ASBMB today

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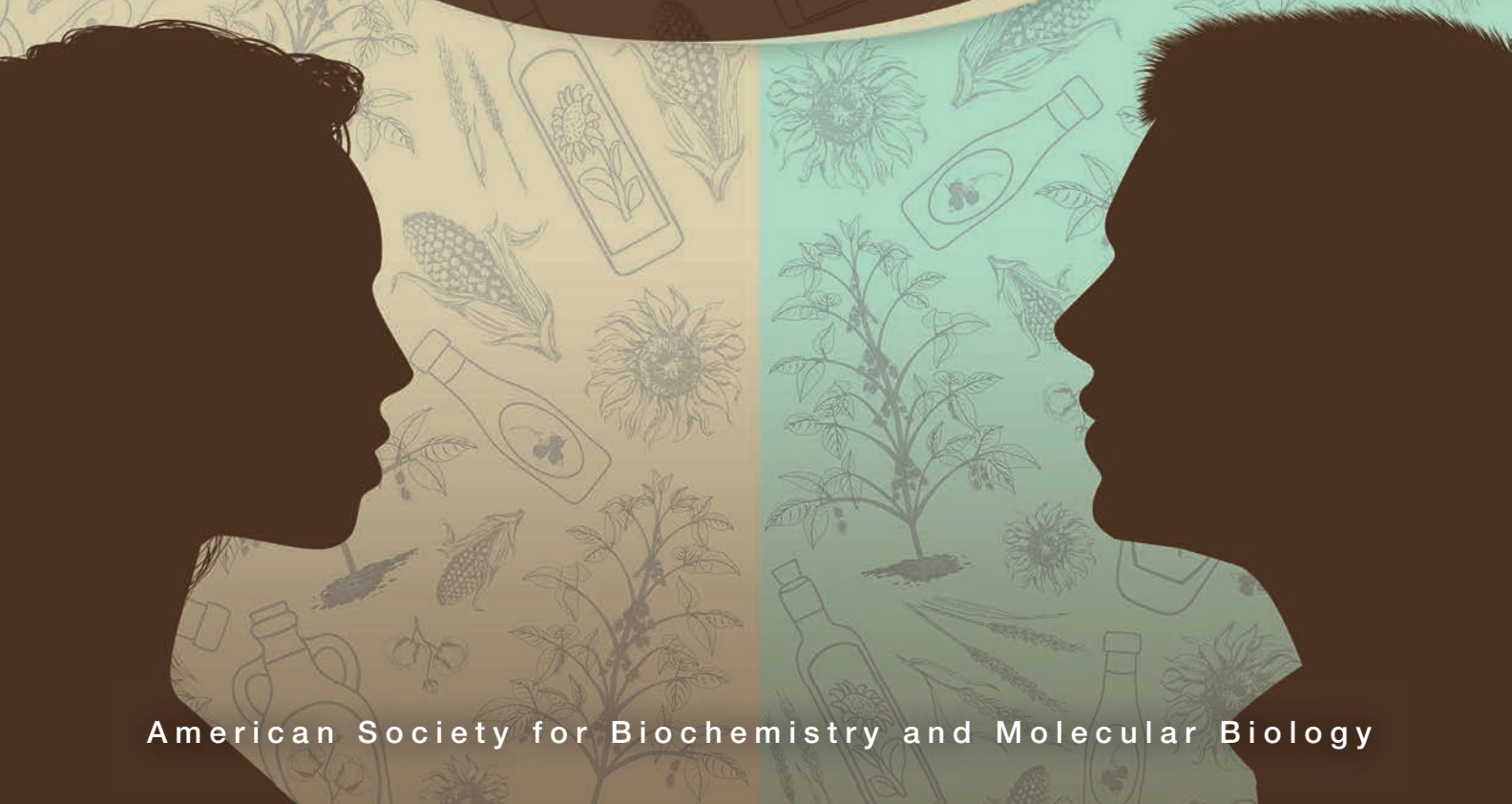
OMEGA-6 DEBATE



American Society for Biochemistry and Molecular Biology

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DECEMBER 2012

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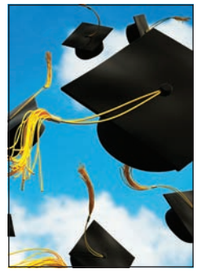

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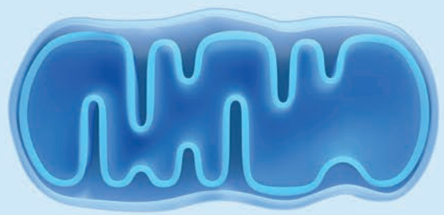
open channels

Which cellular organelle would get your vote?
Brad Graba, a biology teacher in Illinois, took advantage of the election-season hype and engaged his students on campus and on Twitter in a campaign that pitted organelles against organelles. See a selection of the some of the tweets from the activity on Page 32.



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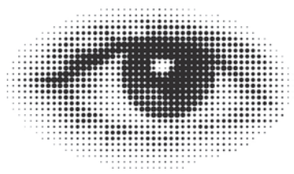
NINDS workshop produces recommendations for reporting animal studies

The National Institute of Neurological Disorders and Stroke has released a set of recommendations for scientific papers and grant applications describing preclinical animal studies. Published in the Oct. 11 issue of the journal Nature, the report recommended that all preclinical animal studies include details about research methodology, including randomization, blinding, sample-size estimation and data handling. Visit http://bit.ly/RGW1nk for more of this story.

Garfunkel, partners offer a $2 billion gold prize for blindness cure



Singer Art Garfunkel has teamed up with two of his former college buddies to put $2 million worth of gold bullion on the table for whoever can find a cure for blindness by 2020. The prize will be given to the person or persons "most responsible for ending blindness" by Dec. 13, 2020, according to the prize website. Garfunkel's partners in the endeavor are his former Columbia University roommates: Sanford "Sandy" Greenberg, an investor and chairman of the Wilmer Eye Institute's Board of Governors at Johns Hopkins University School of Medicine, who was blinded by glaucoma as a college junior, and Jerry I. Speyer, a real estate magnate and philanthropist in New York. Find out more at http://bit.ly/Tqa7v5

Milk offers possible defense against the deadly bioterrorism agent ricin

What if a glass of milk contained the antidote to one of the most deadly toxins known to man? Well, it turns out that this common household beverage, often recognized for its role in promoting strong bones, also may be a strong inhibitor of the highly toxic compound ricin. Read more about findings reported in the Journal of Biological Chemistry at http://bit.ly/Upa7lp.

president's *message*

The field of (Nobel) dreams

BY JEREMY BERG

Every year in the first week of October, when the Nobel Prize winners are announced, the world is much more focused on science than usual. This year, the fields of biochemistry and molecular biology were well represented in the awards. The Nobel Prize in chemistry was awarded to longtime American Society for Biochemistry and Molecuar Biology member Bob Lefkowitz and 2013 ASBMB Earl and Thressa Stadtman Distinguished Scientist awardee Brian Kobilka for "studies of G-protein-coupled receptors" (1, 2). These investigators integrated biochemical approaches to purify the receptors for key substances such as adrenaline, molecular biological techniques to clone cDNAs and genes that encode these receptors, and crystallographic methods to determine their three-dimensional structures. The Nobel Prize in physiology or medicine was awarded to Sir John Gurdon and Shinya Yamanaka "for the discovery that mature cells can be reprogrammed to become pluripotent" (3). Yamanaka was recognized for discovering that introducing four genes into differentiated cells through the use of molecular biological methods could induce the cells to dedifferentiate into pluripotent stem cell-like cells, while Gurdon used cell and developmental biological methods many years earlier.

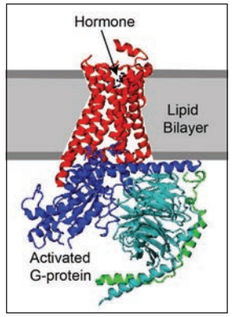
The Nobel Prizes were established in Alfred Nobel's will (4), where he wrote:

> *"The whole of my remaining realizable estate … shall constitute a fund, the interest on which shall be annually distributed in the form of prizes to those who, during the preceding year, shall have conferred the greatest benefit to mankind. The said interest shall be divided into five equal parts … one part to the person who shall have made the most important discovery or invention within the field of physics; one part to the person who shall have made the most important chemical discovery or improvement; one part to the person who shall have made the most important discovery within the domain of physiology or medicine; one part to the person who shall have produced in the field of literature the most outstanding work in an ideal direction; and one part to the person who shall have done the most or the best work for fraternity between nations, for the abolition or reduction of standing armies and for the holding and promotion of peace congresses."*

Of course, biochemistry and molecular biology were not mentioned, as biochemistry was just emerging as a field in 1895 and the concept of molecular biology was still more than half a century away. Nonetheless, biochemistry and molecular biology have been quite well represented in both the chemistry and physiology or medicine prizes over the years. By my count, 67 of the 104 chemistry prizes and 56 of the 103 physiology or medicine prizes have included major components of biochemistry or molecular biology.

The inclusion of biochemistry goes back to the beginning of the Nobel Prize program. In 1902, the second Nobel Prize in chemistry was awarded to Emil Fischer "in recognition of the extraordinary services he had rendered by his work on sugar and purine syntheses." Fischer was a chemist's chemist (recall, for example, Fischer projections from organic chemistry) (5), and he also proposed the lock-and-key model for enzyme specificity in addition to his syntheses of many important biochemicals, including glucose and caffeine. The first biochemical physiology or medicine prize was awarded to Albrecht Kossel in 1910 "in recognition of the contributions to our knowledge of cell chemistry through his work on proteins, including nucleic substances." Kossel discovered the nucleobases and made major contributions to understanding the chemical nature of proteins and their amino acid constituents (6).

Despite the long inclusion of biochemistry as a subject for recognition by the chemistry Nobel Prize, concerns are occasionally heard (including this year) regarding whether the science that is being recognized "is really chemistry." The initial question that Lefkowitz and Kobilka were addressing was certainly a medical and physiological one, namely, "What is the mechanism by which hormones such as adrenaline induce their biological effects?" Lefkowitz's laboratory (including Kobilka, then as a postdoctoral fellow) purified a receptor protein to homogeneity, determined its partial amino acid sequence, and used this sequence to clone the cDNA and the gene for the receptor. Analysis of the



complete deduced amino acid sequence revealed this protein to be homologous to the visual protein rhodopsin, with seven characteristic presumed transmembrane helical regions. These proteins turned out to be members of a vast protein family (the G-protein–coupled receptors) that are central to many biological processes and are estimated to be the targets of approximately half of all drugs in use today.

Consideration of the mechanism of action of these receptors led to a fundamentally chemical question: How does the information that a hormone has bound to a receptor from one side of a lipid bilayer get transmitted to proteins on the other side of the bilayer? Considerable progress had been made on this question, but the most definitive answer came with the determination of the structure of a receptor caught in the act of activating a G protein.

