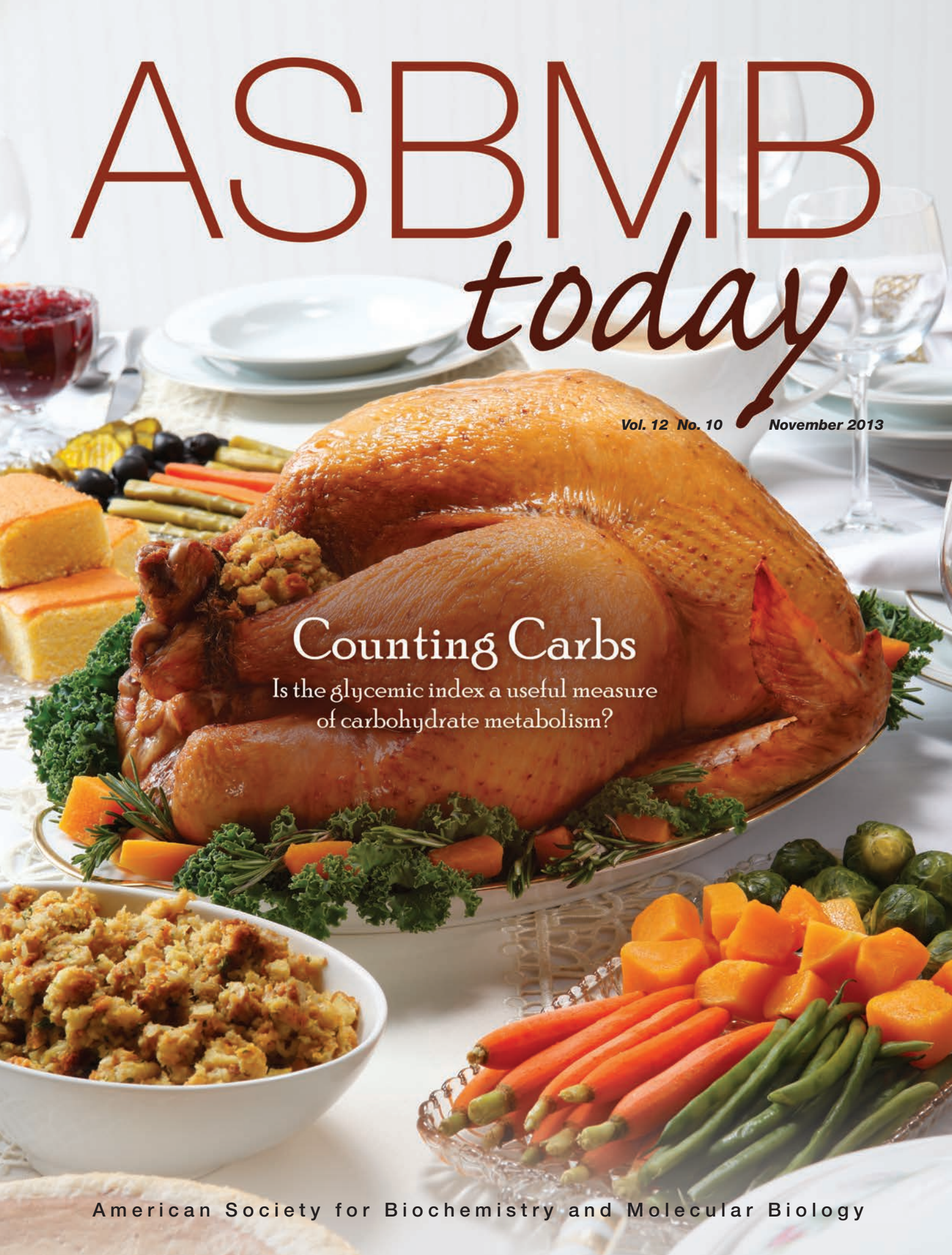
ASBMB today

Vol. 12 No. 10 November 2013



Counting Carbs

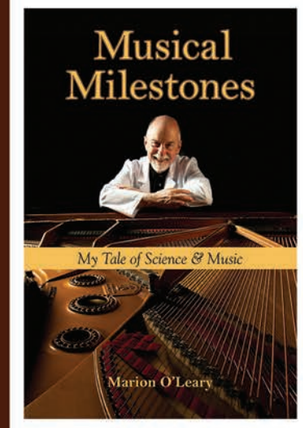
Is the glycemic index a useful measure of carbohydrate metabolism?

American Society for Biochemistry and Molecular Biology

OPEN LETTERS

Call for submissions: open letters

For ASBMB Today's 2014 essay series, we want your letters – ones addressed to someone or something but intended for public dissemination. We welcome letters of all sorts – serious, sentimental and maybe even silly. Send yours to asbmbtoday@asbmb.org by Dec. 31.



A Tale of Science & Music

Many scientists are also serious musicians—in some cases professionals, in some cases dedicated amateurs. *Musical Milestones* is the story of one such scientist—Marion O'Leary—and how he balanced his two passions, along with the added challenges of family, teaching, and university administration. His stories are a lesson for other scientists who search their busy lives for time and energy to pursue a life in music.

MORE INFORMATION
For more information about *Musical Milestones*, or to read sample chapters, go to www.marionoleary.com.

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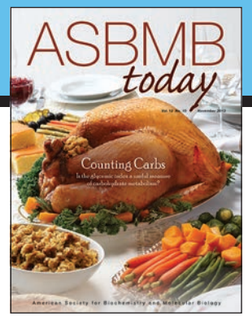

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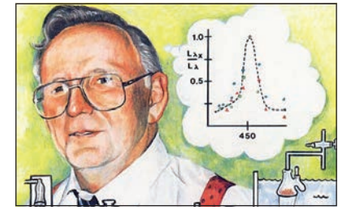

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ASBMB today

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

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Career alternatives, not alternative careers

BY JEREMY BERG

The topic of alternative careers comes up frequently these days in the context of training programs. The term "alternative careers" tends to have a pejorative connotation that many, including me, feel is unjustified.

I'm often asked to give talks about careers, and at each, in addition to presenting general data about career options, I describe the outcomes for the 24.9 graduate students who have worked under my supervision over the course of my career.

I looked at this group because I have direct knowledge of their careers and have at least some insights into how and why they pursued the paths that they did. Of course, I do not know to what extent my experiences are representative, but I have no reason to believe that they are vastly different from those of others.

In describing their career outcomes here, I will use four categories: faculty positions in academia with both research and teaching responsibilities, other active research positions, nonresearch activities using deep scientific knowledge, and other, keeping in mind that this is not the only way of binning career outcomes and that even within these categories placement of some individuals may be ambiguous.

Within these categories, my students fall as follows:

- faculty positions: 7
- other active research positions: 7
- nonresearch science positions: 8
- other: 2.9

You probably are wondering about the 0.9. That corresponds to a student who completed all of the research for his thesis but then, against my strong advice, elected not to write up his dissertation. Instead, he went in a very different direction, spending a year selling wine and then opening his own restaurant. With plenty of hard work, this proved to be a great success, as did his second restaurant. As he approached his 50th birthday, he was considering retirement. The remaining two in the "other" category chose to pursue nonscience careers directly out of graduate school.

Each of the remaining categories is quite diverse. The nonresearch science positions include a patent attorney in private practice, a patent attorney working as an examiner in the patent office, an associate editor at a major science journal, a science writer in the pharmaceutical industry, an M.D./Ph.D. physician primarily in private practice, and two faculty members at purely teaching institutions. In about a quarter of these cases, the individuals who pursued these paths knew that they wanted to pursue careers outside of research-focused academia from fairly early in their graduate training.

The nonfaculty research positions include individuals in many sectors and at many career stages. These include three research leaders in biotechnology companies, two senior investigators in major pharmaceutical companies, the director of a core facility at a university, a chemist running her own consulting company and a post-doctoral fellow who took a decade off after graduate school to care for his children. I believe that most of the students who went into the biotech or pharmaceutical sectors were interested in this career path from early in their graduate student days or before, although one left a blossoming faculty position for an exciting opportunity in a young company and has thrived there.

The details of the faculty positions also are remarkably diverse. Two students are now in departments focused on biochemistry and are working on projects that align at least to some extent with the sorts of research they did as graduate students. Two more who worked with me when I was a chemistry faculty member are in departments of biological sciences, one working on plants and the other on viruses. One used his training in protein nuclear magnetic resonance methods and moved into magnetic resonance imaging and is now a professor of radiology. Finally, two M.D./Ph.D. students are pursuing careers in academic medicine, one in pediatrics and one in oto-laryngology. The diversity of these academic career paths reflects both my rather eclectic research interests and my time in a medical school.

I am immensely proud of my students. Almost all of them are using their scientific training to contribute to society in important ways from discovery to technology development to teaching. Each has found his or her own way, sometimes in a straightforward manner and sometimes by a more circuitous path, to a position that plays to his or her skills and interests and provides an appropriate work-life balance.

I am immensely proud of my students. Almost all of them are using their scientific training to contribute to society in important ways from discovery to technology development to teaching. Each has found his or her own way, sometimes in a straightforward manner and sometimes by a more circuitous path, to a position that plays to his or her skills and interests and provides an appropriate work-life balance. Some of them have risen to high positions within their organizations, including one who is now a dean.

As I hope I have illustrated above, students with training in biomedical sciences can and do go on to a wide range of different careers that depend on their scientific training. That is not to say that all career alternatives meet this criterion.

The shortage of job opportunities for scientists completing their graduate studies and postdoctoral training is a major driver of the current discussion.

Remarkably, National Institutes of Health Director Francis S. Collins and Deputy Director for Extramural Research Sally Rockey recently wrote, "We are, however, firmly committed to the premise that bioscience Ph.D.s provide invaluable contributions to a whole variety of fields. Furthermore, there is no definitive evidence that Ph.D. production exceeds current employment opportunities" (1).

I clearly agree with the first statement, but the second is painfully disconnected from reality. Almost anyone who has talked with or tried to help young scientists launch their independent careers knows that current employment opportunities are extremely competitive in all sectors.

This is truer than it was a decade or even five years ago, and the number of people competing for each

position is the major culprit. The number of biomedical Ph.D.s trained increased by nearly 50 percent from 2002 to 2009 (2).

This was not driven by an analysis that revealed a shortage of Ph.D.s. Rather, more students were trained because of the increase in the NIH research budget and the fact that scientists in training are the major workforce in the academic biomedical research enterprise.

Regulating the number of trainees is more complicated in biomedicine than it is in most other fields. The duration of biomedical training presents a major challenge.

In law, for example, where career opportunities changed significantly concomitant with the economic downturn, many schools responded by decreasing their class sizes by 20 percent or more. However, completion of a law degree takes only three years, so the job market usually does not change dramatically from the initiation of training to its completion. In biomedicine, with an average of more than five years for a Ph.D. and then three to six years of postdoctoral training for many positions, the job market can change dramatically over the training period.

A student who started a Ph.D. program in 2002 – with the NIH budget doubling in progress, many academic institutions adding faculty positions, and opportunities in the pharmaceutical and biotechnology industries relatively strong – completed his or her training within the past few years and emerged in a completely different environment. Furthermore, regulation of training class sizes is less direct in biomedicine than it is in some other fields.

Nonetheless, denial of the issue is not an acceptable option. Students must be made aware of the wide range of career options and also current job prospects in all sectors prior to or early in their training so that they can make informed decisions.

Steps should be taken to reduce the strong coupling of research activity with training so that such activity does not inevitably lead to more young scientists competing for scarce positions. Seriously addressing these issues is a key component of building a sustainable biomedical research enterprise, a topic on which the American Society for Biochemistry and Molecular Biology is taking a leadership role (3).

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Keep an eye out for these legislative measures

BY SHAILA KOTADIA

While the government shutdown concentrated on the budget and debt ceiling, many bills remained stalled in the legislative pipeline. Here are a few pieces of legislation that may help or hinder scientific progress:

Next Generation Research Act

U.S. Sen. Tammy Baldwin, D-Wisc., in September filed a bill to support young researchers. While well-intentioned and supportive of existing programs for young investigators, this legislation is vague in its proposals of new initiatives. The bill proposes preparing a report, to be completed no later than five years from the bill's enactment, to identify the barriers preventing young researchers from progressing successfully into academic positions. The idea is to generate new policies from the report; however, within five years, the climate of the field may have changed dramatically. The bill has been referred to the Senate Committee on Health, Education, Labor and Pensions and may be referred to the House for a vote.

Immigration reform

The U.S. Senate passed a complex, comprehensive immigration-reform bill in June. For workers in the fields of science, technology, engineering and mathematics, the bill would remove certain visa limitations for noncitizens receiving graduate degrees, increase the number of H1-B work visas and establish an education and training account that would fund scholarships for low-income STEM students through an increase in the H1-B visa employer application fee. Overall, the bill would increase the number of foreign-born scientists with advanced STEM degrees who are allowed to work and live in the U.S. The House has yet to propose its immigration-reform bill due to partisan disagreements, and until it does, this bill is stalled.

