning of each semester, his small class, with an enrollment limit of 22, typically ends up with a waiting list twice that size, while at the end of the semester, the Creativity in Science course regularly receives the highest marks in year-end reviews.

"I've had people ask me if I can teach this course to a thousand students each year and not just 22," he jokes. And while he won't go as far as switching the class to a big auditorium lecture, he is open to considering ways to bring the course to a wider audience.

However, he is worried about the loss of intimacy if the format is changed to accommodate more students; furthermore, he already has a full plate managing an active research group and teaching a graduate-level course in critical analysis of the scientific literature.

"As much as the students hopefully get out of this course, I get even more," he says. "I get to take part in lively debates, meet some fascinating university faculty, and see young people discovering their passion and expressing their own creativity."



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For more information:

To see videos of student presentations from Ragsdale's class, go to the online version of this article at http://bit.ly/ATodayCreativity.



feature story

Rebooting science outreach

Online RNA design game garners unexpected interest from nonscientists.

BY ALAN CHEN

t was a typical lab meeting. The latest RNA synthesis results were in, and they were puzzling. The data indicated deviations from the target fold in unexpected ways despite the fact that all eight designs were highly optimized variants of a previously successful design. It looked like another round of synthesis would be inevitable, and the floor was open for suggestions.

"This is different than the RNAFold prediction, at least using the Turner 1999 parameters."

"Yes, the frequency of the MFE in the ensemble doesn't track with what's going on in the leftmost 1x1 loop."

"Could there be an error in the SHAPE analysis?"

"No, position 50 is highly accessible in several similar designs, so it's not a one-time glitch. But that means we have no idea what position 41 is bonding to..."

The thing was, I wasn't in lab. I wasn't even talking to scientists. I was playing an online RNA folding game called EteRNA, and my fellow labmates consisted of computer analysts, project managers, stay-at-home moms (and one dad), retirees and home-schooled teenagers from around the world. And none of them had any formal education in biochemistry.

EteRNA is a National Science Foundation-funded joint effort between an RNA lab at Stanford University and a computer science lab at Carnegie Mellon University. It's very slick and well executed; you can dive right into designing RNAs without knowing anything about molecular biology or bioinformatics. It's all about brightly colored dots, wiggling bonds and getting a higher score than your peers, at least at first. Indeed, 95 percent of the players probably are just substituting EteRNA for their nightly round of Sudoku or Bejeweled.

The other 5 percent

What sets EteRNA apart from other games is the lab portion. Each week, top players create sequences designed to fold into a target shape. They then vote for eight sequences to be synthesized at Stanford and assayed for secondary structure content using the SHAPE primer extension assay (which measures 2'-OH accessibility). Every week, eight lucky players anxiously await the arrival of the experimentally observed secondary structure of their RNA design. When it's not at all what they expected, they become intrigued, hooked and obsessed. Suddenly, they find themselves spending hours each night in intense online discussions with fellow designers, crunching spreadsheets, looking for patterns and bouncing around ideas for the next round.

In short order, players who had never heard of Turner's Rules proved that the underlying energy algorithm acted only on nearest neighbors. They created online charts showing all possible permutations of adjacent base pairs and their free energy contributions as measured by exhaustive in-game enumeration. Shortly thereafter, they discovered that bulges and loops could be stabilized with a dangling purine at the 3' end of a helix and that certain tetraloop sequences got a bonus. Most significantly, they concluded that strategies that worked for the canned puzzles did not work for the actual design challenges.

One might think, given the game's emphasis on points and rankings, that players would hoard their best tricks to themselves — just as the gentleman-scientists of antiquity were loath to publish their most significant findings. But that's not how events have unfolded. Each new insight is posted, analyzed and heatedly discussed in public online forums. Credit for ideas always is duly attributed. Massive design spreadsheets annotated with musings from the top players are freely shared. Most impressively, this cadre of elite players devotes countless hours showing the ropes to newbies so that they, too, can get synthesized and ultimately contribute fresh ideas to the fold — even if it means giving up their own coveted synthesis slots!

How many of us card-carrying scientists honestly can claim to adhere to the same ethos?

Unexpected curiosity

There were obstacles, however, to creating this self-sustaining ecosystem. The small, overstretched team of graduate students responsible for day-to-day operations of the game soon found themselves inundated by requests for more detailed explanations of the underlying science. What does free energy mean, anyhow, and why did designs with extremely negative free energies fail to synthesize in the lab? What is a suboptimal fold? Why is RNA only shown in 2-D? Players were getting frustrated and were quickly losing interest. So I decided to stop being a passive observer. I linked review articles on folding algorithms, some key primary literature and other bioinformatics tools they could use to analyze their designs. I started logging in late at night to field random questions from curious players about anything and everything, from "What's a tetraloop?" to "How can RNAs be used to treat cancer?"

It was like pouring gasoline on a fire.

The resulting flurry of activity in the forums and chat rooms proved something I had suspected all along. Ordinary citizens can read and absorb primary literature; they can formulate hypotheses, test them and analyze data. In other words, ordinary citizens can participate in science! They just need to be introduced to an interesting problem, provided with the right tools, and given access to someone willing to answer their questions. EteRNA already provided two of the three.

Providing an outreach opportunity

To be fair, EteRNA is a research project about crowdsourcing to optimize RNA folding algorithms. It was not envisioned as an outreach project, judging by the lack of educators on staff and the lengths taken to shield players from the details of the underlying science. And while such measures were necessary to appeal to casual players, the need to provide detailed explanations to sustain the interest of the most talented players initially was overlooked. This has been addressed as of late, as players now are being allowed to participate actively in improving the game itself. There even is a planned series of Q&A sessions with actual RNA researchers.

Perhaps the real problem is that we are all guilty of systematically underestimating the public's appetite to be meaningfully engaged in science. Consider that millions of gamers donate CPU time to distributed computing projects like Folding@ home despite the pinch of electricity bills. Some actually purchase separate computers solely to contribute more CPU cycles to research they find fascinating. How many of them would jump at an opportunity to participate actively in that science, to have it be more than just a pretty screensaver?