This structure revealed key aspects of the conformational changes that couple hormone binding to structural features of the opposite side of the membrane that result in changes in the interacting G protein at a nearly atomic level. In addition, the crystallization of this membrane-protein complex required the use of specialized, synthesized detergents and a deep understanding of the physical chemistry of lipid solutions. Thus, while medicine and biology supplied the questions, chemistry provided the answers. I commend the current president of the American Chemical Society, Bassam Shakhashiri, for his appreciation of this accomplishment in the context of chemistry (7).

This October also included another important event for American science, the DeWitt Stetten Jr. Symposium (8) held in the Ruth Kirschstein Auditorium at the National Institutes of Health in honor of the 50th anniversary of the National Institute of General Medical Sciences. In his introductory remarks at this symposium, NIH Director Francis S. Collins noted that NIGMS had supported 75 Nobel Prize winners over its 50-year history (9). This represents 55 percent of the 137 total Nobel Prize awardees the NIH has supported. Yet NIGMS distributes only about 8 percent of the NIH budget.

Recalling that Nobel Prizes are issued to recognize contributions of "the greatest benefit to mankind," this puts the tremendous return on the investment in basic research in quantitative terms.

Biochemistry and molecular biology reflect the combination of scientific fields that were once considered distinct. Of course, such fusion and recombination applies to other fields. This year's Lasker Award in Basic Medical Research was awarded to Mike Sheetz, Jim Spudich and Ron Vale "for discoveries concerning cytoskeletal motor proteins, machines that move cargoes within cells, contract muscles, and enable cell movements" (10). Key to these discoveries were techniques adapted from physics for examining single molecular motor proteins in action. Indeed, some of the key studies were performed in collaboration with Nobel laureate Steven Chu, who was recognized in 1997 for developing laser-based methods for trapping and controlling single atoms.

My own training was in chemistry, and my dissertation project, although motivated by biological questions, was solidly in the mainstream of chemistry. First while a postdoctoral fellow and then while an assistant professor, my approaches moved into biochemistry and molecular biology, driven by the questions in which I was most interested. These changes were quite exhilarating scientifically but occasionally ran into some cultural barriers. At a scientific meeting, a chemist colleague of my Ph.D. adviser came up to me and said, "I understand that you have become a biologist." I was involved in another discussion, and I responded without thinking, "No, just a modern chemist." I do not believe he attended my talk. Many key scientific questions will continue to come into sharper focus only through the continued blurring of traditional scientific boundaries. We should all be careful to avoid being too ensconced in our own traditional fields.

Jeremy Berg (jberg@pitt.edu) is the associate senior vice-chancellor for science strategy and planning in the health sciences and a professor in the computational and systems biology department at the University of Pittsburgh.

REFERENCES

1. http://www.nobelprize.org/nobel_prizes/chemistry/laureates/2012/
2. http://www.asbmb.org/Meetings_01/2013mtg/2013Annualmtgint.aspx?id=17174
3. http://www.nobelprize.org/nobel_prizes/medicine/laureates/2012/
4. http://www.nobelprize.org/alfred_nobel/will/will-full.html
5. http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1902/fischer-bio.html
6. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2599350/pdf/yjbm00317-0091.pdf
7. http://www.huffingtonpost.com/bassam-z-shakhashiri/nobel-prize-chemistry_b_1955580.htm
8. http://videocast.nih.gov/summary.asp?Live=11948
9. http://www.nigms.nih.gov/Education/Factsheet_NIGMSNobelists.htm
10. http://www.laskerfoundation.org/awards/2012basic.htm

news from the hill

Congress' unfinished business

BY CHRIS PICKETT

By most measures, the 112th Congress has been one of the least productive in recent history. However, the current lame-duck session gives lawmakers one final chance to make progress on some serious issues facing the biomedical research community. Here are a few of the legislative topics that we'll be following as the 112th Congress comes to a close.

Sequestration

The fiscal cliff is rapidly approaching, and only a Congressional compromise on tax cuts, spending cuts and the debt ceiling can prevent the national economy from plunging over. Should sequestration, or across-the-board budget cuts, go into effect Jan. 2, the National Institutes of Health will see an 8.2 percent cut to its budget.

Will it happen? We see a 70 percent chance of a compromise plan that averts sequestration altogether, a 20 percent chance that legislators postpone sequestration and debate these cuts at a later date, and a 10 percent chance that sequestration happens.

The best scenario for biomedical research? Sequestration is averted and the NIH is funded at or above the level proposed in already-approved appropriations bills.

Immigration

Two bills have been proposed recently that could make it easier for Ph.D.s in science, technology, engineering and math disciplines to remain in the U.S. after receiving their degrees. However, the bills would redefine STEM to exclude the biomedical sciences. The reason for this exclusion is not clear, but it seems to ignore the important contributions foreign-born Ph.D.s make to public health and the U.S. economy.

Will it happen? We give it a 40 percent chance of becoming law. Keeping scientists and engineers in the U.S. after they've received Ph.D.s has bipartisan support, and the bill is scheduled to come up for debate during the lame-duck session. Congress has many bills of national importance to consider, though, and it is not clear if this bill will rise to the top or get lost in the shuffle. Check out our blog, the ASBMB Policy Blotter, for updates.

The best scenario for biomedical research? A bill is passed to allow all STEM Ph.D.s, including biomedical Ph.D.s, to participate in the new immigration policy.

Primate research

In June, the U.S. Senate passed the Great Ape Protection and Cost Savings Act that effectively bans all research done on primates. There is a provision that would allow for experimentation on chimpanzees in response to an emerging or re-emerging threat of serious infectious disease.

Will it happen? We give this a 25 percent chance of becoming law. This legislation doesn't have the kind of bipartisan support that the STEM immigration bill does and may not even be on the lame-duck session's radar. However, it could be attached to another piece of legislation that has a good chance of passing.

The best scenario for biomedical research? The bill is defeated.

Travel

Travel to conferences for face-to-face communication and demonstration of new technologies and findings is an essential part of scientific progress. However, Congress is considering legislation that would severely curtail travel for all government employees. This would restrict the travel of scientists from the NIH and other federal research agencies to only one conference per year.

Will it happen? We give this an 80 percent chance of becoming law. The restrictive travel language is contained in an amendment to a Senate bill designed to maintain the fiscal solvency of the U.S. Postal Service. There is little opposition to the travel restrictions or the plan to save the U.S. Postal Service.

The best scenario for biomedical research? An exception will be included, as proposed by several groups, to exempt scientists from these travel restrictions.

Chris Pickett (cpickett@asbmb.org) is the science policy fellow at the ASBMB.

Three ASBMB members get NIH funding for single-cell analysis

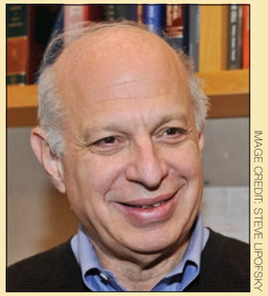

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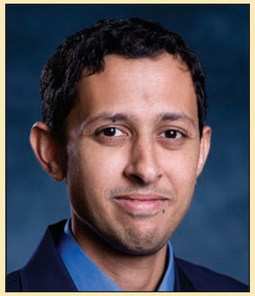
IMAGE CREDIT: STEVE LIPOFSKY


SIMS


VARADAJARAN

Three American Society for Biochemistry and Molecular Biology members won grants from the Single Cell Analysis Program at the National Institutes of Health. Marc Kirschner at Harvard University, Peter Sims at Columbia University Health Services and Navin Varadajaran at the University of Houston were among the 26 recipients of awards supported by the NIH Common Fund.

The NIH intends to invest more than $90 million over five years to promote the development and application of single-cell analysis. The SCAP's goal is to understand what makes individual cells unique and to accelerate the development of clinical therapies based on disease mechanisms at the cellular level. The program has three parts: one to support three research centers, one to create new laboratory-based single-cell technologies and one to generate clinically relevant methods.

"The development of new technologies that can detect differences between individual cells within the same tissue is crucial to our understanding of a wide variety of diseases," said NIH director Francis S. Collins in a press release. "This Common Fund program is an excellent example of how the NIH can accelerate the pace of biomedical discovery."

Kirschner's and Sims' projects belong to the program sector that plans to support new methods for single-cell analysis. Kirschner's aim is to establish a method that simultaneously can profile more than 1,000 cells in each run of a fluorescent-activated, cell-sorting instrument. The method, largely based on existing technologies, will measure tens of proteins and 100 to 200 mRNA levels simultaneously in single cells. Sims' project will develop single-cell proteomics by creating a new technology for protein identification that combines single-molecule fluorescence microscopy and a microfabricated array platform.

Varadajaran's project is among those designed to accelerate the translation of technologies from the laboratory to the clinic. Varadajaran obtained an R01 grant to study single-cell biomarkers in genetically modified T-cells. These cells are being tested in clinical trials to treat leukemia and lymphoma. Varadajaran's aim is to validate the tools for investigating how well the modified T-cells can target tumor cells and use that information to understand better their therapeutic benefits.

Ono named president of University of Cincinnati


ONO

Santa Jeremy Ono was named president of the University of Cincinnati after a unanimous vote by the school's board of trustees in late October. He had been serving as interim president since August and served before that as the senior vice president for academic affairs and provost. He's a professor of pediatrics at the College of Medicine and a research faculty member at Cincinnati Children's Hospital Medical Center. Before arriving at UC, Ono was part of the administration at Emory University and a faculty member at Emory's medical school. Ono has served on the editorial board of the Journal of Biological Chemistry.

AAMC honors Gordon for pioneering gut microbiome work


GORDON

Jeffrey I. Gordon of Washington University in St. Louis School of Medicine won the Association of American Medical College's 2012 Award for Distinguished Research in the Biomedical Sciences. Gordon studies how the gut microbiome affects our physiology and metabolism. A pioneer in the field of metagenomics, Gordon has developed several important experimental and computational approaches, and his work has changed the way we view our mutually beneficial relationships with gut microbes. The AAMC award each year goes to a medical school faculty member who has done outstanding basic or clinical research. Gordon heads up the Center for Genome Sciences and System Biology at WUSTL, where he's been on the faculty since 1981. He's a member of the National Academy of Sciences, the American Academy of Arts and Sciences, and the Institute of Medicine.