America COMPETES Act

The America COMPETES Act was enacted during the Bush administration and reauthorized in 2011 to direct the National Science Foundation and other federal funding agencies, excluding the National Institutes of Health, to invest in STEM education and research and development to maintain U.S. global competitiveness. Now the act is up for reauthorization – this time possibly under the name the Einstein America Act. While the American Society for Biochemistry and Molecular Biology supported the act in the past, it is now concerned that some objectionable language from the draft High Quality Research Act (1) may end up being included in the reauthorization bill. The HQRA had provisions that would alter the peer-review process at the NSF and other funding agencies, and inclusion of those provisions in the Einstein America Act could be detrimental to the foundations of the grant-review process. We'll just have to wait and see the bill.

Sequestration

The government shut down after no continuing resolution was agreed upon for fiscal 2014. In FY13, the Budget Control Act resulted in across-the-board cuts for all discretionary spending. Known as sequestration, this decreased the budgets of the NIH, the NSF and other federal science-funding agencies. With the FY14 budget being so contentious, sequestration may be continued for another fiscal year, which would result in more cuts. At this juncture, the best-case scenario would be a FY14 budget that removes sequestration, restoring the funding agencies' budgets to levels prior to the budget cuts. For the next several months, scientists must make a strong case for the value of their work.

Shaila Kotadia (skotadia@asbmb.org) is an ASBMB science policy fellow.

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Retrospective

Ronald Winfield Estabrook (1926 – 2013)

BY BETTIE SUE MASTERS

Ronald "Ron" Winfield Estabrook, a world-renowned biochemist with a special knowledge of enzymatic reactions related to toxicology and steroid hormone biosynthesis, died at his home Aug. 5. He was 87 and had suffered from congestive heart failure.

An expert in the field of cytochrome P450 biochemistry and biophysics, Estabrook helped transform the University of Texas Southwestern Medical School, as it was called in his day, into a powerhouse. Under his leadership, the biochemistry department became the mecca of cytochrome P450 studies, pushing the field forward from its modest initial findings to become one of the most influential research subjects in biomedicine.

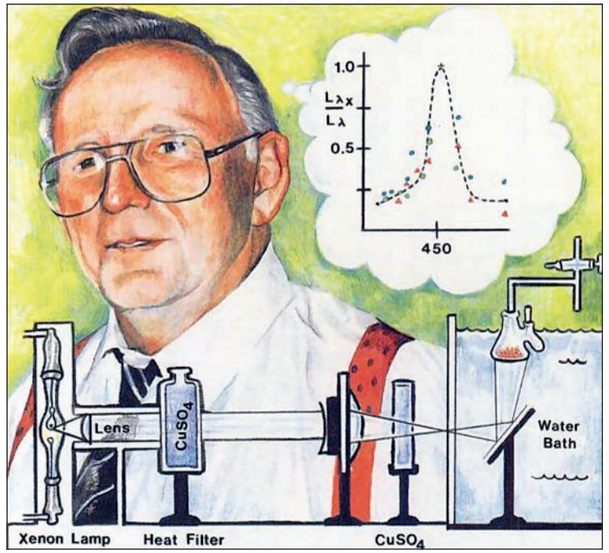

IMAGE COURTESY OF THE FASEB JOURNAL, WWW.FASEBJ.ORG

Image drawn by Dot Roberson

Born in Albany, N.Y., on Jan. 3, 1926, Estabrook attended public schools. He graduated from Albany High School in 1943 and that July joined the U.S. Navy. He attended officer training schools at Princeton and Notre Dame and was appointed to the rank of ensign in March 1945. He was assigned subsequently as a line and gunnery officer on a minesweeper and participated in the Allied occupation of Okinawa Island and Japan.

After World War II, Estabrook earned his undergraduate degree from the Rensselaer Polytechnic Institute in 1950 and pursued graduate training in biochemistry at the University of Rochester under the mentorship of Elmer Stotz, completing his dissertation, "Studies on the Cytochromes in Heart Muscle Extracts," in 1954.

Estabrook then began a long association with the Johnson Foundation at the University of Pennsylvania. He began as a postdoctoral fellow with Britton Chance, during which time he learned sophisticated spectroscopic techniques as they were applied to studies of mitochondrial electron transport. He concluded his time at the foundation as its deputy director. During his tenure at Penn, he spent a sabbatical at the Molteno Institute at Cambridge University with David Keilin, the discoverer of cytochromes. In 1959, Estabrook joined the faculty of the University of Pennsylvania School of Medicine, where he advanced to the rank of professor of physical biochemistry while remaining a member of the Johnson Foundation faculty.

In the early 1960s, Estabrook, together with David Cooper and Otto Rosenthal of the University of Pennsylvania department of surgery, performed pioneering experiments that resulted in the discovery of the functional properties of a unique hemoprotein species, now known as cytochromes P450, and proved their roles in the metabolism of steroids and drugs.

The technique, originally used by Otto Warburg in showing that cytochrome oxidase (Atmung's ferment) was the terminal oxidase in the mitochondrial respiratory chain and known as a photochemical action spectrum (figure 1), was applied to preparations of endoplasmic reticulum, called microsomes. The technique involved reversing the CO inhibition of either drug metabolism or steroid hydroxylation activity of the cytochrome P450 by specific wavelengths of light. The wavelength at which the CO adduct of the enzyme demonstrated the maximum absorption of light and the maximal reversal of the CO inhibition was 450 nanometers, thus the name of this class of enzymes.

The significance of these oxygenating cytochromes P450 in toxicology, environmental health and endocrinology is immeasurable, and the determination of their functional importance was a fundamental discovery. For these studies, Estabrook was elected to the National Academy of Sciences and later, for his contributions to the field of medicine, to the Institute of Medicine of The National Academies. He also was awarded a Doctorem Medicinae Honoris Causae from the Karolinska Institutet in Stockholm.

Estabrook was the first of a number of basic science chairs who were recruited to UT-Southwestern under the direction of Donald Seldin, then chairman of medicine, and Charles Sprague, then dean of the medical school. He arrived in 1968 to serve as the Virginia Lazenby O'Hara professor of biochemistry and chairman of the biochemistry department.

Estabrook recruited four young assistant professors at that time, of which I was one, and forged ahead with a tour de force as he hired more faculty members over the next few years to fill out his roster. The biochemistry department became a hub for cytochrome P450 studies, as numerous scientists from throughout the world spent sabbaticals in Dallas to pursue biophysical and biochemical studies of these all-important enzymes. The evolution of the cytochrome P450 field is legendary, and it is not possible to read about the side effects of any therapeutic drug without mention of the role of these enzymes in the context of drug-drug interactions. During his 14 years as a chairman, Estabrook built a world-class center of research revolving around the cytochromes P450 and their biological and biophysical properties. During this period, Estabrook also served as the first dean of the Graduate School of Biomedical Sciences.

Not only was Estabrook an outstanding mentor of faculty members, having nurtured the careers of a number of future department chairs including Thomas E. Smith (Howard University), Louis B. Hersh (University of Kentucky), Michael R. Waterman (Vanderbilt University), Russell A. Prough (University of Louisville) and me (Medical College of Wisconsin), but he also was a prime mover in the founding of several societies and associations, including the Association of Medical and Graduate Departments of Biochemistry and the International Society for the Study of Xenobiotics. He was the charter treasurer of The Academy of Medicine, Engineering and Science of Texas when it was founded in 2004. He served as treasurer of the American Society for Biochemistry and Molecular Biology from 1985 to 1991.

Estabrook was well known for the insightful questions he always asked and for his incredible ability to sum up at the end the important messages of talks at innumerable scientific meetings. He loved to challenge speakers regarding the meaning of their studies. After his retirement in 2006, when he was named the Ashbel Smith professor emeritus of biochemistry, he kept busy with his many avocations, including photography, genealogy, stamp collecting, and traveling and still attended scientific meetings on occasion.

But most of all he will be remembered for his tender heart, his support of the underdog, and his unending support of those whom he had a role in training or with whom he collaborated. For these reasons, he became known to many of us as "Uncle Ron."

He is survived by his wife of 66 years, June Elizabeth Templeton Estabrook of Dallas, as well as his children, Linda Ann Estabrook Gilbert of Charlotte, N.C.; Laura Elizabeth Estabrook Verinder of Schertz, Texas; Jill Kathleen Estabrook Wisehart of Denver; and David Edward Estabrook of Dallas. Ron was proud of his extended family and shared much of his leisure and travel time with his seven grandchildren and five great-grandchildren, often including his family members on trips abroad. Those of us who were fortunate enough to be touched by his generosity as well as his guidance will miss him greatly.

Bettie Sue Masters (masters@uthscsa.edu) holds the Robert A. Welch Distinguished Chair in Chemistry in the biochemistry department at the School of Medicine at the University of Texas Health Science Center in San Antonio.

ASBMB TODAY LOOKS BACK

We have had the privilege of publishing over the years dozens of Retrospective articles about the great men and women who have contributed to our current understanding of biochemistry and molecular biology. This summer we launched a special collection of those remembrances and biographies on our website. Visit **www.asbmb.org/asbmbtoday** and click on "Collections" to see ones you might have missed or could use in the classroom.

Two more Tabor young investigator award winners

Stem cells to treat corneal disease

BY MITHU MAJUMDER

Vivien Jane Coulson-Thomas was named the winner of Journal of Biological Chemistry/ Herbert Tabor Young Investigator Award in late August at the 8th International Proteoglycan Conference in Frankfurt am Main, Germany, for her work on the use of human umbilical cord mesenchymal stem cells in treating corneal disease.

Coulson-Thomas, a postdoctoral fellow at the University of Cincinnati, was recognized for her work that sheds light on how transplanted umbilical cord mesenchymal stem cells, or UMSCs, participate in extracellular glycosaminoglycans turnover and enable host keratocytes to catabolize accumulated GAGs products. Her research suggests that UMSC could be a novel alternative for treating corneal defects associated with mucopolysaccharidosis and other congenital metabolic disorders in lieu of corneal transplantation. She currently is studying the role of proteoglycans in corneal epithelial wound healing and corneal development.

Vivien Jane Coulson-Thomas was named winner of a Tabor award at the 8th International Proteoglycan Conference held Aug. 25 – 29 in Frankfurt, Germany, and attended by Vincent Hascall, a Journal of Biological Chemistry associate editor.

Coulson-Thomas completed undergraduate and doctoral studies in Brazil at the Federal University of São Paulo, where she worked under the guidance of Helena Nader. Her doctoral work focused on the role of proteoglycans in cancer cell invasion and the design of different co-culture models to study tumor and fibroblast crosstalk.

Mithu Majumder (mithumajumder@gmail.com) is a research scientist at Case Western Reserve University in Cleveland, Ohio.

Adaptable metabolic pathways

BY MARIANA FIGUERA-LOSADA

Ursula Loizides-Mangold was issued the Tabor award by George Carman, an associate editor for the JBC, at the 54th International on Bioscience of Lipids in Bari, Italy.

Ursula Loizides-Mangold received the Journal of Biological Chemistry/ Herbert Tabor Young Investigator Award at the 54th International Conference on Bioscience of Lipids in Italy in September for her work on lipid metabolism.

Loizides, a senior scientist in Howard Riezman's laboratory at the University of Geneva, uses mass-spectrometry-based lipidomics to dissect the role of lipids in cell function and the effects of nutrition on whole body metabolism.

Working with Bernard Thorens' group at the University of Lausanne, Loizides studied the L-peroxisomal bifunctional enzyme, or L-PBE, which has been associated with steatohepatitis, insulin resistance and diabetes.

They found that L-PBE is required to prevent dietary toxicity of medium-chain fatty acids, such as the ones found in coconut oil. These fatty acids induce production of dicarboxylic fatty acids, which accumulate due to L-PBE deficiency resulting in liver failure, inflammation and fibrosis.

These results highlight DCAs' potential toxicity and suggest that specific metabolic pathways can be activated by different nutrients to adapt the organism to the available resources.

During Loizides' postdoctoral studies, she worked on the regulation of polyamine biosynthesis. She said she was inspired by Herbert and Celia Tabor's work on polyamine metabolism and that it is a very special honor for her to receive the Tabor award.

Mariana Figuera-Losada (fmariana@hotmail.com) is a postdoctoral fellow at the Johns Hopkins University.

2013 Nobel Prize in physiology or medicine


ROTHMAN


SCHEKMAN


SÜDHOF

Three American Society for Biochemistry and Molecular Biology members won the 2013 Nobel Prize in physiology or medicine in October for their work in vesicle trafficking.

James Rothman of Yale University, Randy Schekman at the University of California, Berkeley, and Thomas Südhof at Stanford University share the prize "for their discoveries of machinery regulating vesicle traffic, a major transport system in our cells," said the Nobel Assembly in its announcement.