This experience really has forced me to think hard about how we, as scientists, go about fulfilling our mandates to be involved in public outreach. Should we really pat ourselves on the back when we open our lab doors to straight-A high school students from dual-doctorate households or ambitious premeds looking to buff their resumes? And when we dazzle little kids with explosions and freezing flowers in liquid nitrogen — is that education or just entertainment? Is this really what the NSF has in mind when they ask us to detail our broad impacts to society?

Meanwhile, out in cyberspace, stay-at-home moms and college dropouts have arrived at their own, home-grown scientific method for creating RNA designs that work—despite being invisible to traditional venues of science education. Maybe, someday, one of these gamers will consider a career in science. Whether or not that occurs, the NSF— and the public that funds it—has gotten a fantastic return on this investment.



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For more information:

- EteRNA: http://eterna.cmu.edu/content/EteRNA
- Folding@home: http://folding.stanford.edu
- The NSF Broader Impacts criteria: http://www.nsf.gov/pubs/gpg/broaderimpacts.pdf

Got grants? continued from page 12

rin mutation" and Emory University associate professor Stefan Lutz's "Directed evolution of hydrogenase for efficient light-driven hydrogen production via quantum dot-enzyme hybrid systems."

The 2011 Scialog program focuses on fundamental research, at the molecular and nanoscale levels, that shows high potential to impact advanced energy technologies. $\Sigma \Sigma \Sigma$



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feature story

Teaching disconcerting scientific ideas

Explaining the scientific process will help the public understand why scientists trust their own conclusions.

BY MIKE KLYMKOWSKY

ver the years, scientists have come to accept some deeply weird ideas, many with uncomfortable ramifications (see sidebar). They accept these ideas because of the scientific process, a process that is not well appreciated by the general public. A lack of understanding of how science actually works has significant implications when it comes to teaching and the role of science in economic, political and personal decisions. Efforts like the recent bill to allow teachers to teach controversial topics such as biological evolution (1) do as much to befuddle students as they do to make religious zealots appear to be either fools, ignoramuses or charlatans. Unlike religions, which are based on what amounts to personal revelations, and which many come to or are forced to accept through threat of ostracism, torture or even death (2), science is a voluntary communal activity. It is, in theory at least, accessible to all (unlike religious revelation). New observations, provided that they can be repeated and extended by others, can lead to the revision of past ideas without violence. There are few, if any (sane) scientific fundamentalists, devoutly

Strange Scientific Ideas

- Matter is composed of atoms, which are mostly empty space.
- The universe emerged out of nothing (about 13,700,000,000 years ago).
- There are billions of galaxies, each containing billions of stars.
- Time and space are not distinct.
- All organisms are built from similar building blocks called cells.
- All cells are derived from pre-existing cells in a continual lineage that extends back about 3,500,000,000 years.
- The heavier atoms in our bodies were formed within stars or exploding stars.
- Matter and energy are different versions of the same thing.
- The universe is running down yet expanding at a faster and faster rate.
- Random noise can produce complex structures.
- At the molecular level, everything is reversible.
- A collection of cells can, by itself, produce a self-conscious entity that thinks it is more than a collection of cells.

defending a small, static, young and geocentric universe, a nonatomic model of matter, a phlogiston model of heat, a nonevolutionary model of terrestrial life or a supernatural (soul-based) model of consciousness. Reproducible data coupled with dispassionate, rational and skeptical inquiry leads to conditional, albeit empirically supported and highly accurate, conclusions about the world. These are ideas that are difficult to dismiss no matter how hard they may be to believe.

While science occurs within societies, many individuals are not willing or able to accept some of the most well-founded scientific ideas and their implications (3). In part, this is because these ideas, while not directly ruling out the supernatural, certainly are difficult to reconcile with the existence of an all-knowing, all-powerful and all-good God. It has been suggested that "Science and religion are not in conflict, for their teachings occupy distinctly different domains" (4), but this ignores the fact that many well-established scientific ideas (such as big bang cosmology, biological evolution, atomic theory, plate tectonics, the laws of thermodynamics and the physicochemical nature of the mind) can, when taken seriously, provoke a spiritual vertigo that, in the view of some members of the religious community, has highly undesirable and corrosive effects. As an example, the response by religious fundamentalists to human (biological) evolution focuses largely on the premise that evolutionary mechanisms, driven as they are by random events and selection, demean humans by viewing them as just animals, sharing the same nature as other animals. This implies that there is no more meaning associated with being human than there is with being a trichoplax: Both are the product of a mindless (godless) process. Given that calling someone an animal rarely is viewed as a compliment, we can understand their objections, even though from a scientific perspective, they are irrelevant.

As scientists and educators, our challenge is to stay true to the ideals and implications of a scientifically established world view while not gratuitously alienating some of the very people we expect to pay for our work. While some scientists and scientific writers have gone so far as to claim that science has disproven the existence of God (5 - 7), this is, on its face, a silly and totally nonscientific claim. Science cannot disprove God's existence but can render it essentially irrelevant. Consider the earth's place in the universe as illustrated by the "Known Universe" video developed by the American Museum of Natural History. Two points emerge: how unimaginably tiny the earth is in the context of the known universe and, given the limits to the speed of travel, how completely inaccessible and irrelevant this universe is to our day-to-day existence. We must be content to rely on poorly constrained speculation when it comes to models for the origins of life or its prevalence in the universe, notwithstanding often exaggerated scientific claims to the contrary. As scientists and science educators, we need to recognize and explicitly address how current scientific ideas influence our daily lives: where they are useful or irrelevant, and where they might leave us disoriented and alienated.

Science works because it eschews (and actively questions) personal authority; it relies on logic and the assumption that the only authority that matters is that provided by the repeated testing of ideas against a disinterested reality. As such, it provides a bulwark against vested interests, prejudices, superstitions and comforting but unwarranted assumptions. Science and other skeptical and evidence-based positions often are viewed as threatening (think Socrates) and actively suppressed by totalitarian regimes of the (largely secular) left and the (often religious) right (8). Activists who uncritically oppose new technologies or actively back pseudoscientific positions can end up condemning millions to poverty, disease and death (9, 10): Witness the effects of irrational and myopic opposition to vaccines, pesticides, genetically modified organisms and (well-regulated) nuclear power plants.