Dufau wins Argentina's RAICES Prize


DUFAU

Maria L. Dufau, chief of the molecular endocrinology section of the National Institute of Child Health and Human Development, received last month Argentina's RAICES Prize, an award established in 2010 to recognize outstanding Argentine scientists working abroad who have promoted ties that have strengthened science and technology initiatives in Argentina. Dufau was recognized for her dedication to training Argentine fellows and for welcoming Argentine collaborators to her lab over the years. After receiving her award in Buenos Aires, Dufau gave a talk titled "Mi Jornada," or "My Journey." RAICES stands for "Red de Argentinos Investigadores y Cientificos en el Exterior," and the acronym means "roots." The prize is an outgrowth of a program by the same name that was established in 2003. "This great program supports cooperation of Argentinian scientists living and working abroad with colleagues within the country," Dufau said. "It also promotes repatriation and provides support for returning fellows after their training abroad to establish their independent careers." Since the program's inception, more than 800 scientists have returned to Argentina. Dufau has been an ASBMB member for more than 30 years and served two terms on the editorial board of the Journal of Biological Chemistry. Her research focuses on the regulation and function of luteinizing hormone and prolactin receptors, as well as gonadotropin-regulated genes. Her lab discovered a gonadotropin-regulated testicular RNA helicase, GRTH/DDX25, which is essential for spermatogenesis. Most of the seminal findings by her lab in these areas of research were published in the JBC.

Kundu's group wins first place in Merck Millipore competition

Tapas Kundu, a professor at the Jawaharlal Nehru Centre for Advanced Scientific Research in Bangalore, India, and an editorial board member of the Journal of Biological Chemistry, was on the team that won the top prize in the first annual Merck Millipore India Innovation Awards for life science research and innovation. Kundu's team, which focuses on the mechanism of transcription regulation through chromatin, will share the prize of about $56,000. "I congratulate Merck Millipore for this idea," Kunda said in a statement. "This will encourage young minds across India. It gives us an opportunity to work together for the need of science, the need of technology and the needs of the Indian society." The second prize was issued to a team from the International Centre for Genetic Engineering and Biotechnology in New Delhi. That team, led by Dhiraj Kumar, was recognized for work recently published in the JBC (doi: 10.1074/jbc.M111.266239). Merck Millipore, a life sciences division of the global pharmaceutical and chemical company, is headquartered in Billerica, Mass.

Bonini, Cleveland, Dixit elected to the IOM


BONINI


CLEVELAND


DIXIT

Three ASBMB members were inducted into the Institute of Medicine during the organization's 42nd annual meeting in mid-October. They were

- Nancy M. Bonini, a Howard Hughes Medical Institute investigator and a professor of biology at the University of Pennsylvania, Philadelphia;
- Don W. Cleveland, a professor of medicine, neurosciences, and cellular and molecular medicine at the Ludwig Institute for Cancer Research in La Jolla, Calif., and the chairman of the department of cellular and molecular medicine at the University of California, San Diego, School of Medicine; and
- Vishva M. Dixit, vice president overseeing physiological chemistry at Genentech Inc. in San Francisco.

Seventy new members and 10 foreign associates were elected by current members this year.

Mizzou's Hazelbauer gets Curators' Professorship


HAZELBAUER

Gerald Hazelbauer, chairman of the biochemistry department at the University of Missouri, was selected for his institution's Curators' Professorship, a prestigious appointment that carries with it a raise and a stipend. Upon learning the news, Hazelbauer said, "It's very nice to be recognized by my colleagues and institution. Like every 3-year-old, all of whom I see as scientists, my research group and I kept asking how, who, what and why." Hazelbauer, who studies transmembrane receptors and sensory transduction, was on the Federation of American Societies for Experimental Biology Board of Directors for four years and recently received a MERIT Award from the National Institutes of Health.

Protecting biomedical inventions through patents

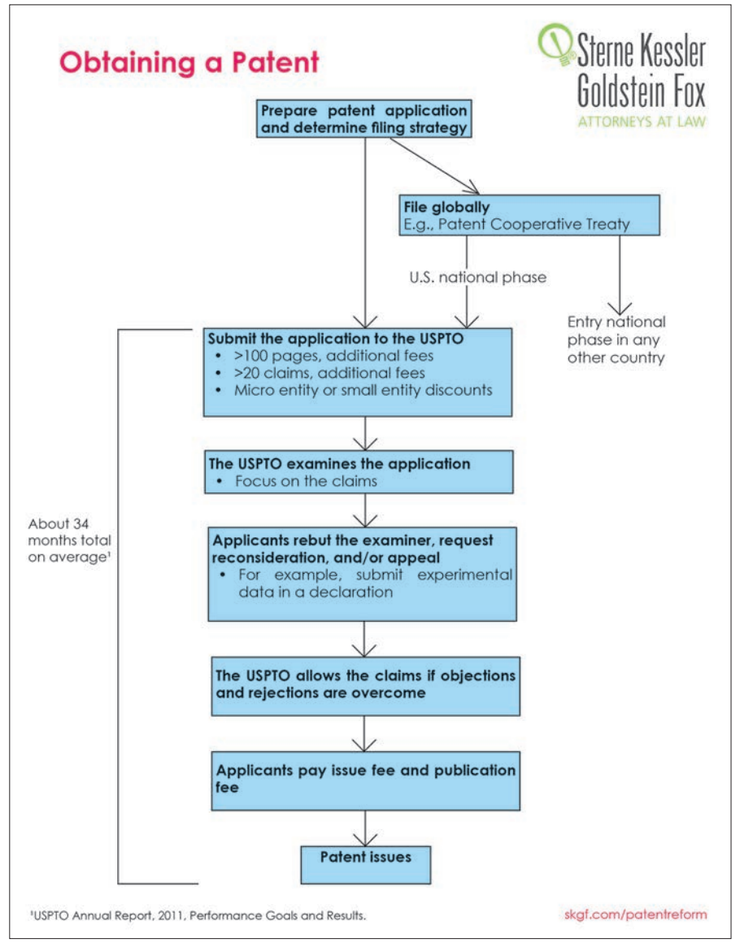
BY CHENGHUA LUO AND GABY L. LONGSWORTH

Many biomedical innovations have the potential for commercialization. As there is usually a lag between initial conception of ideas and commercialization of a developed product, it is important to develop a strategy at an early stage for protecting inventions. One way is to obtain a patent.

A patent is a form of intellectual property granted by the government to the inventor. Once a patent is granted in a country, the patent owner has the legal authority to exclude others from making, using or selling the invention in that country without a license. In the United States, patent rights exclude others from making, using, offering for sale, selling or importing the invention in a limited time period. Patents can attract investment and generate income for patent owners because of the granted monopoly rights.

Patent protection in one country does not extend to other countries. Thus, inventors need to obtain patents from each country or territory to protect their inventions. Usually, a nation's patent office is in charge of the granting of patents in that country. The United States Patent and Trademark Office is the government agency responsible for the examination of patent applications and the granting of patents in the U.S. There are international treaties, such as the Patent Cooperation Treaty (administered by the World Intellectual Property Office and covering more than 140 countries), that centralize some portions of the filing and examination procedures.

The process of obtaining a patent is called patent prosecution. In the U.S., the first step in prosecution is to file a patent application with the USPTO. A patent



application generally contains the following:

- the title of the invention,
- the background of the invention,
- a brief summary of the invention,
- a brief description of the drawing(s) of the invention (if any),
- claims, which define the invention the applicant is seeking to protect, and
- an abstract.

A patent application does not have legal force until it is granted and issued as a patent.

The USPTO examines a patent application for compliance with several legal requirements as discussed below.

First, the subject matter of a given claim must be eligible for a patent. Examples include non-natural products or materials, such as genetically engineered polynucleotides, polypeptides and organisms, humanized antibodies, compounds isolated from nature, and new chemical compounds. Claims that are directed to "laws of nature, natural phenomena and abstract ideas" are not eligible. For example, methods of analyzing a gene sequence in a patient and comparing it with the normal sequence to identify the presence of disease-predisposing mutations are not eligible, because such methods set forth laws of nature – namely, the relationships between gene sequences and the likelihood of developing certain diseases.

In addition, the invention defined by the claims must have utility; in other words, the claimed invention must be useful for any particular practical purpose that would be considered credible by a person skilled in the relevant area of technology. The claim language must also clearly point to and define the boundary of the subject matter that will be protected by the patent. Furthermore, the application needs to adequately describe the claimed invention and provide a description of how to make and use the invention in sufficient detail for a person skilled in the relevant area of technology to make and use the invention. For example, if a patent application claims to have a newly identified mammalian protein, the application needs to disclose the amino acid sequence of the protein from different mammals as well as how to make and use the protein. These requirements ensure that the scope of patent protection granted matches the disclosure provided by the patent. Moreover, the invention must be novel and not obvious based upon what is already known in the field.

In the context of the legal requirements discussed above, the USPTO examination focuses on the claims, which define the scope of protection afforded by a patent. If the USPTO rejects or objects to the claims for failing to meet any one of the legal requirements, the applicant can provide technical data to rebut the examiner, request reconsideration and/or appeal the USPTO's objections as necessary. A patent will be granted after the objections are overcome and the required fees are paid.

Biomedical inventions, laws governing patentability and patent office proceedings are complex. Careful planning and execution are required to obtain strong patents, which are essential tools in the commercialization process. Bringing biomedical inventions to market and building strong patent portfolios can generate significant economic rewards for both inventors and research institutions.

Gaby L. Longsworth is a director with the law firm of Sterne, Kessler, Goldstein & Fox P.L.L.C. Chenghua Luo is an associate with the same firm. Longsworth and Luo concentrate their practice in patent law.

Meet Peter Cresswell

New associate editor for the Journal of Biological Chemistry

BY RAJENDRANI MUKHOPADHYAY

In August, immunologist Peter Cresswell at Yale University joined the Journal of Biological Chemistry as an associate editor. One of his laboratory's research interests is antigen processing by major histocompatibility complexes. Among his many professional honors, Cresswell is a member of the National Academy of Sciences and the Institute of Medicine of the National Academies. He is also a fellow of the Royal Society in the U.K. Cresswell spoke with ASBMB Today about his research interests, his thoughts on the JBC and his career path. Below are edited excerpts from the interview.

Q: Briefly explain what your research group currently is studying.

The major interest in the lab has been historically in antigen processing, which is basically how peptides bind to major histocompatibility complexes, which are then recognized by T-cells. I'm interested in the biochemistry and cell biology of what controls the assembly of MHC molecules and peptides. There are two kinds. One is MHC class I, and the other is MHC class II. We finished up with MHC class II more or less a few years ago with not much in the way of biochemical questions left to ask.

The last few years have been much more focused on MHC class I. There is a whole set of complicated assembly processes, which involves endoplasmic reticulum chaperones, some dedicated proteins and a not-well-characterized mechanism that facilitates the exchange of peptides so that you end up with the highest affinity peptide possible before the class I molecule can get out of the endoplasmic reticulum and be expressed on the cell surface. We're trying to understand that mechanism in absolute detail.

Much more recently, we've become interested in an interferon-inducible protein, which we call viperin. We've recently discovered that human cytomegalovirus (HCMV) uses this viperin molecule to facilitate infection of cells. The virus rapidly induces viperin expression, and a protein encoded by HCMV actually binds to viperin and takes it to the mitochondria, where viperin has some pretty significant metabolic effects. It shuts down fatty-acid beta-oxidation and induces more fatty-acid biosynthesis, which we're currently interpreting as a mechanism for making lots of membrane that the virus can use to envelop itself. That's now a major focus of the lab. We're trying to understand what viperin normally does to allow HCMV to make this adaptation.