Vesicle trafficking "is the mode by which proteins move from place to place within the cell. This includes the process of internalization, in which receptors at the cell surface move inside the cell, as well as the reverse process, in which proteins, such as hormones, are secreted from cells," explains Steven Caplan at the University of Nebraska, who studies the process. "Such movement is essential for the normal functioning of every cell, and impaired vesicle trafficking leads to a host of diseases. More than anything, this Nobel Prize is a boon to those of us in the field and acknowledges the importance of understanding fundamental biological questions."

Schekman, who also recently won the Otto Warburg Medal from the German Society for Biochemistry and Molecular Biology, used yeast genetics to identify more than 20 genes that are critical for vesicle trafficking. He showed that these genes could be classified into three categories of vesicle-transport regulation based on location: in the Golgi complex, in the endoplasmic reticulum and at the cell surface.

Rothman used biochemical approaches to establish the function of SNARE proteins. He demonstrated how different combinations of these proteins formed complexes to control cell fusion and properly delivered the cargo inside the vesicles to the right destination.

Südhof (who recently won the Lasker Award in Basic Medical Research along with Genentech's Richard H. Scheller) became interested in how vesicle fusion machinery was controlled. He worked out the mechanism by which calcium ions trigger release of neurotransmitters and identified key regulatory components in the vesicle fusion machinery, such as complexin and synaptotagmin-1.

"Together, Rothman, Schekman and Südhof have transformed the way we view transport of molecular cargo to specific destinations inside and outside the cell," said the Nobel Prize press release.

Defects in vesicle trafficking have been linked to conditions such as neurological diseases, diabetes and immunological disorders.

– RAJENDRANI MUKHOPADHYAY

Gilbert gets NIH MERIT Award


GILBERT

Susan Gilbert at Rensselaer Polytechnic Institute won a Method to Extend Research in Time Award from the National Institutes of Health's National Advisory General Medical Sciences Council in recognition of her research contributions throughout her career. "Susan is to be congratulated for a very significant and rare achievement in earning an NIH MERIT award," said Laurie Leshin, a dean at Rensselaer. "It's a well-earned recognition of the long-standing, extremely high quality of her research. The award provides her the freedom to explore cutting-edge scientific ideas in ways that wouldn't otherwise have been possible. The National Institutes of Health are to be commended for working to enable their researchers to seek paradigm-shifting breakthroughs." Gilbert's work focuses on the structure and mechanisms of microtubule-dependent ATPases.

IN MEMORIAM: Ellen Fanning (1946 – 2013)


FANNING

Ellen Fanning, a faculty member at Vanderbilt University since 1995 and a Howard Hughes Medical Institute investigator, died in September at the age of 67. Fanning, who headed the molecular biology department at Vanderbilt between 1999 and 2002, studied DNA replication in mammalian cells. A dedicated mentor, she used her HHMI award in 2002 to establish what she called a "Community of Scholars," which offered hands-on research opportunities to undergraduates. Fanning served on the editorial board of the Journal of Biological Chemistry and was a fellow of the American Academy of Microbiology.

NIH funds three projects focused on characterizing microbiota in disease

BY SOO HEE LEE

The Human Microbiome Project, funded by the National Institutes of Health Common Fund, is entering its second phase with three research projects focused on understanding changes in microbiomes in disease. Two members of the American Society for Biochemistry and Molecular Biology will lead one of the projects.

The first phase of the HMP started in 2007 and focused on characterizing microbial communities of different body sites, including skin, nasal and oral cavities, and gastrointestinal and urogenital tracts.

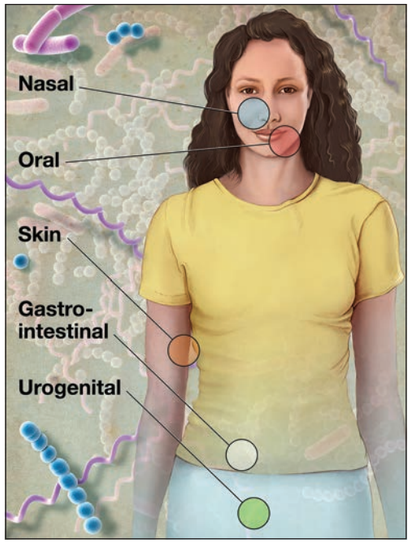

IMAGE CREDIT: NIH

The body sites that were sampled as part of the Human Microbiome Project healthy cohort study.

The new studies will harness the technological tools of the -omics revolution – genomics and metagenomics, transcriptomics, proteomics and metabolomics – to capture coordinated snapshots of the dynamic changes in the microbiome and in the individual during disease progression.

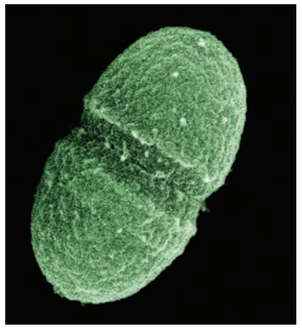

IMAGE CREDIT: NIH

The bacterium *Enterococcus faecalis* is one of many commensal microbes that live in the human gut.

One project, led by Gregory Buck of Virginia Commonwealth University and funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, will characterize urogenital tract bacteria in pregnant women and their babies to gain insights into preterm birth.

A second project, led by Ramnik Xavier of the Broad Institute of Massachusetts Institute of Technology and Harvard University and Curtis Huttenhower of Harvard School of Public Health, will assess populations and physiological activities of gut microbes in people with Crohn's disease and ulcerative colitis, the two major forms of chronic inflammatory bowel disease. The project is funded by the National Institute of Diabetes and Digestive and Kidney Diseases.

ASBMB members Michael Snyder of Stanford University and George Weinstock of Washington University at St. Louis will lead the third project, also funded by the NIDDK. They will examine changes in gut and nose microbial communities in a cohort over three years, sampling the same individual in periods of good health and during viral infections as well as other stresses. The study will focus on people at risk for diabetes, adding another dimension of analysis, and will include blood glucose measurements. In all, more than 1,080 different physiological states will be analyzed.

The project builds upon the expertise of the two teams. Snyder is a leader in the field of functional genomics and proteomics, having led one of seven research groups participating in the ENCODE project, which aimed to identify all functional elements in the human genome. Weinstock led one of the first bacterial genome sequencing projects and was an investigator in the HMP precursor project, the Human Gut Microbiome Initiative.

Soo Hee Lee (shlee0909@gmail.com) received a Ph.D. in biochemistry from the Johns Hopkins University School of Medicine and undertook a Jane Coffin Childs Memorial Fund postdoctoral fellowship at the Yale University School of Public Health.

Researchers identify new potential drug to combat fatal infantile disease

BY LYMOR RINGER

Researchers at the National Institutes of Health have identified a new potential drug that could help treat Batten disease, a fatal neurodegenerative disease in children. The research team, which included American Society for Biochemistry and Molecular Biology members Anil B. Mukherjee and Goutam Chandra, performed mouse studies that suggest this drug may extend the lives of children with Batten disease. Their findings were recently published in the journal Nature Neuroscience.

Batten disease is a group of rare neurodegenerative lysosomal storage diseases that affect one in 12,500 children. In the infantile type of the disease, children are generally born without symptoms but begin to show psychomotor retardation by the time they're 11 months to 18 months old, and they're often blind by the age of 2. These children lose all brain activity and eventually die at around 3 to 5 years old. There is no effective treatment for children with Batten disease.

Children with infantile Batten disease have a deficiency in the PPT1 protein, or palmitoyl-protein thioesterase-1. This deficiency leads to a buildup of waxy substances called ceroids in the cells of many tissues including the brain and eye.

Mukherjee and his colleagues performed a drug screen for derivatives of hydroxylamine, which is known to mimic PPT1 and reduce ceroid buildup but cannot be used clinically due to its high toxicity. They found a derivative called N-(tert-Butyl-Hydroxylamine), or NTBuHA. This compound was effective at significantly extending the lifespan of PPT1 knockout mice without any side effects due to toxicity.

This research team at the Eunice Kennedy Shriver National Institute of Child Health and Human Development also is investigating two additional drugs, known by the brand names Mucomyst and Cystagon, for the treatment of infantile Batten disease patients. Like NTBuHA, these drugs act by breaking down ceroid deposits. The findings are a promising step forward for the treatment of patients with Batten disease, and the researchers hope to begin clinical trials with these drugs soon.

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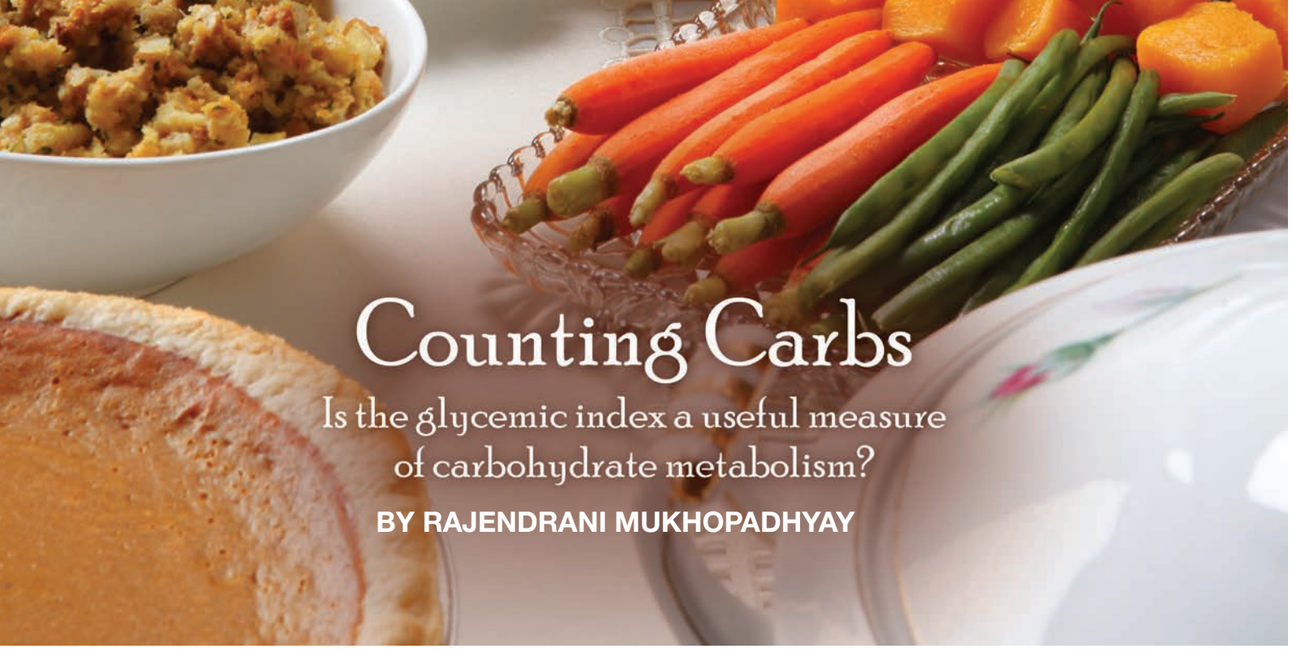


Counting Carbs

Is the glycemic index a useful measure of carbohydrate metabolism?

BY RAJENDRANI MUKHOPADHYAY

Which is better for you: a sugary cereal or a baked potato? According to the glycemic index, the cereal would win because it scores lower.

Since its inception in 1981, the glycemic index – a measure of the changes in blood-glucose levels in response to the consumption of a food containing carbohydrates – has been a source of contention.

Experts tend to fall into one of two camps. One camp believes that a low-glycemic-index diet helps weight loss and keeps chronic illnesses, such as cardiovascular disease, Type 2 diabetes and age-related macular degeneration, at bay. This camp has been pushing for labeling foods with their GI values. The index has been used as the basis of several commercial diets, including the Nutrisystem diet, which has been endorsed by celebrities such as Marie Osmond and Dan Marino.

The other camp counters that glycemic index doesn't clearly delineate between healthful and unhealthful foods: Because some junk foods show up on the lower end of the GI scale, which is thought to be better, the critics argue, the glycemic index confuses consumers. They also contend that the evidence for the health benefits of the glycemic index just isn't consistent. Joanne Slavin at the University of Minnesota was part of the 2010 committee that did the most recent analysis of the U.S. dietary guidelines. "We did the review on GI," she says. "There was strong evidence that the GI isn't linked to health outcomes in healthy people." (See the excerpt from the 2010 U.S. dietary guidelines on page 15.)

This summer, the regulatory authority Health Canada issued a white paper to say that it has decided the index is not going to be put on food labels in Canada (1). "GI is confusing," says Alfred Aziz of Health Canada, the first author on the paper. "We don't feel it's a good labeling measure." Health advocacy organizations in the U.S., such the American Heart Association and the American Diabetes Association, haven't yet adopted the glycemic index. The Canadian Diabetes Association has advocated that Type 1 and 2 diabetics use the measure in its 2013 Clinical Practice Guidelines (2).