The key is an explicit return to Enlightenment values in the science classroom. Scientific ideas need to be presented in all of their weirdness so that their implications as well as their limitations are recognized. There is little to fear from such an approach, since, even when dealing with superficially controversial topics such as evolution by natural selection, the scientific evidence is overwhelming. We would do well to follow the spirit of Tom Paine, who said, "You will do me the justice to remember, that I have always strenuously supported the right of every man to his own opinion, however different that opinion might be to mine. He who denies to another this right, makes a slave of himself to his present opinion, because he precludes himself the right of changing it. The most formidable weapon against errors of every kind is Reason," and by extension a humble, circumspect, but explicit and rigorous devotion to scientific ideals. Explaining the scientific process will help the public understand why scientists trust their conclusions: that evolution has shaped us, that vaccines are safe and that genetically modified organisms may help much more than harm. XXXA



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REFERENCES

- 1. Reardon, S. Bill Allowing Teachers to Challenge Evolution Passes Tennessee House. *ScienceInsider*, April 7, 2011.
- 2. Paine, T. (1794) The Age of Reason: Being an investigation of true and fabulous theology. Barriois, London.
- Berkman, M. B., and Plutzer, E. (2011) Defeating creationism in the courtroom, but not in the classroom. Science 331, 404 – 405.
- 4. Gould, S. J. (1997) Nonoverlapping magisteria. Natural History 106, 16 22.
- 5. Dawkins, R. (2006) The God Delusion. Bantam Books, London.
- 6. Hawking, S., and Mlodinow, L. (2010) The grand design. Bantam Books, New York.
- Stenger, V. J. (2007) God: The failed hypothesis, how science shows that god does not exist. Prometheus Books, New York.
- Ferris, T. (2010) The science of liberty: Democracy, reason, and the laws of nature. HarperCollins, New York.
- 9. Gray, J. (2010) The Man that saved a billion lives: Norman Borlaug and GMOs. *The Toronto Globalist.*
- 10. Ridley, M. (2010) The Rational Optimist. Harper, New York.

A major step forward with many more ahead

continued from page 13

prisingly, women are noticeably underrepresented among holders of patents and as founders of technical startup companies. The uneven playing field in this arena is documented dramatically by recent studies of venture capitalists, who fund very few women-owned businesses in science and technology.

No, our work is not done! While AWIS is heartened by the

tremendous progress reported by MIT and other academic institutions (e.g., those funded by the NSF ADVANCE program), we remain committed to the ongoing tasks needed to ensure full participation by women in the STEM disciplines.



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feature story

Nine quick fixes for scientific talks

Some tips on how to design and deliver an engaging and concise research talk. BY SCOTT MORGAN

As a scientist, at some point in your career, you will be asked to give an oral presentation about your research. Whether it's a thesis defense, a job talk, a lecture at a meeting, or just a simple presentation of results to lab mates, it's important to be able to get your point across in a concise and interesting manner. The following is a simple checklist that will help you organize and prepare your talk. The points are not in presentation order, but in preparation order for the added benefit of time efficiency.

Single theme

The theme provides the objective of the entire talk. It also can be referred to as the take-home message, gist or bottom line. It should be the single most important idea that you want the audience to remember. For example, "The female T-cells are immunized against the Y antigen during pregnancy" is scientifically specific, brief, and to the point. It omits explanatory material that would be defined earlier in the talk. Likewise, "GATA 3 coregulates with ER" does not need to remind us of the acronym for estrogen receptor. These examples also avoid using vague phrases such as "the role of" and "the effect of," by using action verbs that actually describe the role or effect (i.e., immunized, coregulates). A precise take-home message is both more accurate and more interesting than a broad one and thus more memorable. For example, "Cytosol components directly participate in the membrane fusion between MLV and its host cell," is more memorable than "Cytosol components are important in membrane fusion."

Single focus

Despite its centrality to the presentation, the take-home message would be a confusing place to begin the talk itself. "Adult CD4 cells undergo partial polarization under CD3/CD28 costimulation with cytokine priming" clearly lacks context and a frame of reference. Therefore, to pinpoint the main question or focus of the talk, ask yourself the following questions: What was the aim of the study? What were the experiments trying to prove? Also, be

cognizant of the time constraints — the take-home message should answer the main question in the allotted time.

A good main question typically is open-ended, beginning with "how," "where," "what," "when" or "why." Like the take-home message (theme), the main question (focus) is an information filter. Since a common speaking mistake is to cram too much information into the talk, both audience and speaker are relieved by a clear and defined scope.

3

The money slide

Presentation time always is a factor, so it is important to select images that are clear, accurate and most representative of the work. Unfortunately, most speakers are not particularly discriminating at this stage of preparation. Their impulse is to include every piece of data, perhaps on the assumption that a high concentration of information indicates thorough science. Alas, the opposite is true. Data that does not pertain to the main question is perplexing for the audience and runs the risk of clouding their understanding and overloading the talk. Therefore, I suggest beginning the selection process by picking the single most important figure or "money slide." This is the one that would make grant adjudicators fund your project. The money slide could be the most important finding or one that encompasses all the results, but it should represent the most salient data point. This preparation step ensures that the most important piece of information is included in even the shortest of talks. During the presentation, the money slide also reminds you to give the central finding heightened emphasis.

Appropriate slide count All other images, schematics, graphs, charts and photographs will in some way relate to or support the money slide. You should follow the two-minutea-slide rule as a general precept for how many total slides should be in a presentation (not counting the title and acknowledgment slides). I'm sorry, but there simply is no such thing as a simple slide. Each one needs, and deserves, ample time to be described fully.