What have been the highlights of your career?

We identified a number of molecules that are critical for the process of antigen processing. There's a catalyst for peptide exchange from MHC II molecules that is called DM. We actually showed how that worked in a cell-free system. Just with DM

and MHC class II molecules, we could push the exchange of peptides.

We also discovered the protein in the MHC class I pathway that is called tapasin and catalyzes peptide exchange in that system. We eventually were able to make that work in a cell-free system too, but that proved to be much more complicated. It took a lot of years and the energy of one particularly talented postdoc to make that work.

Tell us about your academic background and research training.

I was an undergraduate in chemistry at University of Newcastle Upon Tyne in the U.K. (and) not totally delighted with it. I liked organic chemistry and not much else. I didn't like lab work. I thought labs were fairly boring. You're always following a recipe, kind of like cooking.

Then I did a master's degree … in an area called microbiological chemistry, which was sort of a combination of chemistry and biochemistry. Getting into the master's degree was the turning point. It was the first time I did an experiment where I didn't know the answer. I didn't know what the result was going to be. All of a sudden, I was fired up. I thought it was really interesting to try to design experiments to answer questions when you didn't know the answer in advance. It was a major intellectual stimulus.

Then I moved into immunology for my Ph.D. (at London University), not really knowing what I was getting into. I thought it was interesting and, at the time, a very poorly understood physiological response. I then moved to the USA for a postdoc to work with Jack Strominger at Harvard University, where my life as a biochemist working on MHC molecules really started.

Who do you consider to be big scientific influences?

That's a tough question. I think my Ph.D. adviser, Arnold Sanderson, taught me how to do experiments. He taught me the importance of good controls and good experimental technique. My postdoc adviser, Jack Strominger, showed me how important it is to choose a difficult question. Not to do the trivial; do the difficult things.

When I got my first faculty position at Duke University, the chief of the division of immunology was a very talented guy called Bernard Amos, who was probably one of the nicest people you could ever meet. He had this way of treating everyone, from the janitors to professors, exactly the same way. I thought it was just wonderful and very different from anything I'd ever experienced before. I try to follow that principle myself.

What was your reaction when you were asked to join the ranks of the JBC associate editors?

I was pleased to be considered. I've had the pleasure of working in an area that combines biochemistry, cell biology and immunology, and I've served in editorial positions in the latter two fields. To be asked to do the same in biochemistry was a real honor. I remember Jack Strominger considered his greatest early accomplishment to be publishing three papers in the same issue of the JBC.

How is the new role going so far?

It's interesting. There are a lot of papers that you get as an (associate editor). I'm surprised by how many of them are in areas about which I really don't know much. Even though they are immunology, they cover an eclectic mix. There are some things I know very well, and I can immediately pick up a reviewer and say So-And-So is perfect. And then there are things where I have to sit down and think, "Oh my God. Who on Earth am I going to get to review this?" That requires some PubMed searching and checking around to try to find the appropriate reviewers. It's a little more difficult than I imagined it was going to be.

What do you do outside of the lab?

I'm pretty much a scientist most of the time. I do play acoustic guitar, which is a good way of relaxing after a bad day. I started playing guitar when I was about 14. I played popular music at that time, and I was just playing whatever people played at the time. When I was an undergraduate, I heard some albums by some British folk-blues guitar players, particularly a guy called Bert Jansch, who died last year. Once I heard that music, I thought, "I have to learn to play this stuff!" I started to work on playing a complicated finger style of playing, which I still do.

But I find what I do professionally so enjoyable that I don't feel the need for a serious interest outside the lab.

For younger scientists, do you have any words of wisdom?

Pick a difficult project that is important, use your imagination and be persistent. Remember that you are more dependent on your students and postdocs than they are on you.

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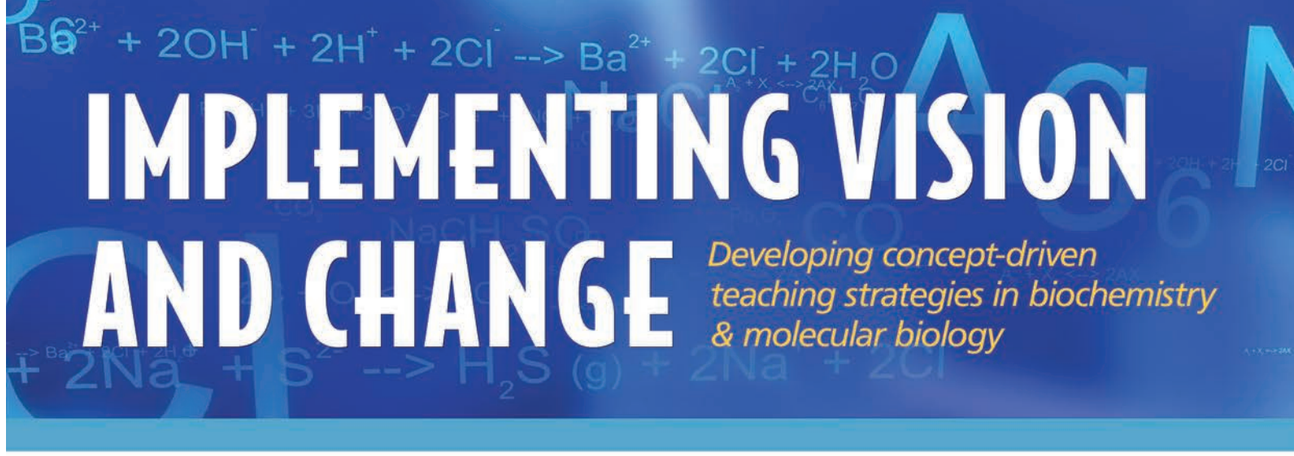

The American Society for Biochemistry and Molecular Biology (ASBMB) launched the Biochemistry and Molecular Biology (BMB) Concept Inventory project in 2011. This is a five-year NSF-funded project, ***Promoting Concept Driven Teaching Strategies in Biochemistry and Molecular Biology through Concept Assessments,*** built on the idea of bringing together a large and diverse network of undergraduate faculty and researchers to develop a central, web-based resource that will serve as an inventory of biochemistry and molecular biology assessment tools developed based on foundational concepts, discipline specific knowledge and essential skills necessary to prepare students to take on the challenges of molecular life science research in the twenty-first century.

During the first year of the grant, regional workshops brought together faculty who teach Biochemistry and Molecular Biology to identify those foundational concepts that define the discipline. In the second year, similar regional meetings transformed those concepts into expectations for student mastery. This year, a series of regional workshops have been developed to focus on assessing student mastery of foundational concepts, and identifying associated best teaching practices.

2012-2013 BIOCHEMISTRY AND MOLECULAR BIOLOGY CONCEPT INVENTORY WORKSHOPS – *Assessing Student Learning*

The following workshops have been scheduled. These workshops are hosted by project PIs and partners across the country.

Saturday, January 12, 2013
Marymount Manhattan College, New York, NY

Saturday, February 23, 2013
University of Alabama, Tuscaloosa, AL

Saturday, March 2, 2013
St. Mary's College of Maryland, St. Mary's City, MD

Registration is available through our website at **www.asbmb.org/bmbconcept.** Registration for all workshops is free. Space is limited.

*To learn more about the ASBMB Concept Inventory project visit **www.asbmb.org/bmbconcept.***
*If you are interested in hosting a workshop, contact Weiyi Zhao at **wzhao@asbmb.org.***

AN ESSENTIAL DEBATE

BY RAJENDRANI MUKHOPADHYAY

A controversy over a dietary recommendation for omega-6 fatty acids shows no sign of resolving itself.

Is a particular dietary recommendation harming people in the U.S.? For almost 20 years, scientists have been arguing over whether Americans and others on a typical Western diet are eating too much of omega-6s, a class of essential fatty acids. Some experts, notably ones affiliated with the American Heart Association, credit our current intake of omega-6s with lowering the incidence of cardiovascular disease. Others, which include biochemists, say the relatively high intake of omega-6 is a reason for a slew of chronic illnesses in the Western world, including asthma, various cancers, neurological disorders and cardiovascular disease itself.

At the center of this dispute is how omega-6s and their cousins, omega-3s, are biochemically processed in the body and the physiological outcomes of the metabolism (see box on the EFA naming convention). Both camps agree that a healthy diet requires both omega-3s and omega-6s. Omega-3s are sorely lacking in Western diets, so people need to increase their consumption of them. But the split comes over omega-6s: Are we or are we not eating too much of them?

To make their case, both camps point to the same body of biochemical and clinical trial data but say the other camp is misinterpreting the data. "It's a real can of worms," says Norman Salem Jr., a biochemist at DSM Nutritional Products, a company that makes essential fatty acids and other food supplements.

OPENING THE CAN OF WORMS

In 1985, Artemis Simopoulos, then the chair of the nutrition coordinating committee of the National Institutes of Health and now the president of the Center for Genetics, Nutrition and Health, described how, from the 1950s onward, Western diets were becoming dominated by omega-6s at the expense of omega-3s. Fish intake, a critical source of omega-3s, had dropped considerably, even among American Catholics after Pope Paul VI decreed in 1966 that Fridays no longer had to be meatless (1). "By 1985, fish consumption was minimal. Something like 25 percent of the U.S. population did not eat any fish at all," says Simopoulos. "In the meantime, agriculture and agribusiness had changed animal feeds. The omega-3 fatty acids that are normally found in grass-eating animals had disappeared because the animals were fed corn." Corn and other grains are generally high in omega-6s.

The oils people consumed also changed. People began to eat more corn, soybean and safflower oils, which are high in omega-6s and plentiful in industrially processed foods. Another source of the dietary change came from the work of Ancel Keys. In 1965, Keys and his colleagues at the University of Minnesota published an equation that quantified the relationship between saturated fats, polyunsaturated fats and serum cholesterol levels (2). The equation helped to sway public health dietary emphasis toward the polyunsaturated fats, which include EFAs, to lower blood cholesterol levels. But the Keys equation treated all unsaturated fats the same. It didn't distinguish between omega-3s and omega-6s. But biochemical studies, such as those by Nobel laureates Bengt Samuelsson and Sune Bergström at the Karolinska Institute in Sweden and John Vane at the Wellcome Foundation in the U.K., were demonstrating that the two classes of EFAs formed different kinds of bioactive eicosanoids.

In 2009, the dispute over omega-6 consumption came to a head when the American Heart Association recommended that omega-6s comprise at least 5 percent to 10 percent of the energy intake in a diet (3). If omega-6 intakes were less than that, said the AHA, the risk of cardiovascular disease likely would increase. According to data from the National Health and Nutrition Examination Survey overseen by the Centers for Disease Control and Prevention, the average American currently gets 6.5 percent of his or her energy intake from linoleic acid, the major omega-6 in the diet.