Supporters of the index decry Health Canada's decision as well as the judgments of the glycemic index detractors. "The criticisms are uninformed," says Jennie Brand-Miller, director of the University of Sydney's GI testing service, SUGiRS. She and others believe that unfortunate circumstances have plagued the glycemic index. "Some of it is the politics of food, and some of it is the politics of science," says Brand-Miller. "Some of the controversy is because GI didn't come out of America. It was from Canada and Australia, and that set up these opposing forces." (See box for all sources' conflicts of interest on page 16.)

WHAT IS THE GLYCEMIC INDEX?

The GI is a measure that ranks foods containing carbohydrates according to their potential to raise blood-glucose levels after being consumed. To get a measure of a food's GI, participants in a study are given the test food to eat. The test food contains a known amount of carbohydrate, usually 50 or 100 grams. The participants' blood-glucose levels are measured by finger-prick tests over the course of two hours after they've consumed the food. Then, on three different days, the participants are given the equivalent amount of glucose powder dissolved in water, which acts as a reference. (Sometimes, researchers use white bread).

The changes in blood-glucose level after eating the test food are plotted as a function of time, and the area under the curve is calculated. The same is done for glucose. The value of the area under the curve for the test food is divided by the average value of the areas under the curve for the reference and then multiplied by 100. The resulting number is a unitless measure, a ratio of the blood-glucose response between the text and reference sample.

Foods that score 70 and above are classified as high on the glycemic index. Foods that score 55 or less are classified as low, and those in the middle are classified as medium.

A PERSONAL RESPONSE?

Because the measurement is done in people, critics argue that this makes the glycemic index susceptible to variation.

"People who want to push the glycemic index make claims on the assumption it's an absolute quantity, which is dependent entirely on the food that you're eating and does not reflect in any way a person's metabolism," says William Whelan at the University of Miami. "They are assuming that it doesn't matter who you are – if you eat this particular food, you're going to get this particular glycemic response. That's nonsense."

Whelan's view is that glycemic response is highly specific to how an individual processes carbohydrates. The rise in blood glucose "causes a release of insulin. Insulin then works to drive the glucose in the direction of fat synthesis," says Whelan. "The extent to which that affects any individual depends on his or her own individual glycemic response."

Whelan's research has shown that a person has a set baseline in his or her response to carbohydrates. Two people can eat the same quantity of the same food, but one person can have a higher spike in blood-glucose level than the other person. This observation, which he made in healthy undergraduate students recruited from the University of Miami, cuts across all kinds of carbohydrate-containing foods.

Whelan asserts that proponents of low-GI diets don't acknowledge this biological fact. "Their message is valid only for that section of the population that naturally, from their own metabolism, for whatever reason, has a low glycemic response to whatever they eat."

But Brand-Miller counters that the GI holds steady across different population subsets. "We've been able to show that if a food is low GI in a normal, healthy young individual it's also low GI in elderly people, children, people with impaired glucose tolerance or people who are overweight."

Thomas Wolever at the University of Toronto says that critics confuse the glycemic index with the glycemic response. "Often times, when people criticize GI, they are not actually talking about GI. They are

talking about a glucose response."

VARIATION IS A STICKING POINT

Health Canada pointed to variation when it decided against printing GI values on food labels. "Compared to other measures of food, for example lipids or proteins, where you actually measure them in instruments, the instrument for the glycemic index is the individual," says Aziz. "You can appreciate how you can have such a large variation when you use a person as an instrument to measure a property of the food."

David Jenkins at the University of Toronto and other proponents of GI say the variation issue is overblown. "There are individual differences, but they are not big," states Jenkins, who, along with Wolever, first published the concept of GI (3). "The big difference is basically a difference between my glucose tolerance and yours when it's not indexed" to glucose. What matters, says Jenkins, is the collective response of a group of people to a particular food in comparison with their response to a reference food.

Experts are split on whether the glycemic index helps people make the right food choices.

Proponents of the glycemic index are very much aware that people differ, even day to day. "The human instrument is very imprecise," says Wolever. "But we've developed the method to take that into consideration."

Wolever says his group measures the reference food more than once, because its value is the denominator in the calculation. "We have to measure it several times to try to get a better representation of that subject's true response, because it varies tremendously from day to day," he says. "The GI value you get depends more on the denominator than the numerator. That's why the denominator is important. That is lost on people."

But Aziz counters that the multiple measurements of the reference food don't cut it. Despite the multiple measurements and averaging, he says, "it's still a highly variable measure."

MEANINGFUL MEASUREMENT

Making a reliable measurement can be problematic. Slavin uses carrots as the example. "For me to deliver 100 grams of carbohydrate in the form of carrots in a feeding study, that's like 15 servings," she says. "It's a huge pile of carrots, because you've got to come up with 100 grams! Carrots are mostly water, a little bit of fiber and a little bit of starch. The GI is very nonrepresentative of what people actually eat."

Also, values reported for a given food can be all over the map. Slavin goes back to her carrots example. GI values reported for carrots in the literature "can go anywhere from 50 up to 120. It's all over the place," says Slavin. "There is no government standard of the use – to say 'This is the value for carrots' – because there isn't a value. It's a moving target."

GI supporters agree there is a problem with consistency: The literature is littered with different values for the same foods, because the studies didn't follow the same methodology. Part of the problem with the GI literature is that "the amounts of carbohydrate in the studies vary," says Wolever. "When you look at nutrition studies, they are not all the same. It's not like a drug study."

The other problem is the food itself, says Jenkins. Processed foods are being reformulated continuously. This means measurements made with previous iterations of a product become useless. "We've got a real problem with changing food supplies," says Jenkins. "Imagine if you're responsible for trying to keep a database of foods that have all been tested for groups of healthy individuals. How can you keep that database up to date and relevant?"

Another problem "stems from the fact that we're often looking at small differences in GI. You need very large numbers of people to show differences in outcome," says Jenkins. Aziz adds that many studies also don't pay attention to the race and ethnicity of the participants. People of different racial and ethnic backgrounds are known to have different metabolic patterns. "Ideally, you need to have equal representation of different ethnic groups in your sample size to be able to have a more meaningful and accurate GI value," says Aziz. With researchers using a few individuals in their studies and old GI measurements, Jenkins says, it's not surprising that the data are riddled with problems.

Jenkins argues that GI becomes most important in people who suffer a metabolic disorder. He says that much of the controversy surrounding GI is rooted in the fact that many of the studies were done in healthy individuals who probably can weather the ups and downs of diet better than people with some sort of disorder. For better assessments of the impact of GI, "don't try looking at healthy people. You'll find it very difficult, because nothing makes much of a difference. They've already got very good insulin and glucose tolerance. There's not much room to change," says Jenkins. "The worse shape you're in, the more you're going to magnify the effects" of changing your diet.

Perhaps that is why the Canadian Diabetes Association concluded in its 2013 Clinical Practice Guidelines, "Meta-analyses of controlled feeding trials of interventions replacing high-GI (carbohydrates) with low-GI (carbohydrates) in mixed meals have shown clinically significant improvements in glycemic control over 2 weeks to 6 months in people with Type 1 or Type 2 diabetes … This dietary strategy also leads to improvements in cardiovascular risk factors" (2).

OTHER ISSUES

GI doesn't capture the interactions of other foods, the critics object. "You never consume foods by themselves," Slavin notes. "If you eat a piece of bread, you probably have butter or peanut butter on it. The GI is much lower because you've put fat on it." Fat is thought to slow down the breakdown of foods and the release of glucose.

EXCERPT FROM THE 2010 US DIETARY GUIDELINES

"Strong and consistent evidence shows that glycemic index and/or glycemic load are not associated with body weight and do not lead to greater weight loss or better weight maintenance. Abundant, strong epidemiological evidence demonstrates that there is no association between glycemic index or load and cancer. A moderate body of inconsistent evidence supports a relationship between high glycemic index and Type 2 diabetes. Strong, convincing evidence shows little association between glycemic load and Type 2 diabetes. Due to limited evidence, no conclusion can be drawn to assess the relationship between either glycemic index or load and cardiovascular disease."

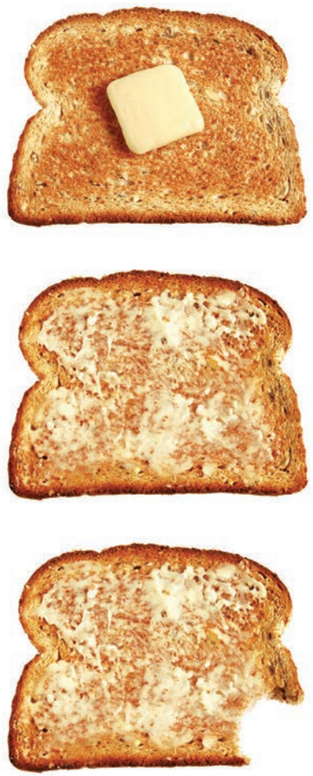
Source: http://1.usa.gov/1gnFLVa

The glycemic index's supporters counter this notion. "They will say when you add butter to bread, you change its glycemic index. You don't," counters Wolever. "Bread is bread! Its GI hasn't been changed. The glycemic impact of the meal has been changed."

Because the index is simply a measure of blood-glucose levels in response to a known amount of carbohydrate, everything else, such as protein and fat, is not considered. For this reason, critics say a pizza can have a low-GI crust but then have salty and fatty ingredients, such as pepperoni and cheese, as toppings, which won't count toward the index.

The fact that unhealthy foods can appear with low GI values is a big concern, say the critics. The example repeatedly brought up is fructose, found in many processed foods. Upon ingestion, fructose goes to the liver and enters the glycolytic pathway. "It elicits a low glycemic response, and hence it has a low GI value," says Aziz. Because of that, a can of soda, which contains fructose and glucose, can have a lower GI value than a baked potato, which is mostly starch that gets broken into glucose.

The subject of junk food exasperates Wolever. "We're not talking about chocolates! That's not the point," he says. "Let's look at our staple carbohy-



drates, the things we're supposed to be getting 45 (percent) to 60 percent of our energy from, and which one of those are the ones with a low GI. Those are ones that we should be focusing on."

But the detractors counter that that doesn't help the public seeking a label to help them decide what to eat. Slavin says the glycemic index makes it hard to send a one-size-fits-all message. Its message is more nuanced – that certain carbohydrates with particular glycemic index values should be chosen over others.

Brand-Miller disagrees that the message is complicated. "My message is simpler than you think. People don't have to remember a whole lot of numbers. There's a need for food labeling," she says. "Just exchange a high-glycemic-index bread for a low-glycemic-index bread, and the same thing for breakfast cereal and rice. Try to have more of the lowest-glycemic-index foods, like legumes, pasta and dairy."

DECLARED CONFLICTS OF INTEREST AND FINANCIAL GAINS

- Jennie Brand-Miller is president of a non-profit glycemic-index-based food-endorsement program called the Glycemic Index Foundation and the director of the University of Sydney's GI testing service, SUGiRS. She is a co-author of "The Glucose Revolution" and "The New Glucose Revolution" book series (Marlowe and Co., New York) and "The Low GI Diet" book series (Hachette Australia).
- Thomas Wolever is the president, the medical director and a scientist at Glycemic Index Laboratories Inc., a contract research organization. He is also president and an owner of Glycaemic Index Testing Inc., which provides services to GI Labs. He receives royalties as co-author of a number of books on GI under the general title of "The Glucose Revolution" and consulting fees from Tamasek Polytechnic for advice related to GI research. In the past three years, he has consulted for McCain Foods Inc. and Bunge.
- David Jenkins consults with and has accepted funding from numerous food companies and organizations, such as Barilla, Kellogg's, Quaker Oats, Coca-Cola, The California Strawberry Commission and Agrifoods and Agriculture, Canada. His wife, Alexandra Jenkins, is director and partner with Wolever at the Glycemic Index Laboratories, which tests foods that Jenkins uses in his studies
- William Whelan has accepted funding for his GI research from the Agatson Foundation, established by Arthur Agatson, who developed the low-carbohydrate South Beach Diet. He also has co-authored a paper on GI with Agatson (*IUBMB Life* **62**, 637 – 641(2010)).
- Alfred Aziz, Joanne Slavin and Allen Taylor declared no conflicts of interest.

HEALTH BENEFITS?

Despite doubts about the usefulness of the GI on food labels, experts say the index is useful to explore how diet affects health outcomes in a research setting. For example, Allen Taylor at Tufts University is interested in the link between a high-glycemic-index diet and glycation of proteins. Sugars can react with proteins through the Maillard reaction to produce advanced glycation end products, which "accumulate with accelerating rates with age," explains Taylor. The implication is that these accumulated glycated end products jam up the proteolytic machinery.