Minimal text

You need to make certain that all text is in bullet form, not in full sentences. The options in presenting text-heavy slides are to read the words aloud or hope that every member of the audience reads at the same pace. However, the lifeblood of a presentation is the contact between speaker and audience, and in a public speaking setting, we all would rather listen than read. Another problem is that you cannot easily deviate from scripted words. Even a minor adjustment forces the audience to hear one explanation while reading another. Above all, it is better not to commit to a precise set of words that will undoubtedly change for the better during the presentation. As you have no doubt noticed, text slides primarily are used for the presenter's benefit rather than to facilitate the audience's understanding. In other words, they function as cue cards. So I would recommend removing the verbs from all slides and using index cards with short reminders for yourself. For further explanation of this phenomenon, see the model of working memory developed by Alan Baddeley and Graham Hitch.

Common ground The best way to achieve an immediate connection with the audience is to address the collective problems that you share with the group: call it the common denominator, the collective puzzle or common ground. It may be tempting to start with definitions or statistics, but they are dry, generalized and bland. Common ground is a more powerful choice because it immediately concentrates on current topics and dilemmas in the field while respecting the audience's knowledge base.

Ask yourself the following questions:

- What are the most relevant scientific issues that I share with this audience?
- Of these, what issue do I focus on? Why?
- What solutions are the most logical? Why?
- Specifically, what am I looking for?

Including the answers to these questions in the introduction will draw a conceptual link between the daily work of the audience and your own.

Brief title

Identifying the main question and common ground also provides excellent headway for crafting an engaging title. Common ground acknowledges the bigger picture; the main question suggests your contribution.

Here is an example of a title: "The Design and Application of

Tagging SNPs in Neuronally Expressed Voltage-Gated Sodium Channel Genes to a Cohort of Caucasian Epilepsy Patients."

In an attempt to be specific, the author has added too many details for a talk. "To a cohort of Caucasian epilepsy patients" implies that the presentation only is relevant to those studying epilepsy among Caucasian patients. "Epilepsy" is important, but the fact that they are Caucasian is not. "The design and application" and "patients" are implicit and can be removed. "Neuronally expressed" might be too detailed; "to a cohort" may be obvious, while the coolest part — tagging SNPs — is diffused by its length. An improved title would be "Tagging SNPs: Voltage-Gated Sodium Channel Genes in Patients with Epilepsy."

Final thought

The final thought is a quick technique to help you end a talk gracefully. A fully memorized sentence can seem canned and overly rehearsed, so I suggest a single trigger word to remind yourself that the final comments should be as strong and well organized as the rest of the talk. For example, the final idea, "Our goal over the next several months is to test this single-chain protein in assays to assess human response. We will also insert this gene into the patients' own B cells to test whether they are either tumor-specific or idiotype-specific CTL," could be simply noted to yourself as "idiotype-specific CTL."

Teach

Lastly, I would like to point out that a good scientific talk is not about you but about the education of the audience. These tools are designed to make the process of speaking less about lecturing and more about teaching. Good speakers are like good teachers - they are impressive because they possess knowledge about highly intricate subjects. But they truly are extraordinary when they can make complicated things seem simple. XXXX



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For tips on giving a good poster presentation, see the March 2011 issue of ASBMB Today.

asbubmeetings

Scenes from the 2011 ASBMB annual meeting





Above: National Institutes of Health Director Francis S. Collins gives a plenary lecture on opportunities and concerns in the biomedical research community.

Right: Students in the Biomedical Research Group at Hillcrest High School in Dallas, Texas, at the opening lecture.

Above right: Meeting attendees pose in the ASBMB knockout mouse cutout.







Want to see more from the annual meeting? Go to http://bit.ly/AToday2011Meeting.



Left: Meeting attendees stop at the American Society for **Biochemistry and Molecular** Biology booth to pick up goodies and buy T-shirts.

Above: ASBMB president Suzanne Pfeffer opens the meeting.





Left: Students from the Pingry School SMART team at the undergraduate poster competition.

Right: Journal of Biological Chemistry associate editor Thomas Vanaman talks to Herbert Tabor/Journal of Biological Chemistry Lectureship awardee George R. Stark.

Below left: Andrew Miles, a senior at Fairleigh Dickinson University, explains his poster.

Below right: The Minority Affairs Committee reception provided a nice respite after a long day of attending lectures.











Left: Carla Mattos of North Carolina State University talks to students at an undergraduate workshop on how to prepare for graduate school.

Right: STEM outreach workshop participants build amino acid sequences using models provided by the Milwaukee School of Engineering Center for BioMolecular Modeling.

Bottom left: Undergraduate poster competition winner Michael Brister of the University of Delaware poses with MAC committee member Phillip Ortiz (left) and Education and Professional Development committee member Mark Wallert.

Bottom right: Journal of Biological Chemistry co-editor Herbert Tabor and his sons Ed, Richard and Stan.





education and training



K-12 outreach opportunities

Don't let excuses get in the way of interacting with teachers and students.

BY J. ELLIS BELL

ne of the more enjoyable and effective outreach activities scientists can engage in is interaction with K-12 teachers and their students. I can't count the number of times I have come across an outstanding first-year student who got into science because he or she was mentored by a teacher who interacted with faculty members at a nearby college or university. Interactions between K-12 teachers and students and science faculty can take many forms, including opening up your lab to summer research projects. This often is supported by funding agencies, professional societies, and colleges and universities in a variety of ways, and in this day and age when high school students know that research experience gives a competitive advantage when it comes to college applications, finding students to participate in summer research is not a problem. Finding teachers interested in pursuing summer research also is not a limitation. The problem is first finding faculty members willing to invest the time and energy in mentoring students and second, making connections between those faculty members and students and teachers.

There are many excuses you can use for not getting involved: it takes time away from writing grants and papers and training students; it doesn't help get grants funded; you've got too much to do already. However, keep in mind that getting K-12 kids and their teachers involved in science will increase public awareness of science and help them understand the need for basic research funding. And since congress members listen to their constituents, outreach actually may help you get your grants. The opportunity to try out experiments without having to make a major commitment is another reason to get involved, and it also provides a chance to help students communicate scientific ideas to a general audience. And finally, there is the satisfaction of seeing students make the right connections between results and ideas and watching them get excited about science.