William Harris, an expert in cardiovascular disease at the University of South Dakota and president of the company OmegaQuant Analytics, says that much of the evidence, both from dietary studies and measurements of blood levels, has shown that higher blood levels of omega-6 are associated with reduced risks for cardiovascular events. Harris, who spearheaded the heart association's scientific advisory group, adds that this is why "the American Heart Association encourages people to eat omega-6 fatty acids and specifically not to buy into this idea that we're eating too much." Walter Willett, an expert in nutrition and epidemiology at Harvard University, goes one step further and calls the asser-

tion that high omega-6 intake is harmful "an urban myth."

But lipid biochemists are alarmed. For example, Floyd Chilton is a biochemist at Wake Forest Baptist Medical Center and a consultant to the company GeneSmart. He says that the AHA recommendation was made without considering the biochemistry of EFAs and solely focused on the outcomes of clinical trials that were not well designed. "I think it led to some very troubling decisions," he says, a sentiment echoed by others, such as Simopoulos, Salem and William Lands, a biochemist at the National Institute on Alcohol Abuse and Alcoholism.

EFAs go through one well-documented biochemical pathway to make eicosanoids. This pathway is also a source of contention between the two camps.

THE BIOCHEMICAL DEBATE

Essential fatty acids were discovered on the heels of vitamins in the early 1900s. In 1929 and 1930, George and Mildred Burr demonstrated that essential fatty acids were critical for the well-being of laboratory rats and discovered the first essential fatty acid, the omega-6 linoleic acid (4). In 1933, one of George Burr's graduate students, Arild Hansen, showed that humans, like the laboratory rats, could suffer from deficiencies in essential fatty acids. Soon both omega-3s and omega-6s were accepted as nutrients like vitamins that had to be consumed through food for optimal health.

EFAs have several functions, which include producing bioactive molecules, making up our tissue composition and contributing to the skin's barrier function. EFAs go through one well-documented biochemical pathway to make eicosanoids. This pathway is also a source of contention between the two camps.

Linoleic acid, the main omega-6, enters the pathway through the Δ6 desaturase. The resulting molecule then gets elongated by an enzyme whose identity has not yet been established. Next, the molecule goes through the Δ5 desaturase. The result is arachidonic acid, a 20-carbon chain that gets converted by cyclooxygenases into eicosanoids, such as leukotrienes, prostaglandins, and thromboxanes, which regulate inflammation and thrombosis. (Aspirin and its fellow nonsteroidal anti-inflammatory drugs inhibit cyclooxygenases.)

α-linolenic acid, an omega-3 fatty acid, also enters the biochemical pathway through the Δ6 desaturase and is transferred to the Δ5 desaturase. The product from the Δ5 desaturase, eicosapentaenoic acid, goes on to form docosahexaenoic acid through additional steps involving elongases. EPA and DHA, like arachidonic acid, help to build eicosanoids. But these eicosanoids are not as potent as the ones made from arachidonic acid.

Here is the contention between the two camps. The camp that believes we eat too much omega-6 says that linoleic acid swamps out the biochemical pathway, not giving α-linolenic acid much of a chance to get to the Δ6 desaturase. All you get with the high linoleic acid amount, argues this camp, is an accumulation of the powerful arachidonic acid, which shifts the body into a state of constant inflammation. But the camp that argues that our omega-6 intake is fine gets frustrated by this argument. Penny Kris–Etherton, a nutrition expert at Pennsylvania State University who was in Harris' advisory group, says the conversion issue goes away if people just eat adequate amounts of EPA and DHA. If EPA and DHA are sufficient in the diet, the need to convert α-linolenic acid into those molecules gets bypassed. "Just eat a lot of fish and we don't have to worry about the conversion issue," she says. Fortified foods that contain EPA and DHA, like milk and eggs, can also be sources of omega-3s.

Even then, says Salem, the products of arachidonic acid compete against those from EPA and DHA for incorporation into complex lipids and into cells and organs. Indeed, arachidonic acid is a better substrate for cyclooxygenases than EPA. William Smith, a biochemist at the University of Michigan at Ann Arbor, says that cyclooxygenase 1 uses EPA at 5 percent to 10 percent of the efficiency of arachidonic acid; cyclooxygenase 2 uses EPA at a somewhat greater efficiency but no more than 20 percent to 30 percent. "If you have a fairly high level of arachidonic acid over EPA, you're opening the floodgates for all the things that prostaglandins do," which includes stimulating inflammation, says Smith.

Even if products from arachidonic acid dominate, Harris argues, products of arachidonic acid can't all be painted with the same brush. He says some of the molecules produced by omega-6s are proinflammatory but some are anti-inflammatory. "One can't certainly say the omega-6s are pro-inflammatory," states Harris. "That's far too simple, because there are several examples of omega-6 metabolites that are either anti-inflammatory or antiplatelet aggregation."

Lands says Harris' point about omega-6s producing both pro- and anti-inflammatory molecules is correct. But as a whole, he counters, the proinflammatory molecules from omega-6s dominate their anti-inflammatory counterparts. These proinflammatory molecules, Lands, Chilton, and others in the camp advocating lower omega-6 levels assert, accumulate in the body and result in several diseases for which inflammation of some sort is the root cause.

Genetics also now has entered the fray. In recent years, Chilton's laboratory has been studying the *FADS* cluster, which codes for the Δ5 and Δ6 desaturases (5, 6). His team has shown that people of African descent have much higher frequencies of genetic variants that efficiently convert linoleic acid to arachidonic acid than people of European descent. As a result, African-Americans have much higher circulating blood levels of arachidonic acid, says Chilton.

This difference in conversion rate is important for an assertion often made by those advocating for the current omega-6 levels. They say that the biochemical pathway self-regulates, turning itself off after a certain amount of arachidonic acid is made. "If we eat more omega-6s in the diet, it doesn't increase arachidonic acid levels, because there is so much regulation," says Willett.

But Chilton says his research suggests an

NAMING CONVENTION

The naming convention for the omega fatty acids is based on the terminal methyl group of the fatty acid chain (the other end has the acid group). This methyl group is designated with the last letter of the Greek alphabet, ω. The position of the first double bond is described relative to the ω position. α-linolenic acid is an omega-3 fatty acid, meaning that the first double bond is between the third and fourth carbons from the terminal methyl group. Linoleic acid has its first double bond between the sixth and seventh carbons; hence, it's an omega-6. Omega-3s and omega-6s cannot be biochemically interconverted; this is the reason both essential fatty acids are needed in a healthy diet.

No one is disputing that we're eating more omega-6 than our predecessors did.

individual's background does matter. "Many people have argued that the system saturates itself at relatively low concentrations of dietary linoleic acid, limiting the amounts of arachidonic acid that can be made," he says. But, he adds, the studies were almost exclusively carried out in European and European-ancestry populations. Given that individuals of African descent have higher frequencies of the variants that convert linoleic acid to arachidonic acid at higher rates than European descendants, Chilton says it is likely that the saturation of the linoleic-acid-to-arachidonic-acid pathway occurs at higher levels of dietary linoleic acid in people of African descent. "With recommendations like that from the American Heart Association, I am particularly concerned we may be driving health disparities," says Chilton.

Lands and other biochemists decry what they see as a complete dismissal of the biochemistry of essential fatty acids in making dietary recommendations. But to that critique, Harris says public health policy should be dictated by clinical trial data. "You don't do it by looking at biochemical pathways," he says. "You look at randomized controlled trials and population cohort studies where disease endpoints are being measured. That's what you care about."

CLINICAL CONUNDRUM

In coming up with its 2009 recommendation, the AHA looked at the literature describing various clinical trials that included omega-6s. The AHA used evidence from observational trials that lasted up to 20 years and randomized controlled trials in which participants were given special diets. Subsequently, biochemist Joseph Hibbeln and clinician Christopher Ramsden at the National Institute on Alcohol Abuse and Alcoholism analyzed the oils used in the randomized controlled clinical trials (7). They asked if the evidence for the AHA recommendation was specific to linoleic acid or if an increase in omega-3s could be responsible for the benefits.

Ramsden and Hibbeln describe the problems they see: The trials involving only omega-6 didn't give any indication of benefit and even suggested a hint toward increased risk; only the trials that increased omega-3s along with omega-6s presented a benefit. The AHA, they say, did not separate the trials involving only omega-6s from those that also increased omega-3s.

"Here's the analogy," says Hibbeln. "Say I give marshmallows infused with penicillin to people who have an infection and they get better. By gram weight, the intervention was mostly marshmallows. But there was penicillin. Do I then overgeneralize, as the American Heart Association has done, and recommend that people eat marshmallows to cure their infections? I don't think so."

Harris doesn't buy that argument. Biochemistry dictates that an excess of linoleic acid should suppress the conversion of α-linolenic acid to EPA and DHA. It must be linoleic acid that is the main factor in preventing cardiovascular disease in these clinical trials, Harris says, adding that the molecule is known to have beneficial effects, such as lowering low-density lipoprotein cholesterol. The onus is still on Hibbeln's group "to explain how a small amount of α-linolenic acid contained in a virtual ocean of linoleic acid" can have cardioprotective effects, says Harris.

But Ramsden counters that the one trial that increased the daily intakes of EPA and DHA to 5 grams, a large amount equivalent to 16 fish-oil pills a day, showed major benefit. If that trial, called the Oslo Diet Heart Study, was excluded from the meta-analysis, none of the other clinical trials showed a benefit from the omega-6s.

There aren't any data showing what happens when linoleic acid in people's diets is dropped to less than 1 percent, an amount at which it's thought that linoleic acid doesn't crowd out α-linolenic acid. What's needed is a clinical trial that carefully tracks a large range of linoleic acid amounts in the diet and catalogues health outcomes.

"That trial will never be done. It would take 10 years or longer and cost perhaps $100 million," says Salem. "No one is ever going to pay for that trial." Harris concurs, saying the randomized, controlled trial would be extremely hard to pull off, because the entire food supply would have to be manipulated to test different amounts of linoleic acid.

'WE'RE THE EXPERIMENT'

No one is disputing that we're eating more omega-6 than our predecessors did. Over the past 100 years, consumption of linoleic acid has increased dramatically in the U.S., mainly through the use of soybean oil. Soybean oil intake has gone up from being 1 percent of calories in the American diet to as much as 10 percent, according to Hibbeln. Lands, Salem and others contend that the rise, driven by the processed food and agriculture industries, has happened without anyone knowing its effects. "If I were now to try to get permission to change 10 percent of the calories in the U.S. diet, I would need a very large body of data unequivocally proving that it was safe," says Hibbeln. "No such body of data exists for soybean oil. But it's in our diet. We're the experiment. It's been a very large, uncontrolled intervention."