"If you feed animals high-glycemic-index diets, sure enough, they accumulate these glycation products throughout their whole bodies, even though they are not diabetic," says Taylor. These glycated products are thought to be cytotoxic, and because they are produced indiscriminately throughout the body, they have effects away from the central metabolic pathways in the gut and liver. Taylor says his group has collected similar data from human studies: People who consume high-glycemic diets develop cataracts, age-related macular degeneration, diabetes and cardiovascular disease at higher rates than normal. "There are seemingly systemic effects of the stress that's caused by diets that deliver sugar rapidly," Taylor says.

Brand-Miller explains the mechanism for Type 2 diabetes. "Beta cells are the most sensitive cells in the body from the point of view of detecting glucose." She adds that the mitochondria "are producing lots of NADH and free radicals when the glucose load is very high. It overwhelms the capacity of the beta cells to quench the oxidative stress."

But more studies, on larger scales, have to be done. According to the 2010 U.S. dietary guidelines, "A moderate body of inconsistent evidence supports a relationship between high glycemic index and Type 2 diabetes … Due to limited evidence, no conclusion can be drawn to assess the relationship between either glycemic index or load and cardiovascular disease."

IMPROVING THE INDEX

Wolever, Brand-Miller and Jenkins say that the arguments that have dogged GI for the past 30 years need to be laid to rest so that the field can move forward. In their view, the criticisms are old and have been refuted by their research. The most important thing now, Wolever says, is making the measurement and application of GI consistent to avoid further obfuscation.

Experts agree that any measure that helps people make better dietary choices is a good one to have. "We acknowledge that carbohydrate-rich foods that result in a lower blood-glucose response or can mitigate the glycemic response after a meal would be beneficial in general," Aziz says. For this reason, he says, Health Canada is developing a guidance document that sets out the criteria for establishing a health claim that the consumption of a food leads to a reduced glycemic response.

The critics agree with Health Canada's assessment. "Everybody wants a measure of carbohydrate quality. I get that," says Slavin. "The glycemic index appears like a good measure." But the problem is that GI doesn't distinguish between healthful and junk foods. As Slavin sums it up, "The glycemic index doesn't really drive the foods we want people to consume more."

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Meet Alex Toker

A new associate editor for the Journal of Biological Chemistry

BY RAJENDRANI MUKHOPADHYAY

Alex Toker at the Beth Israel Deaconess Medical Center and Harvard Medical School in January joined the ranks of the associate editors at the Journal of Biological Chemistry. Toker is a former chairman of ASBMB Today's advisory board. His laboratory focuses on the cellular and molecular mechanisms of cancer progression. The interview has been edited for length and clarity.

Would you briefly explain what your research group is studying?

The work in our lab focuses largely on the cell and molecular biology of cancer progression, particularly breast and prostate cancer. For many years, we have been working on the phosphoinositide 3-kinase and Akt kinase signaling pathway and the mechanisms by which this signaling cascade promotes phenotypes associated with malignancy. We use a variety of approaches to study PI 3-K/Akt pathophysiology in cancer, from basic biochemistry and cell biology to developing and using mouse models of cancer. We are focusing on evaluating how the many genetic lesions that exist in the PI 3-K/Akt signaling pathway mediate cancer progression. We also evaluate new drugs that are being developed to target these enzymes for therapeutic benefit. Being a faculty member in a pathology department at a medical center also allows me to interact with clinical scientists and translate the findings from our discovery-based approaches to human pathophysiology.

Tell us about your academic background and research training.

During my childhood, we moved around a lot in mainland Europe, so I went to many different schools. But we finally settled in London, where I went to university and received a bachelor's degree in biology from Kings College. Immediately thereafter, I embarked on a Ph.D. at the National Institute for Medical Research in Mill Hill (London), where I worked on 14-3-3 proteins, which were relatively obscure and out of the limelight at the time. After my Ph.D., I did what many postgraduates were encouraged to do at the time and sought a postdoc in the U.S.A. I settled on the laboratory of Lewis Cantley, who in 1991 was at Tufts University School of Medicine. But a year after joining the lab, we moved to Harvard Medical School and the Beth Israel Deaconess Medical Center.

I spent six very formative years in the Cantley lab, and it was during this time that my passion for basic research solidified. I joined the lab in the early 1990s, a few years after Dr. Cantley and his graduate student Malcolm Whitman had discovered PI 3-K. At this time, the enzyme was considered relatively obscure and perhaps an oddity in biology. But it was an extraordinary stroke of luck that I was able to do my postdoc in this lab and contribute in some way to discoveries of PI 3-K signaling. Today we know that PI 3-K represents one of the most frequently deregulated pathways in all human cancers and holds significant promise for targeted therapy. My own contribution was to identify the Akt kinase, one of the best-understood effectors of PI 3-K. Akt kinase transduces the signal by binding with high affinity to the PI 3-K lipids PtdIns-3,4-P2 and PtdIns-3,4,5-P3. The Science paper in which this work was published allowed me to move on and begin to establish my own independent laboratory, first at the Boston Biomedical Research Institute. In 2000, I was recruited back to the BIDMC in the department of pathology.

Did anything occur, in a milestone sort of way, that made you choose science as a career?

There was never a particularly strong scientific background in my family, but I do recall that back in the mid-1970s, when we had just moved to London, we lived very close to the Natural History Museum in Kensington. I vividly remember spending entire weekends there, usually by myself, exploring the many halls of dinosaur fossils, insects, meteorites and the whale room. I think it is fair to say that is where my interest in science started.

During grad school or postdoc, did something especially influence you to choose the path you've blazed in research?

My most formative years were as a postdoctoral fellow in Lew Cantley's lab, and I learned an enormous amount about science and interacted with other colleagues. It was a scientifically exciting time, where I also learned the importance of establishing and working in an environment that is serious and fun at the same time. I also was impressed by a concept that I had never really fully appreciated but that was evident in the Cantley lab: The most profound and impactful scientific discoveries often are made serendipitously or because an error or control revealed something unexpected. Also, the freedom to pursue one's scientific curiosity is something that I appreciated very early on and would have a very hard time giving up now.

What does it mean to you, on a personal level, to be an associate editor for the JBC? What was your reaction when you were asked to be an associate editor?

I was extremely honored to be asked to join the board as an associate editor. I recall my first paper as a postdoctoral fellow at Harvard was a JBC paper, which I was very proud of. The journal has a long history of being at the forefront of biochemistry, and many seminal discoveries in the 20th century were published in the JBC. It was very humbling to be asked. When (Editor-in-Chief) Marty Fedor wrote me with the invitation, I was delighted but also a bit concerned about what commitment it would entail. After a chat on the phone, she swiftly laid my concerns to rest, and I said yes on the spot.

How is the new role going so far? Have you been surprised by anything during your tenure with JBC?

It is going very well indeed. My concerns about an enormous workload have not really materialized, and

I do find the number of manuscripts that I deal with to be quite interesting because of the broad range of subjects. Sometimes I will get a manuscript that is so outside my comfort zone that I am a bit worried. But the great thing about the board is its wide-ranging expertise and insight. I know I always will find just the right editors to review a paper. It certainly has presented a steep learning curve, but I now feel quite comfortable with the expectations placed on associate editors and would like to think I provide a fair and balanced assessment of papers.

What do you do outside of the lab? Hobbies? Do you have any advice for balancing life in the lab with life outside of the lab?

With three children, one of them 3 years old, and work, there is really little time or energy for many other activities. I do enjoy cooking and try to prepare something new or different whenever I can. I do think it is important to have at least one or two activities outside of the lab and science, whether those activities focus on family, sports or hobbies. My hobby, outside of spending as much time as possible with my kids, is music. I go to many live music shows in the Boston area, which, being a college town, is great with many venues. For the past 10 years, I also have been going to the Coachella Music and Arts Festival in the California desert in April, which allows me to escape from reality for a few days!

For scientists in training, do you have any words of wisdom or a motto?

Take risks. The period of training is designed for just that – to take risks with your projects and do what is exciting, not mundane or safe. Choose an environment where that attitude is encouraged and not frowned upon. As for words of wisdom, there is a quote that I remind my lab of quite frequently, much to their chagrin. It's from Earl Stadtman, one of the great biochemists of the 20th century, who famously said to his own trainees that "progress in science is directly proportional to the number of experiments you do."

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With funding becoming scarce, scientists are looking to the public for help

Crowdfunding is one way to finance projects and increase public awareness of research

BY MARK STEWART

Faced with having to lay off lab members and yet still having to make progress on research projects, in spring 2013 Michael Pirrung, a professor of chemistry at the University of California-Riverside, was in search for money and fast.

He began searching for untraditional sources of funding so that he could have his anticancer drug synthesized and sent to the National Cancer Institute for tests. Sadly, Pirrung's situation is becoming commonplace among scientists in light of continual flat funding at the National Institutes of Health and deeper cuts due to the Budget Control Act of 2011. Scientists are losing jobs in record numbers, and some are considering careers in other countries (1).

But some researchers, including Pirrung, refuse to leave any stone unturned when it comes to finding money for their research projects and labs. While these scientists have not hit the streets asking for money just yet, they are doing it in the digital world: They're turning to crowdfunding.

CROWDFUNDING 101

Crowdfunding, which solicits funds from the public for projects, is not new. It was even used in 1885 to raise money to build the pedestal that the Statue of Liberty stands on today. More recently, it has been used primarily in the arts – to fund musical work, smartphone apps or even movies.

It is now taking off in the sciences. The process begins with a researcher posting a project on a crowdfunding website (Table 1). Each project includes a description, an explanation of its importance, a video, updates on progress and comments from project donors. Researchers also provide a budget and set a funding goal.

Each website has different constraints for the funding timeline and how the money is dispersed to the researcher. Some crowdfunding sites require that the funding goal be met or surpassed (the all-or-none funding model) to receive the money.

SUCCESS WITH CROWDFUNDING

Already there have been dozens of projects successfully funded by the crowd. These projects include developing new imaging techniques for surgeons, studying the impact of gun-control laws, and studying pollution in waterways.

Elizabeth Iorns, co-founder and chief executive officer of Science Exchange, funded a project aimed at preventing the transmission of a BRCA mutation,

a gene that can increase the likelihood of breast cancer.

Iorns chose this funding mechanism because she had left academia to start her company and thought she had little chance of obtaining funding through a traditional grant application. But professors at universities also use this type of funding. During Pirrung's search for funding to synthesize a kidney-cancer drug, he used crowdfunding to start the project. Without crowdfunding, it is likely both projects would not have been initiated.

GETTING THE WORD OUT

Crowdfunding sounds simple, right? Well, not so fast! There are several things that researchers should be aware of when using crowdfunding sites.

Pirrung says he "initially thought the website would bring thousands of eyes" to his project and that "everyone would donate a dollar or $5." This proved not to be the case.

Public outreach is a necessity for a project to be funded successfully through crowdfunding sites. It isn't necessarily about the project details; it's the project's ability to garner the public's attention that leads to its success. Both Iorns and Pirrung appealed to cancer groups to help gather funds for their projects.

Attracting various patient advocacy groups provides an immediate crowd in which to pitch your research ideas. "It is a lot of work," says Iorns, who primarily used social media outlets. Pirrung took another route and searched for an influential science blogger to write about his project and post a link to the project website.

Most crowdfunding sites coach users on how to create an interesting project summary and how to reach out to the public. Clearly, scientists who are present in their local communities and online are more likely to be successful than those who have little interaction with the public or lack online presences. Tips for increasing your Internet presence were presented in the August issue of ASBMB Today (2).

CROWDFUNDING PROVIDES A PODIUM

By pitching ideas for crowdfunding, scientists are able to interact with the public. Public donors will have personal investments in these projects, and they will learn what exactly is happening in the labs. Researchers are encouraged and sometimes required to keep donors updated on their progress. This allows donors to obtain knowledge and may help provide a new outlook on the science enterprise. Scientists often leave the public out, though it is public money that helps fund federal grants.

Senior researchers are not the only ones using crowdfunding to help start projects. A number of projects have been initiated by undergraduate and doctoral students and postdoctoral scientists. Doctoral students often have few sources of funding available to them for their projects, but crowdfunding offers a unique opportunity for them to pitch their ideas. Posting projects online teaches students early on how to market their science, and it allows them to build a relationship with the public that can be carried on to their future research positions.

Crowdfunding also advertises the university or research center. This helps institutions engage their local communities, alumni and potential donors.

CONCERNS WITH CROWDFUNDING

There are some concerns that users of crowdfunding should be aware of before pursuing this type of funding.

Most crowdfunding sites lack formal review committees. As this type of funding mechanism rises in popularity, there is a growing concern over how to maintain the legitimacy of projects and keep the public trust. New crowdfunding sites are popping up frequently, and some are beginning initiatives to ward off these concerns.