Several years ago, the American Society for Biochemistry and Molecular Biology reinstated a program to provide funds for K–12 teachers and their students to do summer research with faculty mentors. ASBMB still has money set aside for this initiative and will make up to three additional awards this summer. If you're interested, it's not too late to apply. Contact Weiyi Zhao (wzhao@asbmb.org) to find out more.

In another attempt to foster increased interactions among K–12 teachers, students and society members, ASBMB held a workshop titled "STEM outreach: fostering partnerships between colleges/ universities and junior high schools" at the 2011 annual meeting. The workshop involved a number of faculty members as well as teachers from local high schools interested in finding out more about how to create such connections.

As a follow-up to this workshop, the society, with funding from the National Science Foundation, now is accepting applications for small seed grants to provide incentive and support for the development of outreach programs and partnerships between teachers and researchers. ASBMB plans to award ten grants, of up to \$2,000 each, to teams consisting of one or more junior high school teachers (or other K-12 educators) and one or more research scientists. Seed funds can be used for a variety of purposes, including the purchase of laboratory equipment, materials and supplies; relevant transportation costs; fees associated with pertinent professional development training; and release time to allow one or more partners to participate in planning and training. The application process is not too long and can be found, together with the review criteria, at www.asbmb.org/nsfstem.aspx.

The application deadline is June 15th. More information is at www.asbmb.org/nsfstem.aspx. $\Sigma\Sigma$



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





A changing of the guard This summer, the MAC will get a new leader.

BY SQUIRE BOOKER

As July 1 draws near, with it comes a change in the composition and leadership of the American Society for Biochemistry and Molecular Biology Minority Affairs Committee. For the past three years, the MAC has been chaired by Craig Cameron, who will remain on the committee as past chair, while the responsibilities of chairman will be handed over to me.

MAC has been busy under Craig's leadership and has enjoyed a number of noteworthy accomplishments: the online publication of minority scientist research spotlights that highlight careers of minority scientists and provide inspirational anecdotes on strategies for success; the establishment of the Partnership in Diversity, a registry of minority scientists and others interested in fostering diversity in the biological sciences; the organization of a workshop, funded by the National Science Foundation, to identify barriers that minority scientists share in applying for and obtaining federal funding for their research; and the establishment of the first ASBMB Diversity Award, named after Ruth Kirschstein.

Also of note is the organization of several successful scientific and issues-based symposia at the ASBMB annual meeting. It goes without saying that these accomplishments could not have been possible without a great team of committee members and staff who worked tirelessly to set objectives, outline strategy and secure appropriate funding.

As we transition into this next phase of leadership, the MAC will remain committed to many of the initiatives established during this past term. We also will continue to attend conferences that target aspiring young scientists from underrepresented groups, such as the Annual Biomedical Research Conference for Minority Students and the Society for Advancement of Chicanos and Native Americans in Science annual conference. Each year, the MAC sponsors booths at these and other conferences to provide information about ASBMB and the benefits of belonging to a professional scientific society as well as information pertaining to career development, summer research programs and applying to graduate school. Moreover, the MAC distributes complimentary one-year memberships to students who visit the booths. Our goal in the near future will be to develop strategies to better engage these students in the society so they recognize the benefits of membership and maintain their association with ASBMB. We also will target students who attend the ASBMB annual meeting and will seek to engage them through effective programming and targeted events and workshops. For the past two years, we have enjoyed strong turnout at the annual ASBMB Minority Scientist Networking Reception and have begun to use this event as a hub for pairing students with academic and professional scientists to facilitate communication and mentoring.

The MAC also is committed to furthering the careers of underrepresented minority scientists and elevating the stature of minority scientists within ASBMB. By forming the Partnership in Diversity, we are hoping to create a database of minority scientists in all areas of biochemistry and molecular biology that can be used to identify suitable speakers or organizers for ASBMB thematic programming and as a resource for other organizations interested in identifying minority scientists for various reasons.

In short, the MAC remains vibrant and is looking forward to keeping busy and ambitious during the next few years. $\overleftarrow{\text{VXX}}$



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For more information

- Minority scientist research spotlights: http://bit.ly/MinorityResearch
- Partnership in Diversity: www.asbmb.org/MinorityAffairs/register.aspx
- The ASBMB Diversity Award: http://bit.ly/ASBMBDiversityAward

journal news



Reflections on the biosynthesis of "a small but beautifully organized protein"

BY ANGELA HOPP

Many of us catalogue the chapters of our lives with turningpoint texts — books, articles, maybe even songs — that mark shifts in thinking, tweaks or wholesale reversals in career courses, and revelations when we needed them or, perhaps, didn't expect them at all.

Such was the case for Donald F. Steiner, now professor emeritus at the University of Chicago, who begins his recent Journal of Biological Chemistry "Reflections" article by recalling his chance encounter with the 1938 book "Fearfully and Wonderfully Made: The Human Organism in the Light of Modern Science." When he came upon the tome at the Dayton Public Library, he was a chemical engineering student and working the second shift at a paper mill.

"This book came as a wonderful revelation that could not be ignored, even though I barely understood much of it," he writes. "Indeed, I was so enthralled by its revelations that, within just a few days, I decided that I must somehow gain access to this compelling new scientific field."

Since then, subsequent generations of scientists likely have indexed phases of their lives and research with texts by Steiner, whose many outstanding achievements include the discovery of proinsulin, the characterization of the proinsulin pathway, the isolation of the human C-peptide and the development of the radioimmunoassy for C-peptide used today to measure endogenous insulin production.

Naturally, Steiner's "Reflections" article is full of science – and storytelling – with true staying power.

In one vignette, he recalls a 1964 trip to Europe, during which he stopped in Munich at the Max Planck Institute for Cellular Chemistry to thank Feodor Lynen for earlier extending an offer of a postdoctoral fellowship, which Steiner had turned down to take an assistant professor position at the University of Chicago biochemistry department.