Experts like Harris and Willett say this increase has been to our benefit. "We have seen a massive decline in cardiovascular disease mortality and huge increase in life expectancy," says Willett. "Not all the benefit is due to the increase in linoleic acid, but almost certainly much of it is. It was not an absolute disaster." But the lipid biochemists counter that it's not just cardiovascular disease at stake. They say diabetes, obesity and even psychiatric disorders are some outcomes of a diet heavy on omega-6s.

Both sides agree that there is much more research to be done on the various pathways in which EFAs participate. Ramsden says nonspecialists may have the impression, based on the well-known body of work on prostaglandins and a few other categories of compounds derived from EFAs, that the biochemistry of omega-6s and omega-3s is firmly established. But that is not the case, because "it's really more complex than anyone had ever thought." Ramsden continues: "I look at this field as having a long way to go."

For this reason, the current experts in the field urge more scientists and clinicians to join in the efforts to understand the impact of EFAs on health outcomes and perhaps finally lay the omega-6 dispute to rest. As Harris says, "The more people are tuned into the question, the more research will be done on the topic and the less uncertainty we will have around the issue."

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REFERENCES

1. Bell, F. W. *Amer. Econ. Rev* **58**, 1346–1350 (1968).
2. Keys A., et al. *Metabolism* **14**, 776–787 (1965).
3. Harris, W. S. et al. *Circulation* **119**, 902–907 (2009).
4. Mukhopadhyay, R. *J. Biol. Chem.* doi: 10.1074/jbc.O112.000005 (2012).
5. Sergeant, S. et al. *Br. J. Nutr.* **107**, 547–555 (2012).
6. Mathias, R. A. et al. *BMC Genet.* doi: 10.1186/1471-2156-12-50 (2011).
7. Ramsden, C. E. et al. *Br. J. Nutr.* 104,1586–1600 (2010).

MCP MOLECULAR & CELLULAR PROTEOMICS

Tiny mitochondrial intermembrane space's proteome

BY RAJENDRANI MUKHOPADHYAY

Despite being the smallest of the four mitochondrial compartments, the intermembrane space is important for several of the organelle's functions. Among other things, the IMS oversees the transport and modification of proteins and other entities, regulates the respiratory chain complexes and coordinates apoptosis. But not many details are known about the compartment.

In a recent Molecular & Cellular Proteomics paper (1), a team led by René P. Zahedi at the Leibniz Institute for Analytical Sciences and Chris Meisinger at the Albert-Ludwig University of Freiburg (both in Germany) did the first IMS proteomic profile in yeast (1).

Because there wasn't a straightforward way to purify IMS proteins from those in the other three mitochondrial compartments, "we developed a dedicated strategy that utilizes recombinant mammalian Bax, one of the key components to trigger apoptosis in mammalian cells," explains Meisinger. Bax inserts into the outer mitochondrial membrane to release cytochrome C and most of the soluble IMS proteins. So Meisinger, Zahedi and colleagues exploited this conserved biochemical mechanism to trigger the release of IMS proteins and analyze them by quantitative mass spectrometry.

The investigators identified 49 proteins, of which 20 were novel. Ten of the 20 "had not even been localized to mitochondria before," says Meisinger. The investigators discovered a novel assembly factor for respiratory complex IV, which had been annotated as a protein of unknown function and localization. The investigators call it Coa6. "Another surprise was the identification of thioredoxins and thioredoxin reductases," says Meisinger. "The IMS was thought to provide an oxidative environment. However, these enzymes seem to also provide reductive capacity."

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1. Vögtle, F.-N. et al. Mol. Cell. Proteomics (2012) DOI: 10.1074/mcp.M112.021105.

JLR THE JOURNAL OF LIPID RESEARCH

How high cholesterol levels come in handy during protozoan infection

BY MARY L. CHANG

It has been long impressed on us by doctors and news reports that eating too much fatty food will lead to hyperlipidemia and, worse, potentially deadly atherosclerosis and cardiovascular disease. Statins, now being prescribed by doctors to untold millions of people around the world to reverse these conditions, have made the pharmaceutical industry a multibillion dollar industry. So it is surprising that in the December issue of the Journal of Lipid Research, researchers in India presented data suggesting that hyperlipidemia confers some protection against leishmaniasis, a disease caused by protozoan parasite infection.

JLR Associate Editor Kenneth R. Feingold and editorial board member Carl Grunfeld of the Department of Veterans Affairs Medical Center at the University of California, San Francisco, review the previous literature and this article in a special commentary.

The innate immune system is the nonspecific first line of defense the human body has against infection by foreign invaders. Part of this immune system are Toll-like receptors; present on the surface of macrophages and other cells, they activate this innate response when they recognize conserved products from microbes. Leishmania donovani is transmitted by the bite of the sand fly. The protozoan survives in infected individuals by living in macrophages, depleting cholesterol and disrupting lipid rafts, thus hampering the macrophage's usual action in the innate response of alerting the body to an invader by antigen presentation.

In an article entitled "Hyperlipidemia offers protection against Leishmania donovani infection: role of membrane cholesterol," June Ghosh of the Indian Institute of Chemical Biology and colleagues present data demonstrating that hyperlipidemia protects from leishmaniasis. In a mouse model, apolipoprotein E knockout mice showed a marked decrease in splenic and liver parasite burden six weeks post-Leishmania infection; in contrast, the parasitic burden in wild-type infected mice continued to increase as time went on. Mice fed an atherogenic diet also resisted the spread of infection better than mice fed a normal diet, and as might be expected, when mice received statin treatment, which decreases serum lipid levels, their susceptibility to infection increased. Taken together with previous studies in hamsters, Feingold and Grunfeld suggest these data provide convincing evidence that serum cholesterol levels are important to modulating Leishmania donovani infection. While some microorganisms have been able to use host lipid and lipoproteins to their advantage to survive, the results presented in the article by Ghosh et al. suggest that a carefully balanced approach in adjusting serum lipid levels could be the key to providing protection from Leishmania.

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jbc THE JOURNAL OF BIOLOGICAL CHEMISTRY

Insights into a new therapy for a rare form of cystic fibrosis

BY DANIELLE GUTIERREZ

Scientists at the Hospital for Sick Children in Toronto have established that VX-770, a drug recently approved by the FDA to treat a form of cystic fibrosis caused by a rare mutation, works through an unconventional mechanism. Their results shed light on the regulation of the cystic fibrosis transmembrane conductance regulator and reveal new possibilities for treating cystic fibrosis caused by various mutations.

Cystic fibrosis is a genetically inherited disease afflicting about 70,000 people around the world. It is caused by various mutations in the CFTR protein, a channel found in the lining of many organs that controls the viscosity of the mucus coating them. A characteristic feature of the disease is thick mucus buildup in the air passages, which causes difficulty breathing and recurring infections.

Recently, the FDA approved the drug VX-770, also known by the trade names Kalydeco and Ivacaftor, for peo-

ple with cystic fibrosis caused by a particular mutation in CFTR – the G551D mutation – for whom it effectively eases breathing. But exactly how VX-770 works was unknown.

The established mechanism for CFTR regulation requires phosphorylation of the protein and binding of ATP. However, in their recent Journal of Biological Chemistry "Paper of the Week," Christine Bear and colleagues report that VX-770 opens phosphorylated normal and mutant CFTR channels without ATP. Their results indicate that VX-770 binds to a different site on CTFR than ATP, suggesting that it works through an alternative mechanism. Significantly, this mechanism may be an effective target for treating cystic fibrosis caused by various CFTR mutations that, like the G551D mutation, impair ATP-mediated channel regulation.

Bear's group determined how VX-770 works via the development of a new assay system. Their results demonstrate the potential of this assay system to discover drugs that target the basic defects caused by CFTR mutations, Bear explains. The assay system is useful to identify candidate compounds that interact with rare mutations, such as G551D as well as the major CFTR mutant F508del, Bear said.

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JBC thematic minireview series on HIV and the host

BY CONNOR BAMFORD

Just under 0.5 percent of the total human population carries the human immunodeficiency virus. That's 34 million of us living with a virus for which there is not yet a vaccine. Ten percent of those infected are children, and the biggest disease burden is found in sub-Saharan Africa. Many of those infected will develop Acquired Immunodeficiency Syndrome. In 2010 alone, 1.8 million people died of AIDS-related illnesses.

Having jumped species into humans from chimpanzees in West Africa about 100 years ago, HIV has rapidly spread across the world, transmitted during sexual intercourse, unsterile injections and birth. Yet it was only in 1983 that HIV was discovered and linked to AIDS, a disease described only two years earlier. Since then, tremendous progress has been made into understanding the basic biology, epidemiology and evolution of the virus, and this has allowed us to develop effective pharmacological interventions, to diagnose new infections cheaply and easily, and even to develop a number of HIV vaccine candidates.

However, a number of challenges still lie ahead. Highly active antiretroviral therapy — one of the 20th century's greatest achievements — can extend lifetime considerably, but the specter of drug resistance always looms. Based on past World Health Organization figures, 6.8 percent of HIV infections were drug resistant in low- to middle-income countries compared with more than 10 percent in high-income countries. Also, our most successful HIV vaccine trial in humans gained only modest results.

For these reasons and others, the Journal of Biological Chemistry decided to run a special minireview series about this exciting and important field of research, covering diverse topics spanning the replication cycle of HIV to help researchers continue the investigation of the basic biology of HIV in the hope of better understanding the enigmatic human pathogen.

"HIV remains a major global public health problem," says Charles Samuel of the University of California, Santa Barbara, the convener of the series and a JBC associate editor. "Substantial progress has been made toward achieving a structural basis for understanding HIV virus interactions with host cells and the biochemical mechanisms by which HIV replicates. Hopefully this knowledge will fuel the development of more effective therapeutics and ultimately an effective vaccine."

In his introduction to the review series, Samuel outlines the basic biology of HIV and the need to develop new treatment strategies, taking us through the steps of viral replication: entry, reverse transcription, integration, gene expression and assembly.

In their minireview, Robert Blumenthal and colleagues from the National Institutes of Health discuss the mechanism by which HIV enters its target host cell via viral glycoprotein-mediated membrane fusion, a process essential for HIV infection of target T cells, macrophages and dendritic cells and, hence, disease outcome. They focus their review on the dynamic process — what they call a "multistep dance macabre" — that occurs after viral receptor binding, which facilitates the transport of the bulky viral core through the cell membrane, and how we can study it using protein structure determination, lipid dye tracking and video microscopy.

Stuart F. J. Le Grice from the National Cancer Institute reviews the potential and past successes of HIV reverse transcriptase-targeted drug development. Reverse transcription in HIV — the enzymatic conversion of a single-stranded RNA genome into a double-stranded linear DNA copy that can be inserted into the host's own genome — is an essential step in the HIV replication cycle. It is mediated by a multifunctional protein, RT, that mediates RNA binding, DNA synthesis and also RNase activity. Le Grice notes that many of the Food and Drug Administration's approved anti-HIV drugs are RT inhibitors and that they are being developed as anal and vaginal microbicides to block virus transmission prophylactically.