Larry Lawal, founder and chief executive officer of HealthFundit, started his company with the goal of initiating collaborations with universities to help address legitimacy concerns and issues with the transfer of funds to universities. Lawal believes "crowdfunding can serve as a powerful tool to enable bold research that may otherwise not be possible; however, it's important for investigators to not compromise on scientific review." Overall, because these projects are posted online, the community has the ability to self-police the projects presented on the sites, providing a crowdsourced peer-review process.

The transfer of money from the crowdfunding website to the university has led to some institutional bureaucratic issues. Because people donate the money for the research project, most universities look at it as a gift, so researchers are not required to provide a percentage for indirect costs (money used for building maintenance, electricity or lab space).

In addition, these sites do take a percentage of the money raised for their overhead before giving the money to the university. Some universities object to such a fee. Most universities require that the total amount of money raised be given to the university first, and then site administrators can be reimbursed. Researchers should look into their own institutions' policies before using a crowdfunding site.

Additionally, most projects set their funding targets at anywhere between $1,000 and $20,000. It is clear that crowdfunding does not replace large federal or private foundation grants. Pirrung states, "It is a lot of work for not a lot of money."

Most of the successful projects have clear short-term goals that are easy to convey to the public. Alternatively, some researchers use crowdfunding sites to begin high-risk, high-reward projects that may help them develop successful grants for federal agencies. However, this may lead some to fear that their projects may be stolen by competitors.

Careers in academia are built on obtaining successful projects, funds and papers. Therefore, it is vital that researchers maintain a balance between the information they share with the public and the information they keep to themselves before they publish and submit grants. This is a concern that researchers must face on a case-by-case basis. Another fear is journals turning down manuscripts because data were posted on these sites. In addition, there are concerns about how these online websites will affect intellectual property rights and copyrights that some researchers pursue for specific compounds or techniques created in the lab. All these issues require individuals to speak with officials within their universities or outside their universities to learn how best to limit these side effects.

CONCLUDING REMARKS

Crowdfunding is an exciting new area of opportunity for researchers, but, as noted, there are concerns still to be addressed as this funding mechanism matures. Crowdfunding is a great way to garner public attention in research and build a fan base that researchers can use for future projects.

By the way, Pirrung's story does have a happy ending. His kidney-cancer drug was successfully synthesized and sent to the NCI for comprehensive tests. In addition, he secured more funding to continue his work on developing anticancer drugs and avoid laying off lab members. Pirrung says that it was "crucial to have the crowdfunding work as a bridge" until other funds could be secured.

TABLE 1: CURRENT CROWDFUNDING SITES AVAILABLE TO RESEARCHERS

COMPANY	FUNDING MODEL	WEBSITE
Geekfunder	All-or-nothing	www.geekfunder.com
Kickstarter	All-or-nothing	www.kickstarter.com
Microryza	All-or-nothing	www.microryza.com
Petridish	All-or-nothing	www.petridish.org
Rockethub	Keep-it-all	www.rockethub.com
Superior Ideas	Keep-it-all	www.superiorideas.org

Keep-it-all models allow researchers to keep all of the money donated regardless of whether the goal is met at the end of the timeframe. All-or-nothing models require researchers to reach or surpass their funding goals to obtain the funds.

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MCP MOLECULAR & CELLULAR PROTEOMICS

Fishing out the details of how tilapia tolerate salt

BY RAJENDRANI MUKHOPADHYAY

Tilapia are interesting critters: The fish can change the workings of their gills based on the saltiness of the water they are in. In a recent Molecular & Cellular Proteomics paper, researchers looked into the molecular details of how tilapia change protein expression in their gills to accommodate different concentrations of salt.

There are four species of tilapia, which belong to the large family of cichlids, and they all easily mate with one another. The hybrids are grown in fish farms around the world. "These fish have a large economic value as a source of protein and other nutrients," explains Dietmar Kültz at the University of California, Davis, who was the first author on the MCP paper.

Kültz says the tilapia's ability to adapt easily to the environment has made them an invasive species. They've left their native Africa and are swarming into places in North America, such as Florida and Hawaii.

He also points out that projected effects of climate change include rises in sea levels and more frequent droughts. "Knowing the molecular basis of tilapia's high environmental stress tolerance will offer insight into potential strategies for managing their aquaculture performance and invasiveness," says Kültz. "In addition, such research reveals the mechanisms that equip fish with an extreme capacity for tolerating salinity stress. Those mechanisms will likely be under great selection pressure in many species of fish exposed to future climate changes."

Kültz and colleagues used proteomic methods to analyze many of the proteins in the gills of the fish, the organs that take up water to extract oxygen from it. First, the researchers looked at proteins known to be involved in handling salinity. They found that the expression of mitochondrial proteins, molecular chaperones and ion transport proteins was increased as salt concentrations increased.

Next, the investigators looked for novel proteins involved in salinity processing. They discovered a protein, called NDRG1, whose expression decreased with increasing salinity. This protein never has been implicated in gill reconstruction, although it is known to be involved in cell proliferation and differentiation. The investigators suspect that NDRG1 stalls cell growth: When salinity increases and the fish need more cells in their gills to handle all the salt ions, they turn down levels of NDRG1.

Kültz explains the investigators are now interested in the mechanisms by which the protein expression levels are altered by salinity and how other organs in the fish cooperate with the gills to increase the fish's tolerance to rising amounts of salt.

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JLR THE JOURNAL OF LIPID RESEARCH

New thematic review series begins: 'Living History of Lipids'

BY MARY L. CHANG

The November issue of the Journal of Lipid Research marks the start of a special thematic review series titled "Living History of Lipids." As the title of the series suggests, this set of thematic reviews will explore what is known about lipids, but it will do so in the unique context of recognizing the forward-thinking pioneers whose hard work, determination and, in many cases, accidental yet astonishing experimental discoveries have led to the knowledge of the field as we know it today. The series is being coordinated by JLR Associate Editor Al Merrill of the Georgia Institute of Technology.

The first installment, penned by Daniel Steinberg of the University of California, San Diego, a former editor-in-chief of JLR, celebrates the 100th anniversary of the lipid hypothesis of atherosclerosis. In 1913, a young Russian doctor named Nikolai N. Anitschkov observed that feeding rabbits a high-cholesterol diet caused arterial lesions that looked remarkably similar to those seen in human atherosclerosis. This finding flew in the face of the medical literature up to that time, which described atherosclerosis as an untreatable condition and an unavoidable consequence of aging.

Two subsequent decades of tireless research of rabbit atherosclerosis by Anitschkov and his team resulted in the publication of a comprehensive review of their investigations, which included the identification of foam cells and the observance of cholesterol accumulation, white blood cell recruitment and the conversion of fatty streaks to fibrous plaques. Anitschkov and his group also observed that the severity of arterial lesions is proportional to an increase in blood cholesterol levels; that distribution of the lesions is predictable, most commonly and severely at arterial branch points; and that lesions are, at some level, reversible.

In his review of Anitschkov's lipid hypothesis of atherosclerosis, Steinberg concludes with much admiration that, despite all the technological advances and detractors over the past 100 years, Anitschkov's hypothesis has required little amendment and has stood the test of time.

Mary L. Chang (mchang@asbmb.org) is publications manager for the Journal of Lipid Research and Molecular & Cellular Proteomics.

Thematic series on fat-soluble vitamins continues: vitamin E

BY PREETHI CHANDER

"Dietary factor X (is) indispensable for the production of healthy young." That is how Herbert McLean Evans and Katharine Scott Bishop described vitamin E in their 1922 paper in the journal Science reporting their discovery of the essential nutrient.

Vitamin E is the common name that refers to a group of eight vitamers that include four tocopherols* and four tocorienols. Vitamin E deficiency causes cholestatic liver disease in children, neurological abnormalities and impaired immune response. Due to its strong antioxidant function, this fat-soluble vitamin is used as a supplement to decrease the risk of heart disease.

Continuing the Journal of Lipid Research's thematic series on fat-soluble vitamins, the September issue addresses vitamin E with two reviews covering current research on this topic. In his introduction to this series, editorial board member William S. Blaner describes vitamin E as "the enigmatic one," because we still do not know specific pathways or molecular targets of vitamin E that help explain its role as an essential nutrient.

Of the eight forms of vitamin E, the human body preferentially uses only the alpha-tocopherol form. The liver plays a major role in the control of uptake and circulation of vitamin E into the plasma. The review by Maret G. Traber of the Linus Pauling Institute at Oregon State University describes regulatory mechanisms that prevent vitamin E buildup through the interplay of two separate hepatic systems – the alpha-tocopherol uptake and secretion into the plasma and the cytochrome P450 oxidation systems – that degrade the nontocopherol forms.

The second review, by Moshe Vardi, Nina S. Levy and Andrew P. Levy of the Technion-Israel Institute of Technology, addresses the controversy regarding the cardioprotective effects of vitamin E. After reviewing various vitamin E intervention studies and their clinical outcomes related to cardiovascular morbidity and mortality, the authors con-

A discussion about Vitamin E

"The enigmatic one" is how William Blaner at Columbia University described vitamin E in an editorial he wrote for the Journal of Lipid Research. To learn more about this mysterious molecule, we invited Blaner and Maret Traber at Oregon State University to join the ASBMB Journal Club for an exciting discussion about the latest research into vitamin E. **Watch a video of the chat at http://bit.ly/1cae56Y.**

clude that "the answer appears to be a resounding no when one provides vitamin E indiscriminately to unselected populations."

Using a pharmacogenomics approach, Vardi et al. identified a subgroup for which vitamin E is highly cardioprotective: those individuals who are either on hemodialysis or are diabetic and carry a haptaglobin genotype, Hp 2-2. The article emphasizes the importance of proper patient selection to observe vitamin-E-based protection against the development of cardiovascular disease.

** "Tocos" in Greek means "childbirth," "ferein" means "bring forth," and "-ol" represents the presence of an OH group.*

Preethi Chander (chander.preethi@gmail.com) earned a Ph.D. in structural biology from Purdue University and completed a postdoctoral fellowship at the National Institutes of Health.

FoxO3 and Sirt6 play an important role in regulating SREBP-2 and cholesterol homeostasis

BY KYEORDA KEMP

Cholesterol is an essential component of the cell membrane and serves as a precursor for the biosynthesis of a number of molecules found in eukaryotes, such as sterol hormones, bile acid and vitamin D. While cholesterol is crucial for eukaryotes to function, hypercholesterolemia, or abnormally high cholesterol levels, is strongly associated with heart attack, stroke and peripheral vascular disease. Therefore, cholesterol levels must be maintained and regulated carefully.

Because of cholesterol's importance in cell structure and function and its role in numerous biological pathways, understanding how host systems regulate cholesterol synthesis is a major focus of research. An important regulator for cholesterol biosynthesis is sterol regulatory element binding protein 2, or SREBP-2. Synthesis of cholesterol is controlled in a homeostatic manner and is linked to the levels of cholesterol present; SREBP-2 plays a crucial role in regulating this process. SREBP-2 functions as a transcription factor to control the expression of a number of genes involved in cholesterol biosynthesis, and until recently, the epigenetic regulation of this molecule gene was not understood.

In a recent article in the Journal of Lipid Research, a research team led by X. Charlie Dong at Indiana University School of Medicine reported that Sirt6 plays a critical role in the regulation of SREBP-2. Loss of Sirt6 results in elevated SREBP-2 and increased cholesterol levels, while overexpression of Sirt6 decreases SREBP-2 and cholesterol levels. Moreover, the researchers found that Sirt6 interacts with forkhead box O3 transcription factor 3, or FoxO3 (which has been linked to cholesterol synthesis in the liver) to modify the SREBP-2 gene locus and regulate the expression of the SREBP-2 gene. In addition, the authors found that overexpression of Sirt6 can improve hypercholesterolemia in mice.

According to the Centers for Disease Control and Prevention and the World Health Organization, heart disease is the leading cause of death in the United States, and cardiovascular diseases are the leading cause of death worldwide. The findings of this study not only improve our understanding of cholesterol homeostasis but may have a lasting impact on the fight against cardiovascular diseases.

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jbc THE JOURNAL OF BIOLOGICAL CHEMISTRY

Francisella tularensis: a biological weapon

BY KHYATI KAPOOR

The bacterium Francisella tularensis, which causes tularemia, is categorized as a class A bioterrorism agent, putting it among the likes of plague, smallpox and ebola.

Known in some parts of the world as rabbit fever, the bacterial infection can cause large die-offs of rabbits, hares and rodents. Francisella is transmitted to humans by arthropods, including ticks, and can enter the body through damaged skin, if infected animal carcasses are handled, or through inhalation, if those carcasses are mowed over, which explains why it also has been called lawnmower disease.

Upon infection, the bacterium lives as an intracellular pathogen and can survive in a multitude of cells, including macrophages, thus winning over the body's first and second lines of defense, resulting in a lethal infection.

This Gram-negative bacterium has four known subspecies, which have varying degrees of virulence in humans. Tularensis is the most virulent; holarctica can infect humans but rarely is fatal; novicida is usually nonlethal; and mediasiatica – well, it's still a bit of a mystery.