"When I arrived ... I asked one of the students where Lynen's office might be, and he replied with something like, 'Ach, der hohe Adler (Oh, the high eagle!) — He is around the corner in that direction!' A bit mystified by such veneration, I arrived at his office to find his very excited secretary, who told me he had just received word that morning from Stockholm that he had received the Nobel Prize and she couldn't reach him, as he was away at a meeting," Steiner writes. "Just then, the phone rang, and she spoke excitedly for a few minutes, then turned to me and asked: 'Do you know who is this fellow Konrad Bloch, who shares the Nobel Prize?' ... I informed her that he was an American scientist, now at Harvard University, who had also done outstanding work on cholesterol biosynthesis. She then passed this information on to a newspaper reporter. Having thus served as Konrad Bloch's pro tempore press agent, I left a brief congratulatory note for Lynen with her, and then my two companions and I continued our European explorations."

Later in the article, Steiner weighs in on the current conditions under which young investigators must operate, saying "the steady erosion of opportunities" troubles him greatly.

"It is clearly imperative to make more openings available at the entry level so that individuals do not have to wait for positions and resources while their most creative years evaporate. Early placement of promising young investigators in responsible positions must become one of our highest priorities if we wish to preserve the unparalleled scientific productivity that we have achieved. This is one of the greatest challenges we face today in science," Steiner writes. "Unfortunately, I have no easy solutions to propose, other than the observation that, clearly, we older scientists must reduce our consumption of resources in order to make room for the young to flourish."

To find out more about Steiner's work and life, read the complete¹ "Reflections" article, "Adventures with Insulin in the Islets of Langerhans," online at www.jbc.org or in the May 20 print issue. $\Sigma X X \lambda$

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

FOOTNOTE:

'Don't miss some of the best passages of the piece just because they are tucked away in the footnotes. For example, Steiner writes, "As beautiful symmetrical peaks of labeled proinsulin began to emerge just as hoped, I heard myself exclaiming 'wow' and 'gee whiz.' Suddenly, I remembered that Gene Kennedy had once remarked, 'There are only two kinds of scientists— those who say "gee whiz" and those who say "so what" when something new and exciting appears.' I am clearly one of the former!"

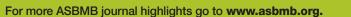


Food for thought: commentaries on the kinetics of fatty acid transport

BY MARY L. CHANG

Commentaries are a special, semiregular feature of the Journal of Lipid Research, where experts in various fields of lipid research highlight the findings of a new article being published

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in the journal and provide their own unique perspective. In the June 2011 issue of JLR, we have not one but two commentaries that together provide an opposing viewpoint to the data presented in "Plasma apolipoprotein C-III metabolism in patients with chronic kidney disease," a patient-oriented research paper by Esther M. M. Ooi and collaborators published in April.

The first commentary, "Complexities of plasma apoliprotein C-III metabolism," by Frank M. Sacks, Chunyu Zheng and Jeffrey S. Cohn, calls into question a key conclusion made in the April JLR paper. Specifically,

Sacks et al. cast doubt on the one-pool model of plasma apolipoprotein C-III that Ooi and colleagues propose to account for the similarity of enrichment-time curves for apoCIII in very low density lipoprotein as well as in high density lipoprotein (sometimes referred to as "good cholesterol"). The model suggests apoCIII "'jumps off' lipoproteins," according to Sacks et al., before they are delivered to cells.

In addition, Ooi et al. reported that apoCIII in VLDL in patients with chronic kidney failure was broken down at a lower rate in comparison to healthy counterparts, but the authors drew this conclusion by utilizing the rate of apolipoprotein B (apoB) in VLDL as a reference. Sacks, Zheng and Cohn, suggesting that the model offered by Ooi et al. may be too simplistic, point out that there are three physically different forms of apoCIII, each with its particular rate of breakdown, and that apo-CIII is present in different percentages across naturally occurring lipoproteins in the body, so that relative determination of apoB content may not be an appropriate indicator of apoCIII content. The commentary also points out that free apoCIII is not, in fact, found in plasma.

Associate Editor Henry N. Ginsberg and Columbia University colleague Rajasekhar Ramakrishnan have similar concerns in their commentary, "Investigations of apoCIII metabolism using stable isotopes: what information

can you acquire and how can you interpret your results." They emphasize that until there is methodology to clarify specific fractional catabolic rates and breakdown pathways for lipoproteins, relative measurements may not be reliable.

Since the topic of apoCIII currently is very much in the spotlight, the paper and two commentaries provide very timely, and very worthy, food for thought. The controversy particularly highlights the complexities of performing kinetic analyses concerning the constituents of lipoproteins as they are transported through the body. $\Sigma \Delta \Delta$

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

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career insights

Decisions Going from industry to finance and back again.

BY RALPH THOMAS

he summer before my sophomore year in high school, I opened my sister's biology book in an attempt to prepare for my biology class that fall. I soon found myself lost in the chapters discussing DNA replication and protein manufacture. I was mesmerized by the sections devoted to carbohydrate metabolism and fatty acid production. I waited for biology class to start with great anticipation and couldn't wait to take chemistry the next year. By then I knew what I wanted to do for a living, and I charged through the rest of high school with a laser-like focus on college.

My valedictorian accomplishments were inadequate preparation for freshman year, but I rebounded in subsequent semesters and earned a hard-won Bachelor of Science in chemistry. I then returned to the paint manufacturing company where I had been employed as a workstudy student. My new job as an infrared spectroscopist at the company was truly stimulating for me, but upward mobility was out of the question anytime soon. A colleague who was enrolling in graduate school told me about available scholarship money and a seed was planted. I elected to defer the paycheck and chase my academic calling.

Fast forward to my first postdoctoral appointment. A very long day in the lab had ended. I went home feeling totally confused and very disillusioned. For the first time in my chemistry career, I was stuck. I was impaled on a terribly low-yielding step in a multistep synthesis of a potentially medically useful steroid. My advisor was growing restless. If I couldn't dislodge myself from this jam, then how did I expect to be a promising tenure-track professor loaded with fresh ideas and spewing out papers like a printing press? I feared it wasn't going to happen. What I wanted to do for a living had to be reassessed.