The Dana–Farber Cancer Center's Lavanya Krishnan and Alan Engelman document in their minireview the recent advances in the biochemistry of retroviral DNA genome integration, an obligate step in the virus life cycle and one that leads to the establishment of treatment refractory latent virus reservoirs in long-living host cells. Krishnan and Engelman take a structural perspective on how the viral nucleoprotein complex (specifically the HIV integrase enzyme) catalyses the integration reaction. They describe the growth in the field after the development of high-throughput small-molecule screening of integrase inhibitors.

Ronald Swanstrom and colleagues from the University of North Carolina–Chapel Hill detail the strategies by which HIV processes its single polyprotein (expressed from a genome-spanning open reading frame, a common strategy in small positive-sensed RNA viruses) into the enzymatic and structural machinery it needs to replicate, assemble and exit the cell. They concentrate on the protein–protein interaction domains necessary for the virus to carry these tasks out and discuss the potential for drugs that target these processes despite the rapid generation of antiviral resistance.

The dynamic interactions between HIV and host micro-RNAs are reviewed by Kuan-Teh Jeang and colleagues from the National Institute of Allergy and Infectious Disease. RNA interference, or RNAi, is an evolutionary conserved mechanism of post-transcriptional gene regulation mediated by the RNA-induced silencing complex known as RISC. Given its prominence in RNA regulation, it both targets and is a target of the RNA virus, HIV. This review focuses on the dynamic warfare between HIV and its host RNAi machinery. miRNAs have been shown to specifically target HIV's RNA genome, and deregulated miRNAs are associated with HIV disease outcome. This minireview discusses how this virus could control these processes.

And finally, Reuben S. Harris and colleagues from the University of Minnesota discuss the role of innate restriction factors in defending against HIV. Restriction factors are molecules that negatively modulate viral replication. One necessary response to this is that viruses that infect humans have evolved means to combat these defenses. Harris and co-authors review this ancient evolutionary arms race with specific reference to the host-encoded APOBEC3 proteins, BST-2/Tetherin and SAMHD1 dNTP hydrolase. Comparing the HIV–human interaction to that of its primate cousin, simian immunodeficiency virus, with nonhuman primates, the authors outline how we could use this understanding to develop more effective HIV antivirals.

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The road well traveled together

A joint 'Reflections' by Leonore and Leonard Herzenberg

BY PUMTIWITT MCCARTHY

In their joint "Reflections" article in the Journal of Biological Chemistry, "Our NIH Years: A Confluence of Beginnings," Leonore and Leonard Herzenberg describe their scientific journey from the laboratory of Nobel laureate Jacques Monod in Paris in 1957 to the National Institutes of Health in 1959 and finally to a joint laboratory at Stanford University School of Medicine, where they have been for more than 50 years.

Their formative years at the NIH turned out to be an important stop on their journey. Leonard Herzenberg, who goes by Len, remarks, "I am continually aware of how valuable my NIH roots really are."

The couple's "Reflections" article begins with an

Lee Herzenberg recalls fondly the purchase of her wedding dress: She bought it for $10 off a sample rack in a shop on New York's 14th Street. "It was a tiny size but could have been made to order for me except for being too long," she says. "I made the headdress and veil myself by salvaging applique flowers from the part we cut off the hem. Money was in short supply in those days."

unexpected plot twist. Leonore Herzenberg, who goes by Lee, describes finally starting to feel that their life was stable: finding appropriate child care and enjoying what they thought would be a long-term appointment in Monod's laboratory in Paris studying transcriptional regulation and the LacZ operon.

One day, they received a letter that had been mailed to Len's former address. As a result, it was four months late. This important and very tardy letter was calling Len to report to service in the U.S. Army! The couple thought because he was doing a fellowship overseas, he would be exempt from being drafted until its completion. This was not the case. "There was no appeal at this point. Len was a fugitive, plain and simple," Lee writes.

Monod was able to pull a few strings and set up Len to join the laboratory of Harry Eagle at the NIH as a Public Health Service appointee. The couple returned to the United States, and Len "was on his way to a new life and career 'carrying a pipette for his country' at the NIH (instead of carrying a gun in the army)."

The Eagle lab was at the forefront of mammalian cell culture and was the first to develop the proper media and growth conditions to cultivate, most famously, HeLa cells as well as other tumor-derived cells. This work eventually led to the President's National Medal of Science for Eagle.

When Len joined the lab, he helped improve growth conditions for different kinds of cells. This work later led to one of his greatest accomplishments: the development of the fluorescence-activated cell sorter, or FACS, for which Herzenberg won the Kyoto Prize in 2006.

FACS is an automated cell-sorting system that allows separation of different cell types from a heterogeneous cell mixture. The cells are sorted one at a time and quantitated based on the light-scattering and fluorescence characteristics of each particular cell. This has been a powerful tool in the field of immunology and cancer biology.

While Len's place at the Eagle lab had been prearranged, Lee wasn't so sure what the next step was for her. She writes, "NIH was not so welcoming for husband-wife teams … I was basically cut adrift." Luckily, Bruce Ames, a former colleague of Len's who later would develop what is now known as the Ames test, was at the time just embarking on his independent career at the NIH. Lee successfully obtained a permanent position in the Ames lab.

Ames' research focused on bacterial genetics and the histidine biosynthesis pathway in Salmonella. This work was similar to the work Lee had conducted in the Monod laboratory, so it was a smooth transition. Interestingly, Len and Lee's bacterial gene regulation work in Paris with the LacZ operon had many parallels to the histidine operon Lee worked on in the Ames lab. Both systems were examples of bi-stable systems. She explains, "They operated either in an 'on' or the 'off' position – they could not and did not operate for any length of time in the middle."

The Herzenbergs describe the NIH in those days as a wonderful environment. Scientists who had made great discoveries within their fields were often right down the hall or across the campus. Many fruitful conversations and collaborations grew from corridor and cafeteria conversations. One such collaboration, with Mike Potter, became an important cornerstone of Len's career. He always had wanted to study a cell line that could be used to determine cell-surface antigens and suspected that these antigens could be used as markers for genetic studies in cell culture. He needed a "cell line that was close to a normal, accessible cell type." Potter's laboratory had the answer. Potter had a cell line, P388, derived from mouse lymphocytes from chemically induced tumors. Len's group used the cell line for many years after the initial collaboration.

Toward the end of Len's Public Health Service appointment, the couple decided it was time for him to negotiate for a permanent position. Len was successful in securing a local offer, and the couple was happily ready to settle at the NIH. But again fate stepped in.

In a twist that may make current job-seekers green with envy, Len received a letter that contained a job offer for a position he never had applied for. Future Nobel laureate Joshua Lederberg had been tasked with starting the genetics department at the Stanford University School of Medicine. Lederberg wanted Leonard to be his first faculty appointment. The two had met briefly in Paris and at the NIH, but nothing foreshadowed the job offer, Len recalls. The Herzenbergs mulled it over and decided this was too good an opportunity to pass up, so they packed up and moved to California, where they have had a joint laboratory since.

Though they left the NIH many years ago, the Herzenbergs have continued work that relates to their time there. The couple writes, "We recently realized how important it now is to protect cultured cells against mutagenesis while they are being cultured." Len's work in improving cell-culture growth conditions in Eagle's lab has made an indelible mark on their research trajectory. One member of their group, Kondala Atkuri, gives an informative summary in the "Reflections" article of their current efforts to grow mammalian stem and other therapeutically useful cells at oxygen concentrations that more closely mimic levels found in vivo and that are much less likely to induce dangerous mutations.

Although the Herzenbergs have been away from the NIH for many decades, it is a cherished part of their history. Len writes, "As I look back, I realize that the people I met and the focus on mammalian biology, genetics and human disease that they transmitted to me is really the enduring legacy of our NIH years."

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Zombies, beer and family-friendly, sun-filled afternoons

Anything is possible during a science festival

BY BEN WIEHE

San Francisco

They lined up by the hundreds, their ashen faces spattered with blood. Some were horribly disfigured. Others were undergoing inexplicable mutations. All were thirsty.

Thankfully, there were two bars at the entrance and more inside just past the dance floor and DJs, ready to serve the almost 4,000 20- and 30-somethings in full Halloween regalia at the Zombie Night Life event at the California Academy of Sciences. To the right, a short presentation by a neuroscientist was getting under way. Off to the left were more lines of participants eager to learn about brains using real specimens. Out back, the stage was being set for the horror costume and drag show.

The bustling Thursday night zombie party boded well for the 2012 Bay Area Science Festival, which still had more than 70 events to go in its 10-day schedule. Over the next several days of my visit, a familiar feeling of whiplash set in as I zipped around San Francisco Bay; each new event stood out in distinct contrast with the previous one.

On Friday evening, I was at the headquarters of Wired magazine with members of the press and local nerd-herders. (Nerd-herders? Oh, yes. These are the influentials in your community who convene science and tech gatherings for an enthusiastic public.) We learned about the impact of beer on technology and history while sampling the specially brewed science festival beer, dispensed from a mobile cocktail robot, of course.

On Saturday, I waited at a public transit station with numerous families from the Oakland area. One of many shuttles arrived to take us up from urban streets through peaceful woodlands to the Chabot Space and Science Center for a free day of exploration made possible by Chevron, one of the festival's biggest sponsors.

IMAGE CREDIT: COURTESY OF THE BAY AREA SCIENCE FESTIVAL

The line for face painting wound past neuroscientists presenting brain specimens.

Shortly after experiencing the wonder of seeing solar plumes through a telescope alongside children at Chabot, I was taking photos outside the Castro Theater. The marquis announced the headline act, "Alton Brown and the Bay Area Science Festival," while swarms of boisterous Halloween revelers navigated a sold-out line that stretched for blocks.

Sunday started early with a long drive to the hills and volcanic domes of Clayton for a small group hike led by field scientists. Sunday evening took me north to San Rafael for a multimedia presentation by a Pixar animator enjoyed by a popcorn-munching audience in a historic movie theater.

Joining scientists in the field for discovery.

IMAGE CREDIT: BEN WIEHE

By Monday at lunchtime, I was at the prestigious Commonwealth Club in downtown San Francisco with my best shoes on for a talk on synthetic biology by George Church of Harvard Medical School.

Many days and scores of events later, the celebration culminated with Discovery Day, a massive, free, family-friendly day featuring interactive exhibits by more than 150 companies, schools and organizations – including the American Society for Biochemistry and Molecular Biology. This year Discovery Day was again held at AT&T park, home of the World Series-winning Giants, and drew close to 30,000 attendees.

I could go on, but this isn't about just the Bay Area.

Grassroots growth across the nation

Science festivals are popping up across the country. Each is different for all of the same reasons that your own community is a unique source of pride. (It may be that a zombie drag show in the name of science won't go over in quite the same way where you live.) Some of the festivals are large initiatives requiring annual six-figure fundraising drives. Some are more modest in scale.