Recent papers in the Journal of Biological Chemistry and the journal Molecular & Cellular Proteomics report probable mechanisms by which Francisella leads to a lethal infection.

Writing in the JBC, Meenakshi Malik's group at Albany College of Pharmacy and Health Sciences reported how tularensis represses inflammasome during early stages, thus resulting in an infection. The team used naive macrophages for infection with a mutant of F. tularensis. This mutant bears a gene that encodes for OmpA-like protein, which is responsible for the repression of inflammasome activation, delaying the death of infected macrophages.

Although this OmpA-like protein checks early activation of inflammasome, the authors witnessed an increased activation after 24 hours. This increased activation might be happening via another independent pathway. The results reinforce that there is a lot to be learned about the mechanism of infection by this pathogen.

Meanwhile, a research team led by Fred Heffron at Oregon Health & Science University used F. novicida to manifest a tularemialike disease in animal models. The team reported in the MCP that it used isobaric tags for relative and absolute quantification to analyze alterations in the host cell phosphoproteome as Francisella invades. It takes just four hours for the bacterium to escape from the phagosome to the host cell cytoplasm. This infection in the host cell involves all three types of cytoskeleton filaments.

The entry of Francisella into the host cells triggers the signaling pathways, resulting in massive changes in the phosphoproteome of the host cell. Heffron's team pointed out that tristetrapolin, a component of mRNA degradation machinery, is inhibited due to hyper-phosphorylation, which affects the regulation of cytokine production, resulting in apoptosis of host cells.

The ability of Francisella to breach the defense mechanisms of the human body could be exploited in biological warfare. These two studies enhance our knowledge of the bacterium's mechanism of infection and might help to one day design drugs against this deadly organism.

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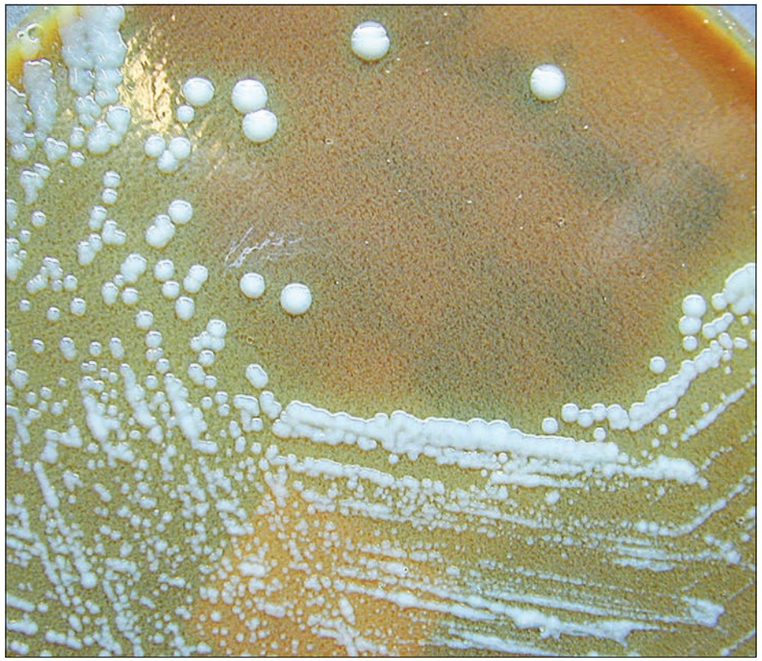


IMAGE CREDIT: CDC/LARRY STAUFFER, OREGON STATE PUBLIC HEALTH LABORATORY OF WIKIMEDIA COMMONS

Colonization of Francisella tularensis on cysteine heart agar after 72 hours.

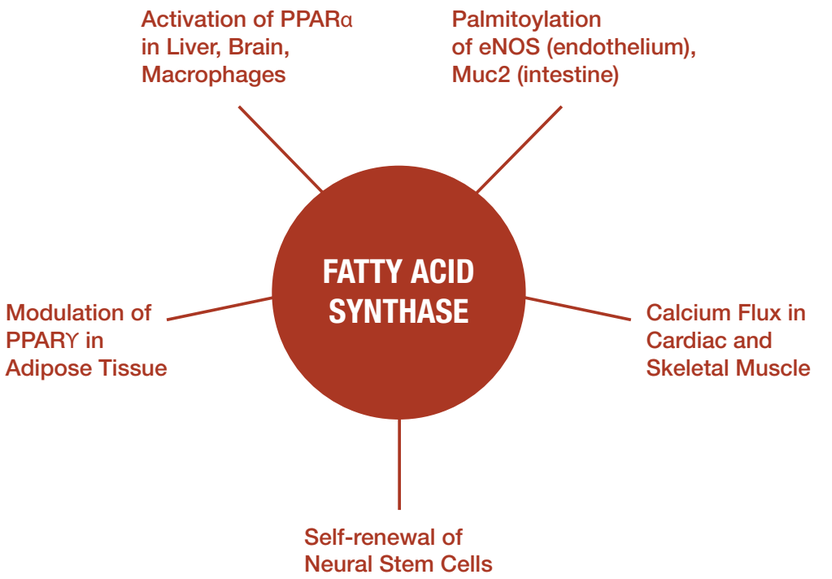
Fatty acid synthase and Galen of Pergamon

BY CLAY F. SEMENKOVICH

A considerable proportion of extant Greek texts are attributed to the physician-scientist Galen (AD 130 to ~210), likely because an army of amanuenses recorded everything he said. He is credited with the notion that disease is the consequence of discrete causes, so the biological pursuit of mechanism may have originated with Galen. His original contributions were substantial, dominating life sciences for 1,500 years, and he was a proponent of the role of lipid metabolism in pathophysiology. His study of the active properties of lipids perhaps began with his appointment as physician to the gladiators of the high priest of Asia when he treated injured muscle with a mixture of olive oil (oleate), beeswax (palmitate, palmitoleate, oleate) and rose petals.

Even before Galen, nature figured out that lipids are critical for biology. Mammalian fatty acid synthase, known as FAS, is a type I fatty acid synthase, indicating that all of the activities required to synthesize palmitate from simple precursors are present in a single multifunctional polypeptide. FAS is required for life, because conventional deletion of the fasn gene in mice is embryonically lethal (1). However, tissue-specific deletion of fasn has revealed an amazing spectrum of biological functions driven by de novo lipogenesis.

Mice with a deficiency of FAS in liver resemble mice with deficiency of the nuclear receptor PPARα (2). Both are prone to the development of fatty liver and hypoglycemia due to defects in fatty acid oxidation and gluconeogenesis. Treatment with chemical PPARα ligands corrects the phenotype in mice with hepatic FAS deficiency, implicating FAS in the generation of an endogenous ligand for PPARα. An FAS-dependent phosphatidylcholine species linked to the Kennedy pathway of phospholipid synthesis was identified as an endogenous PPARα ligand (3).



Mammalian fatty acid synthase (FAS), a multifunctional enzyme that synthesizes predominantly palmitate, has complex tissue-specific effects mediated by several molecular mechanisms.

Connecting FAS (induced by feeding) with PPARα (induced by fasting) initially seemed paradoxical, but recent evidence indicates that FAS is compartmentalized in liver, with different fractions subject to differential regulation of enzyme activity to promote PPARα activation with fasting (4). FAS-mediated activation of PPARα also occurs in the brain (5) and in macrophages (6). FAS affects the function of another nuclear receptor, PPARγ. Deficiency of FAS in adipose tissue decreases the association of certain

Galen of Pergamon

ether lipids (synthesized in peroxisomes) with PPARγ, resulting in protection from obesity through induction of cells resembling brown fat (7).

FAS influences other key processes. It is involved in preserving the integrity of structures that protect mammals from the environment. At the vascular endothelium (8) and at the intestinal epithelium (9), FAS appears to be the predominant source of fatty acids for palmitoylation of proteins (eNOS at the endothelium and Muc2 in the intestine) critical for maintaining barrier function. In neural tissues, FAS is required for stem-cell renewal (10). In cardiac (11) and skeletal (12) muscle, FAS regulates calcium flux, likely by modulating the phospholipid composition of the sarcoplasmic reticulum.

FAS generates palmitate, but exogenous palmitate does not rescue the phenotype induced by FAS deficiency (4, 11). Thus, Galen may have been correct in principle but not in detail. Lipids modulate numerous stress responses, but instead of exogenous fat, endogenous fat produced by FAS and channeled to specific compartments regulates integrative physiology relevant to disease.

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‘You hear the screech of rubber hitting the road’

BY MELODY KROLL

Host it, and they will come. That’s what the University of Missouri bet on when it hosted a regional career symposium focused on science outreach and communication in September.

More than 125 people registered for the one-day event, co-sponsored and co-organized by the American Society for Biochemistry and Molecular Biology, and more than 40 others were turned away due to space limitations. The vast majority of attendees were graduate students, but postdoctoral fellows, faculty members and science-communication professionals also were present. Attendees came from 19 institutions in 12 states, mostly from the Midwest but also New York, New Jersey and D.C.

“The fact that people came from so many places is really encouraging,” said ASBMB member Bruce McClure, a professor of biochemistry at MU who helped organize the symposium. “It really speaks to how much science outreach resonates as something students and postdocs want to embrace as part of their life. That’s exciting.”

That is certainly true for Denise Leonard, a postdoctoral fellow from Washington University in St. Louis who attended the symposium. “I love science outreach. I really enjoy talking to people about the science that I do and how they can become involved in science. I’m looking for career-development opportunities that will help me grow within the science outreach and communication area,” Leonard said.

From left: Hannah Alexander and two speakers, Monica Metzler, and Morgan Thompson.

Matt Windsor, a postdoctoral fellow from Vanderbilt University, attended for similar reasons. “I like communicating. I like trying to explain what I do,” said Windsor, who is particularly interested in public policy. “That’s what I hope to do with the rest of my career.”

The symposium

The science outreach and communication symposium was the idea of Hannah Alexander, adjunct professor of biological sciences at MU and a member of the ASBMB’s Public Outreach Committee.

When approached about organizing a regional ASBMB career symposium at MU, Alexander knew she wanted to do something different.

“Rather than doing a traditional how-to-get-an-academic/industry-job symposium, I wanted to focus on skills that all students and postdocs need to develop to be successful in any scientific career – namely, the ability to write and communicate science effectively, both professionally and to a lay audience,” Alexander said.

Alexander found wide support for her idea on campus. She secured funding and organizing manpower from several academic departments, including biochemistry, biological sciences, and physics and astronomy, as well as several campuswide programs, including MU’s Science Communication Network, the Chancellor’s Distinguished Visitors Program and Mizzou Advantage.

The symposium included sessions on communicating science to audiences from kindergarten through college, tips and tricks for effective science communication, and the role of science and outreach in different scientific careers. It also included a keynote talk by Karen Cone, program director for the National Science Foundation, who spoke about science communication and outreach as they relate to the NSF’s broader impacts requirement on grant applications.

Attendees also heard from individuals implementing outreach programs. Geoff Hunt, public outreach coordinator for the ASBMB and co-organizer of the symposium, shared information about the society’s outreach committee (1) and a forthcoming online science-communication course. Julie and Billy Hudson from Vanderbilt University gave a passionate talk about their outreach to rural communities through the Aspirnaut Initiative (2). The symposium also featured two of the winning teams of the NSF’s Graduate Education Challenge: Eric Hamilton and Melanie Bauer from Washington University in St. Louis and Elyse Aurbach and Katherine Prater from the University of Michigan.

The latter presentations were McClure’s favorites.

“In those talks, you hear the screech of rubber hitting the road,” said McClure. “Those students shared not only their experience with conceiving and executing projects but also the reality of doing it within the confines of their institutions. Giving them the opportunity to share that directly with other graduate students and postdocs is a job well done.”

The symposium also featured 18 posters showcasing the attendees’ innovative programs for science outreach at their own colleges and universities. All of the posters are available on the meeting’s website (3).

According to evaluations and informal feedback from attendees, learning about current programs and networking with others were the best aspects of the symposium. Many attendees said they would have liked to have had even more time for networking and sharing ideas and suggested that future symposia include informal networking sessions and hands-on workshops.

“People enjoyed and were excited by the realization that so many others share their enthusiasm for outreach and communication. That was clear from the registration and from the buzz at the breaks and poster sessions,” Alexander said.

Attendee Denise Leonard said she “absolutely loved” the event. “I don’t think I’ve laughed this much at a conference. It was just so great to interact with so many other graduate students as well as postdocs. It seems like there is such a big need for a bunch of us to get together and talk about our interests.”

A role for professional societies

Alexander said the symposium’s focus on science outreach and communication contributed to the regional turnout.

“The topic is very relevant to students and postdocs while they consider continuing careers. Yet it retained the traditional career-meeting aspect and thus attracted some people who were not interested in science outreach only,” Alexander said.

Eric Hamilton and Melanie Bauer, at the front of the room.