A stint in industry

My second postdoc was much more rewarding, both in terms of laboratory satisfaction and number of publications. But by then I had made up my mind. If I wasn't going to be a professor, then I might as well get paid. I interviewed with Revlon and soon found myself in sunny San Diego at the fledgling Revlon Science Institute. An industrial postdoc, to be sure, but the weather was great, and now I could make and save money. A return on my hard-working parents' investment in education was finally here.

Paradise lasted only two years. The concept of a research and development facility distantly flung from its New York City corporate headquarters wasn't overly novel, but it turned out to be significantly underfunded, and the CEO gradually lost interest. The institute's doors



Ralph Thomas is a freelance and contract tutor in algebra I and II, calculus, geometry, pre-algebra, pre-calculus and chemistry. In 2009 he exceeded his extended service guarantee and prepaid debit card account goals as a rookie tax associate at H&R Block. Before that, he was a senior financial consultant at First Wall Street Corporation. Before his financial services endeavors, Thomas led an interdepartmental team at NAPP Systems Inc. He received his doctorate from Northern Illinois University and bachelor's degree from Illinois Institute of Technology.

were padlocked within three years of its opening. At that point I was carrying a two-month-old mortgage on a downtown San Diego condo in a complex that sat helplessly among soon-to-be-sagging commercial property values. With most of my savings now buried in the condo down-payment and unemployment at hand, I was chasing job leads one day when I received a fateful phone call. It was my panicked investment advisor, who had called Revlon and was told I no longer worked there.



He asked me, "Have you ever considered becoming a stockbroker?" My response: "Not really."

But I had to face the prospect of selling a newly bought condo in a dropping real estate market in order to facilitate a relocation that might permit me to secure a chemistry gig somewhere. There were too many unknowns wholly to dismiss the idea of an abrupt career change. So I decided on a two-track course. I would study the material for the general securities license during that summer while continuing to hunt for chemistry-related employment in San Diego. I passed the Series 7 exam in mid-August with no chemistry job in sight. I began my career as a commission-only full-service stockbroker in late August, and Saddam Hussein invaded Kuwait a week later. No clients, no savings, an almost depleted brokerage account, a relentless mortgage, and southern California real estate was in an official recession.

My career as a stockbroker

Exacerbating an already difficult situation was that the penny-stock boutique firm I worked for demanded 12- to 16-hour workdays and a few hours on Saturdays. Fortunately, my spirits frequently were buoyed by dedicated co-workers, and nothing provided energy quite like making a sale. That boiler room buzz you've seen in movies like "Wall Street" is very real and exhilarating. I quickly grew to enjoy the socialization of a brokerage office as much as a science lab and find (to this day) financial products as fascinating as chemicals.

But the commissions I earned were insufficient to pay the bills, and I was forced to lean heavily on the generosity of sympathetic friends until I could recapture my selfsufficiency. Meanwhile, my brokerage firm was starting to fall into disfavor with securities regulators, and I had to change firms. I was then introduced to the world of the home office. Eventually, I dislodged a job opportunity from a temp-tohire agency. To the rescue rode, of course, chemistry, in the form of a suburban San Diego photo-polymer printing plate company. This operation swiftly breathed new life into my dormant lab skills. No stock sale or mutual fund exchange could erode my ability to perform HPLC and GC or interpret NMR spectra. In a few weeks I successfully reverseengineered a printing plate formula owned by one of the company's competitors and parlayed a threemonth temporary assignment into a full-time job.

Back to science?

Now I can guit the stockbroker business as order has been restored, right? Fat chance. I love researching investments. A stock chart taps the analytical chemist in me as much as an IR or mass spectrum. A Wall Street Journal reads as easily as Chemical and Engineering News. I find Investors Business Daily no more technical than the Journal of the American Chemical Society. Nope, I had creditors – my personal bankers - to repay, so I did both. It was the most ambitious project of my life, and I made it work. Even though market hours (6:30 a.m. to 1:00 p.m. Pacific Time) overlapped my new 8-to-5, all of my investment clients either were mutual fund holders or buy-and-hold stock owners. So I'd check quotes, call clients and, yes, fax trades at breaks, during lunch, in the evenings and on weekends. I became an occupational Casanova.

It all went exhaustingly well until the newspaper company that owned the printing plate company decided to sell us to a larger privately owned chemical company. My responsibilities, which by now had mysteriously morphed away from the core competency that earned this full-time position in the first place, seemed likely to become even murkier under new ownership, assuming they needed me at all. Add to this a recent bad review with my current boss and a client base itching to do more business, and I had all the ingredients for 24/7 entrepreneurship.

Regrettably, the brokerage business grew too slowly to reach the critical mass necessary for sustainability and survival. The compliance grim reaper that had haunted my initial financial services firm finally came calling here. Massive layoffs and withheld contracts followed at this once pristine financial services outpost in San Diego. Had my money under management been sufficiently larger, I would have been spared the blade. I wasn't sunk by the bear market but rather by decisions and nondecisions. It is said in business that whether you occupy the corner office or just one of the cubicles may boil down to a few crucial decisions. Perhaps people are judged less by their decisions and more by how they navigate their consequences, but on occasion, we are forced to summon our inner Indiana Jones just to survive our choices. I currently tutor math and chemistry, and I'm trying to build another self-sustaining client base. Will the next decision be mine? $\nabla \Omega \Delta$

Obesity in Africa highlights this global epidemic

Little to no attention has been paid to the rising challenge of obesity across the life course in Africans.

BY JAMES M. NTAMBI

Globally, obesity has reached epidemic proportions as a major public health problem. In developing countries, obesity often coexists with widespread undernutrition, which is a major problem in children under five years old. Undernutrition often leads to conditions such as Kwashiorkor and marasmus due to protein and energy deficiencies, respectively. Obesity, on the other hand, is a major contributor to the global burden of noncommunicable diseases, including diabetes, coronary heart disease, hypertension, osteoarthritis, fatty liver disease, inflammation, sleep apnea and certain cancers.