The diversity of activity that the festivals represent (there are at least three dozen annual festivals active in the U.S.) makes them impossible to summarize. Still, we can make some generalizations:

- Science festivals engage whole communities and make science and technology a part of the cultural calendar in much the same way that art festivals and street fairs do.
- Most feature scores of events over several days and in many venues, reaching students, families and adults where they live, work and play. Festival programs go wherever necessary to serve hard-to-reach audiences, including both science-inattentive individuals and underserved communities.
- They rally communities to celebrate science as alive and local. By convening as many partners as possible, festivals unite those dedicated to science, technology and education.
- They bring the public into direct contact with scien-

tists and engineers, leading people to seek out more science experiences throughout the rest of the year.

Festivals working together

In 2009, a national network of science festivals — the Science Festival Alliance — formed with support from the National Science Foundation. The basic premise of the SFA is that each festival represents both the capacity to serve local communities and the chance for other festivals to learn something new. The SFA's top priorities are to help independently organized festivals get started and to provide festival organizers with a professional network that lets them share their greatest triumphs.

The SFA also serves as a good first stop for anyone interested in getting involved with science festivals. Intrigued by the idea and interested in finding out more? Sign up to receive Science Festival Headlines (1). Think you may want to partner with a local festival to share your work with public audiences? Find a festival near you using the SFA's map and calendar (2). Wondering why there isn't a festival initiative under way in your town? Contact the SFA to see who else is interested in your region (3). Considering starting a new festival? Check out the SFA's "First Look at Science Festivals" document online (4).

Ben Wiehe (wiehe@mit.edu) is the manager of the Science Festival Alliance and on staff at the MIT Museum.

RESOURCES

1. http://sciencefestivals.org/get-connected.html
2. http://sciencefestivals.org/go-to-a-festival.html
3. http://sciencefestivals.org/contact-us.html
4. http://sciencefestivals.org/news/140.html

The ASBMB 2012 graduation survey

A brief synopsis

Every year, the American Society for Biochemistry and Molecular Biology requests demographic data on students graduating with bachelor's and graduate degrees in biochemistry and molecular biology from more than 800 programs across the United States. The 2012 survey yielded 135 respondents, 94 of whom provided data.

Table 1 shows how respondents characterized their programs. Each "Y" indicates a box checked by respondents. A brief inspection reveals that

- 57 of the responding institutions offered only undergraduate degrees,
- six offered both bachelor's and master's degrees,
- 20 offered bachelor's through Ph.D. degrees and
- 11 offered only graduate degrees.

A majority of the responding institutions characterized their bachelor's degree offerings as biochemistry programs or as biochemistry tracks within chemistry degree programs. Somewhat surprisingly, no institution used the term "biotechnology" to characterize its bachelor's degree programs, although one used the term as a descriptor for its graduate degree programs. (To save space, the biotechnology category is not shown in Table 1).

Table 2 summarizes the demographic data reported. Things to note:

- While females slightly outnumber males overall, males slightly outnumber females among those earning Ph.D.s.
- As in past years, the number of graduates from ethnic groups historically underrepresented in scientific disciplines remains disappointing.
- Particularly troubling was the fact that, for the second year in a row, the ratio of black students graduating with graduate degrees relative to the number of them earning bachelor's degrees was 1:8, a decline from 1:3 in 2010 and 1:4 in 2008. In contrast, this year the graduate-undergraduate ratio for whites, Hispanics and Native Americans clustered around 1:5. While our sample size may be too small to be considered statistically significant, it will be important to examine future surveys for signs of a long-term trend.

A few institutions stood out with regard to the representation of historically underrepresented groups:

- The University of Virginia listed five black graduates, five Hispanic graduates and one Pacific Islander graduate among the 103-strong class of 2012.
- Texas Women's University in Houston graduated 23 black and seven Hispanic students.
- Other schools reporting significant numbers of black students among the class of 2012 include Jackson State University in Mississippi and Oakwood University in Huntsville, Ala.
- The University of New Mexico in Albuquerque and Rice University in Houston graduated eight and five Hispanic students, respectively.
- Native American students tended to cluster at a few institutions, mostly private, such as Simmons College in Boston, Adelphi University in New York, Whitman College in Washington state, the University of Dallas and Mills College in Oakland, Calif. The notable exception to this pattern was the public California State University at San Marcos.

DEGREE(S) OFFERED

PROGRAM TYPE (total)	BIOCHEMISTRY			MOLECULAR BIOLOGY			CHEM (BCHM option)			# OF RESPONDENTS
	BA/BS	MA/MS	PhD	BA/BS	MA/MS	PhD	BA/BS	MA/MS	PhD	
BA/BS only (57)	Y									33
				Y						1
							Y			10
	Y			Y						5
	Y						Y			4
	Y			Y			Y			4
MA/MS only (1)								Y		1
MA/MS + PhD only (10)		Y	Y							4
		Y							Y	1
			Y	Y	Y	Y				3
			Y		Y	Y				1
		Y	Y		Y	Y		Y	Y	1
BA/BS + MA/MS (6)	Y	Y								2
	Y	Y						Y		1
	Y	Y			Y					2
	Y						Y	Y		1
BA/BS to PhD (20)	Y		Y							1
	Y	Y	Y							4
	Y							Y	Y	2
	Y	Y	Y	Y	Y	Y				1
	Y						Y	Y	Y	3
	Y		Y				Y	Y	Y	1
	Y	Y	Y				Y	Y	Y	1
	Y	Y	Y			Y				1
	Y	Y	Y		Y	Y				1
		Y	Y				Y			1
							Y	Y	Y	2
			Y			Y	Y			1

	B.A. or B.S. total (%)	B.A. or B.S. F / M	M.A. or M.S. Total (%)	M.A. or M.S. F/M	Ph.D. Total (%)	Ph.D. F/M
White, non-Hispanic	955 (58.7%)	457 / 498	48 (50.0%)	29 / 19	124 (44.4%)	64/60
American Indian/Alaska native	50 (3.1%)	31 / 19	1 (1.0%)	0 / 1	11 (3.9%)	7/4
Black, non-Hispanic	88 (5.4%)	66 / 22	7 (7.3%)	3 / 4	5 (1.8%)	4/1
Hispanic	61 (3.7%)	35 / 26	2 (2.1%)	1 / 1	9 (3.2%)	3/6
Asian	258 (15.9%)	143 / 115	10 (10.4%)	4 / 6	42 (15.1%)	14/28
Pacific Islander	4 (0.3%)	3 / 1	1 (1.0%)	1 / 0	1 (0.4%)	1/0
International	92 (5.7%)	63 / 29	21 (21.9%)	11 / 10	79 (28.3%)	36/43
Unknown	118 (7.3%)	52 / 66	6 (6.3%)	3 / 3	8 (2.9%)	2/6
TOTAL	**1626**	**850 / 776**	**96**	**52 / 44**	**279**	**131/148**

open channels

Which cellular organelle would get your vote?

Brad Graba, a biology teacher at William Fremd High School in Palatine, Ill., took advantage of the election-season hype and engaged his students on campus and on Twitter in a campaign that pitted organelles against organelles. Here's a selection of the some of the tweets from the activity. Read more at **www.wild-types.wordpress.com**. (Hat tip goes to ASBMB Today science writer Rajendrani Mukhopadhyay for spotting this fun meme and using Storify to capture it on her blog.)

@mr_graba: My students are running election campaigns for cell organelles. Creativity explosion in the classroom!

@ Golgi_Body2012: If you want a healthy nervous system, don't vote for peroxisomes. #Golgi2012

@TheNucleus2012: Why vote for chloroplast? It is something that is only found in plants. Vote for an organelle found in you, me, and your Dog! Vote Nucleus!

@Lysosomes2012: casually digesting some bad organelles #lysosomelife #cellprobs

@PlasmaMembrane4: @mr_graba will obviously vote for us, because we are like border control. The harmful things are kicked out, and the good things are let in!

@VOTE4RIBOSOMES: @mr_graba We make proteins cause we're awesome #livingthelife

@Wholly4Golgi: We package your macromolecules up better than FedEx. #vote4golgibody

@Reticulum_Rocks: Besties! We work together with the Golgi Body and share chemical products! @wholly4golgi

@NuCleanNucleus: @Reticulum_Rocks, when u screw up, you send the person TO the ER! #lol #badsciencejoke

On the Wild Types blog

Show tunes as part of a teaching strategy?

Love and heartache are well-established inspirations for songs. But Kevin Ahern at Oregon State University turns to another source: biochemistry. Take, for instance, the song "Translation," sung to the tune of "Maria" from "West Side Story": *Translation! / I just learned the steps of translation. / And all the things they say, / About tRNA, / Are true.* It gives you a new appreciation for and interest in the subject, doesn't it? That is Ahern's goal.

Fluorescent protein controls enzyme activity

These days, we can't imagine doing molecular biology experiments without green fluorescent protein and other fluorescent tags. In a paper in Science, researchers have made one do more than just work as a tracker. This engineered fluorescent protein can control a protein's activity.

lipid news

Holiday wishes from the Lipid Research Division

Another year has slipped by. I'll resist the temptation to follow that with the usual "slippery grease" references our members often face during this season. But I do want to take this opportunity to wish all of our members peace, health, happiness and great science in 2013!

The Lipid Research Division has had another good year. Our community within the American Society for Biochemistry and Molecular Biology continues to grow. We are now at 510 members. Our representation on ASBMB committees also has grown, and our representation at the annual meeting is as strong as ever. Our small meetings have expanded abroad and attracted new members from other countries. Jordan Scott from Rob Stahelin's laboratory at Indiana University–Purdue University Indianapolis recently agreed to serve as the webmaster of our Lipid Corner website. Jordan is a bright and energetic young scientist, so keep an eye on the Lipid Corner.

Next month, I'll be writing to outline plans for the upcoming year, including the announcement of the new director, who will assume this position in April. I'm looking forward to the new year with great enthusiasm. We do face some challenges, but we also have a strong community ready to meet those challenges. It should be fun and exciting as we move ahead.

-- Dan Raben

ASBMB TODAY ESSAY SERIES:

DERAILED *but* UNDETERRED

DEADLINE: DEC. 31, 2012

ASBMB Today is seeking personal essays for a special series called "Derailed but Undeterred."

The series will speak to the resilience required for success in science. We hope these first-person essays will impart emotion and insight into how scientists endured — or are still enduring — trials and tribulations, both uncommon and widespread.

Share with our readers how you navigated unexpected life events and scientific setbacks that threatened your professional and personal goals. Your story can be humorous, serious or something in between, but it must be, above all, true and personal. We welcome submissions from scientists and students at all stages.

Guidelines: *Essays must be unpublished, between 300 and 1,000 words and emailed to asbmbtoday@asbmb.org by Dec. 31, 2012. Please send your manuscript with a brief cover letter, including the title of your submission, complete contact information and an author bio of no more than 100 words.*