The ASBMB’s support also had a lot to do with it, McClure said. “Just having ASBMB in the name gave it some cachet.”

Providing training on science outreach and communication, Hunt said, is a service that professional societies like the ASBMB can do for their members in addition to publishing scientific journals and holding scientific meetings.

“People are really looking to professional societies for professional development and career-training opportunities. They want jobs, but they don’t know how to get them. That’s our role: to facilitate their professional development,” Hunt said. “Hopefully not too subtly, we were able to hit participants over the head with the idea that science outreach and communication underlies a lot of different career opportunities, whether or not they end up staying in the lab.”

As for Alexander, she hopes other universities will follow suit.

“We hope that our experience will encourage similar regional meetings in other parts of the country and that regional communication networks will continue to grow and interact with each other,” she said.

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Broadcasting scientists

Google's Hangouts on Air give public a seat at the table during scientific discussions

BY BUDDHINI SAMARASINGHE

Science outreach is an extremely important aspect of being a scientist. However, it is an aspect that often is overlooked because of the daily pressures of a scientific career. By not engaging with the public, we fail to fulfill our obligation as humanity's explorers and advisers, and we alienate the very people who fund us. This is the primary reason I engage in science outreach.

Television represents an enormously valuable means of reaching a wide public audience. Science documentaries such as the BBC's "Horizon" or PBS's "Nova" capture the public's imagination, but popularizing science on television requires a significant production effort. This typically is the domain of an established television network, something to which the average scientist does not have easy access.

The social network Google+, meanwhile, has a platform for video broadcasts known as Hangouts on Air (1). HOAs allow video, with up to 10 presenters, to be broadcast live on the Internet. After the event, the video is archived on YouTube. HOAs come with Q&A capabilities, so that the audience can submit questions that can be answered live. This represents a paradigm shift in science outreach and has great potential for reaching millions of people. HOAs are gaining in popularity. Organizations that have used the platform include NASA (2), the Hubble Space Telescope (3), CERN (4), National Geographic (5), Scientific American (6) and the SETI Institute (7), to name a handful. Even the White House is using HOAs (8) to have conversations with the public.

I have been involved in many HOAs, co-hosting them with a variety of scientists in diverse fields – paleontology, string theory, virology, parasitology and more.

My co-host, Scott Lewis, and I also have performed demonstrations of science, the most notable being one with an electron microscope: We were able to image various objects live during the Hangout (9). People across the world were looking at the compound eye of an insect live on air, learning about the techniques involved and being awed.

We've hosted panel discussions covering topics such as the recent controversy surrounding the ENCODE project (10). We used that opportunity to explain some basic molecular biology. Recently, Noah Diffenbaugh, a climate scientist at the University of Stanford, hosted an HOA to discuss his review paper published in Science (11). He explained its findings and took questions from viewers about the data. The Science on Google+ community (12) also has begun hosting Posterside HOAs (13), akin to conferences, during which scientists present their work in 10-minute talks and answer questions.

These example HOAs highlight the platform's potential for science outreach. Although science itself is respected, we scientists have an image problem. The public perceives us as faceless, ethically challenged logic machines. Through Google+ HOAs, we are brought into everyone's home. By being broadcasting scientists, we tear down the ivory tower.

If you have any questions about setting up your own HOA, please feel free to get in touch with me!

Buddhini Samarasinghe (buddhini@knowthecosmos.com) is a molecular biologist with experience in cancer research. She earned her Ph.D. at the University of Glasgow and recently completed a postdoctoral position at the University of Hawaii. She is the co-creator of the science communication website Know the Cosmos (www.knowthecosmos.com). Follow her on Twitter at www.twitter.com/DrHalfPintBuddy, Facebook at www.facebook.com/DrHalfPintBuddy or on Google+ at www.google.com/+BuddhiniSamarasinghe.

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8. http://goo.gl/jPmW5W
9. http://goo.gl/Gdeqcx
10. http://goo.gl/81PlPO
11. http://goo.gl/0TpdkE
12. http://goo.gl/Q1lK7z
13. http://goo.gl/DTtRpr

Assembling a toolkit for biochemistry and molecular biology educators

BY ANN WRIGHT, PAMELA S. MERTZ AND JOHN TANSEY

What is the best way to build a Web-based toolkit for undergraduate faculty members to share best practices, activities and assessments in biochemistry and molecular biology?

Members of the American Society for Biochemistry and Molecular Biology's Research Coordination Network steering committee led discussions to answer this question at two workshops during the Student-Centered Education in the Molecular Life Sciences symposium in August at Seattle University.

During the discussions, a BMB educator toolkit wish list was created. While we're still in the early stages of building the toolkit, here we'll touch on possible content, the submission process, information security, copyright concerns, the peer-review process and database functionalities. We hope to launch the toolkit in 2015.

What content should the toolkit contain?

The toolkit will serve as a central resource for undergraduate teachers of biochemistry and molecular biology. It will provide activities and resources to assist faculty members, especially new ones, with scholarship related to teaching and learning. Resources for new instructors, such as tips on writing syllabi and exams, will be included, as well as educational literature resources, such as those about visualization in science.

The content will be grounded in pedagogical research, and a peer-reviewed process will be implemented. An accepted submission will therefore be considered a peer-reviewed publication.

The content will be divided into the three categories:

1) core principles or foundational concepts in biochemistry and molecular biology;

2) foundational skills; and

3) foundational concepts from physics, chemistry and mathematics, or the allied fields.

Additionally, the website will have a keyword search, and resources will be organized by categories (classroom activity, assessment or others).

Which types of submissions are appropriate?

Guidelines for submission will be made available, and a review committee will be established. The committee will include ASBMB members with an understanding of educational research.

Each submission will be classroom tested, contain clear instructions, state the learning goals and objectives, give the time required for pedagogical material and identify Bloom's level.

Each submission will include the authors' contact info, keywords, the resource category, the level of the course where the material was used, the number of students in the course, students' prior knowledge, guidelines for student misconceptions, the amount of time necessary for completion (in class or out of class) and pre-activity preparation instructions. For laboratory experiments, a supply list and handouts also will be included.

If an assessment is submitted, the type of assessment must be stated, and if it's not a multiple-choice evaluation, a rubric must be provided.

Access and copyright

All published resources will be attributed to their respective authors.

We are considering providing a user-rating and comments feature and highlighting popular resources on the website. The latter would be analogous to the Protein Data Bank's Molecule of the Month.

In the interest of not reinventing the wheel, the following well-established websites will be used as models for the ASBMB online database:

- University at Buffalo's case studies website, sciencecases.lib.buffalo.edu/cs/
- The American Society for Microbiology's new Student Learning Assessments in Microbiology Database, www.microbelibrary.org/about/60

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Turning a failure into a success down the road

BY ELEFTHERIOS P. DIAMANDIS

The famous professional heavyweight boxer Rocky Marciano retired undefeated, scoring 49 wins, a still-standing record. But very few know that Rocky was knocked down twice in his professional career. In both cases, he got up and finally won the fights.

There are numerous other examples of startling comeback wins in almost all sports. Such turnarounds require courage, perseverance and a relentless fighting spirit. But this is not enough.

To succeed in the long term, you also need critical analysis of adversity, thinking and planning for the future.

The three post-failure phases

Every one of us has faced adversity in our professional and personal lives; defeats are part of the game, and turning defeats into wins is not easy. How many of us have failed exams, messed up interviews, been denied jobs or promotions? And how have we coped with such adversities?

An adverse event usually is associated with three phases.

In phase 1, which starts just after the failure, the usual reaction includes devastation, disappointment, denial and anger, sometimes in combination with blaming just about everybody else for what happened. Blaming others might involve saying the examiners were not reasonable or were biased, the questions were unfair or unexpected, and the like. In this phase, even various forms of discrimination may come to mind.

This initial phase is followed, around one to three days later, by the more thoughtful phase 2, in which the event is analyzed further either by the candidate alone or with the help of one or more close friends or family members. A most useful task during this period is to find out why the failure happened. Was it poor preparation, inexperience, stress or something else?

Once the root cause is identified, phase 3, the phase of planning to avoid another failure, is a lot more productive.

IMAGE CREDIT: I FRATELLI ANGELO E GIORGIO BONOMO OF WIKIMEDIA COMMONS

Rocky Marciano's dedication is memorialized with a U.S. stamp and a statue in Italy.

Things to keep in mind

Here are some simple tips that can help turn failures into successes:

1. Do not blame others for your failure. Usually, people are not out to get you.

2. Find out the root cause of the failure. The best people to provide feedback are your judges, and on many occasions, you are allowed to ask them for feedback. They may tell you that your knowledge was not enough or that your response to their questions was not effective. If you can't interact directly with your judges, find an experienced interviewer or reviewer who can listen to your story and provide feedback on the possible causes of your failure.

3. Remember that everybody gets another chance, either for the same opportunity, a related one, or something different. Do not feel that this failure is the end of the world, because it isn't. Just try to prepare better the next time and avoid the mistakes you made before.

4. Ask somebody, preferably somebody who succeeded in a similar scenario, to train you with mock examinations or interview questions. There are many fatal mistakes that can be made during an interview, and good preparation and practice can help you avoid them. For example, responding to a question with a statement like, "I am not sure about the answer, but here is one," will give the impression that you throw answers around to see if they stick. This is usually worse than saying, "I do not know, but I will look it up later."

5. Trust that the failure has given you valuable experience and that the next time, with early and better preparation, you will come a lot closer to success.

6. Keep a positive attitude about the future; do not allow the failure to demoralize you or cause you to question your abilities. Think of your previous successes and persist.

Imagine what would have happened to Rocky if he had not stood up and fought after those devastating knock-downs. He would not have made it into the history books, and nobody would remember him. The fact that he prevailed in those two fights made his career memorable. When you go to the next round of competition, think of Rocky and learn from his courage.

A football player recently was asked how he felt after losing a whole season to an injury, and he had a very positive attitude: "It is a small setback for a big comeback." The same can happen to you. Your next big comeback is just around the corner.

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- University of Delaware's problem-based learning site, www.udel.edu/inst/index.html.

What do you think?

The Seattle workshop participants were graduate students, undergraduate science faculty members and faculty members who are interested in improving undergraduate pedagogy. As this project moves forward, designing a useful and usable BMB education toolkit will depend on input from the ASBMB community.

What are your thoughts about and suggestions for building a BMB teaching toolkit? Email rcn@asbmb.org with your comments.

For more information about the ASBMB's role in developing concept-driven teaching strategies for biochemistry and molecular biology, visit www.asbmb.org/NSF/NSFHome.aspx.

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In case you missed it

In October, the journal Academic Medicine published a letter to the editor (1) by members of the American Society for Biochemistry and Molecular Biology's Education and Professional Development Committee. The letter is reprinted below with permission from the original publisher.

REFERENCE
1. Kennelly, P. *et al. Acad. Med.* **10**, 1405-1406 (2013).

DESPERATELY SEEKING FLEXNER: TIME TO REEMPHASIZE BASIC SCIENCE IN MEDICAL EDUCATION

BY PETER J. KENNELLY, JUDITH S. BOND, BETTIE SUE MASTERS, EDWARD A. DENNIS, CHARLES BRENNER AND DANIEL M. RABEN

The medical education community is currently engaged in an intensive review and revision of current models for physician training. New medical school curricula feature a substantially increased focus on communications, administrative, and teamwork skills designed to enable tomorrow's doctors to interact more effectively with patients and seamlessly collaborate within today's evolving care delivery structure.

These curriculum revisions are occurring as a new age dawns in medicine. Genomics, proteomics, and metabolomics will enable physicians to examine patients with a comprehensiveness unimagined by their forebears. Access to personalized data for each patient will yield more accurate diagnoses and the selection of optimized treatments. The ability to directly observe subtle perturbations in metabolism and gene expression will transform our capacity for the early detection and treatment of cancer, diabetes, atherosclerosis, hypertension, and Alzheimer's, among others.

To leverage these revolutionary developments, future physicians will require the type of firm grounding in basic sciences recommended by Flexner (1) in 1910. Paradoxically, recently many medical schools have substantially reduced basic science education. Although acceleration of the preclinical curriculum has the obvious benefit of giving students more time to develop clinical skills, we believe that this approach will have the unintended consequence of preventing the majority of future physicians from understanding the genomic, proteomic, and metabolomic data that patients can now obtain. In additional to training in clinical and interpersonal skills, we urge our colleagues to reemphasize basic science in the preclinical years. This will allow us to train individuals who will be able to practice molecular medicine and collaborate with basic research scientists to leverage new information and technologies to advance biomedical knowledge and practice.

REFERENCE
1. Flexner, A. "Medical Education in the United States and Canada: A Report to the Carnegie Foundation for the Advancement of Teaching." Bulletin No. 4. (1910).

2014

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ASBMB Topic Categories: #2000 - 2465

Travel Award Application Deadline: November 19, 2013

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