The precise etiology of the many abnormalities that occur in obesity in the African population still is unknown. Multifactorial causes of obesity include genetic, dietary and lifestyle variables that together result in an imbalance between energy intake and energy expenditure. It is clear that a segment of the African population is rapidly adapting to a modernized lifestyle characterized by reduced physical activity and increased consumption of processed food rich in carbohydrates and fat, which has resulted in a dramatic rise in the incidence of overweight and obese individuals. Popular foods among children have shifted to those that are more energy-dense, including fast foods, cereals, breads, potato chips and soft drinks.

African diets have a very high carbohydrate component that can dramatically increase endogenous fatty acid synthesis, and since both dietary and endogenously synthesized fatty acids contribute to the whole-body fatty acid pool, obesity can result from excessive fat or carbohydrate consumption. There also is an increasing body of evidence in support of the Barker hypothesis, which proposes that the origins of obesity may actually occur in utero. In particular, links have been established between reduced birth weight and obesity and the associated risk factors in adulthood. The most widely accepted mechanisms thought to underlie these relationships are those of fetal programming by nutritional stimuli. It is suggested that the fetus makes physiological adaptations in response to changes in its environment to prepare itself for postnatal life. These changes may include epigenetic modification of gene expression.

Little to no attention has been paid to the rising challenge of obesity across the life course in Africans. For instance, much of the data about the extent of obesity in Africa is not published and often is documented in manuscripts in progress or in clinical reports. In addition, there are no well-defined population surveys that have evaluated the linkage of diets to obesity, type 2 diabetes and other symptoms of the metabolic syndrome in Africa. Exacerbating the problem are Africa's meager financial resources and overstretched skilled human resources, as well as existing lethal transmittable diseases such as tuberculosis and malaria.

While there obviously are some universal characteristics of the global obesity epidemic, responding to this health problem in each society requires proper understanding of the local environment and factors involved. For example, food availability and accessibility, which have been suggested by studies in North America as important components of the obesogenic environment, do not seem to play a big role in Africa among lower socioeconomic groups. Emphasis must therefore be placed on the preventive aspects of these diseases in order to economize on Africa's meager resources. Fortunately, many of the chronic noncommunicable diseases listed under the metabolic syndrome are preventable. Both early detection and management of these diseases can help to mitigate costly chronic complications and premature mortality. The challenges are clear, and they also are clearly important.



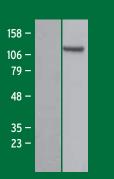
James M. Ntambi (jmntambi@wisc.edu) is the Katherine Berns Von Donk Steenbock professor in the departments of biochemistry and of nutritional sciences at the University of Wisconsin-Madison.

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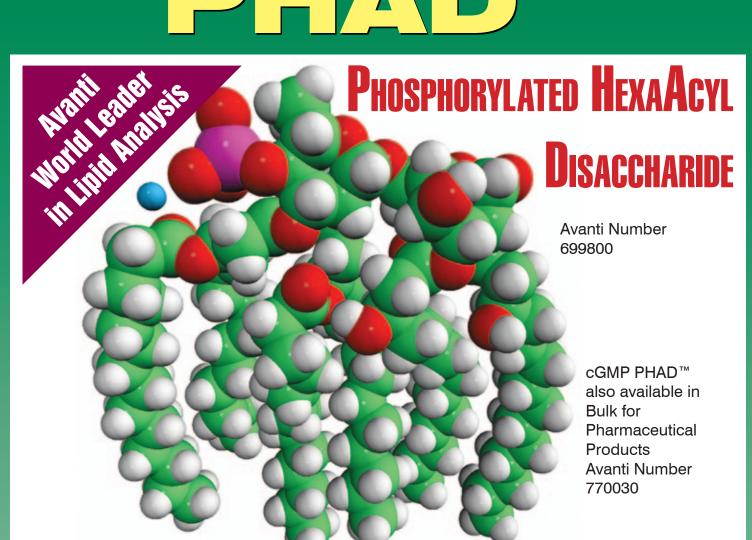
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• Lousada-Dietrich, S., Jogdand, P.S., Jepsen, S., Pinto, V.V., Ditlev, S.B., Christiansen, M., Larsen, S.O., Fox, C.B., Raman, V.S., Howard, R.F., Vedvick, T.S., Ireton, G., Carter, D., Reed, S.G., Theisen, M. (2011) A synthetic TLR4 agonist formulated in an emulsion enhances humoral and Type 1 cellular immune responses against GMZ2 - A GLURP-MSP3 fusion protein malaria vaccine candidate. Vaccine.

• Coler, R.N., S.L. Baldwin, N. Shaverdian, S. Bertholet, S.J. Reed, V.S. Raman, X. Lu, J. DeVos, K. Hancock, J.M. Katz, T.S. Vedvick, M.S. Duthie, C.H. Cleag, N. Van Hoeven, and S.G. Reed, (2010). A synthetic adjuvant to enhance and expand immune responses to influenza vaccines. PLoS One 5:e13677

• Coler, R.N., Bertholet, S., Moutaftsi, M., Guderian, J.A., Windish, H.P., Baldwin, S.L., Laughlin, E.M., Duthie, M.S., Fox, C.B., Carter, D., Friede, M., Vedvick, T.S., Reed, S.G. (2011) Development and characterization of synthetic glucopyranosyl lipid adjuvant system as a vaccine adjuvant. PLoS One 6:e16333.

• Fox, C.B., Friede, M., Reed, S.G., Ireton, G.C. (2010) Synthetic and natural TLR4 agonists as safe and effective vaccine adjuvants. Subcell Biochem. 53:303-21.

• Anderson, R.C., Fox, C.B., Dutill, T.S., Shaverdian, N., Evers, T.L., Poshusta, G.R., Chesko, J., Coler, R.N., Friede, M., Reed, S.G., Vedvick, T.S. (2010) Physicochemical characterization and biological activity of synthetic TLR4 agonist formulations. Colloids Surf B Biointerfaces. 75:123-32.

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