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ASBMB TODAY

THE MEMBER MAGAZINE OF THE AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

Curiosity & Cures

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The science behind this year's Nobel Prizes.

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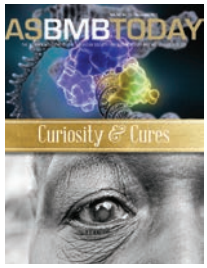

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2015's top 10

By Lauren Dockett

It is a heady thing to look back over a year's worth of publications. At ASBMB Today, it means getting to revisit all those in-depth features, moving personal essays, and a glittering parade of prize-winning ASBMB members (including four Nobels and a Breakthrough prize in just the past two months)! There are more than a few issues from the past year that I've dog-eared and piled into a safe corner so that we might reread coverage of research that we can dig deeper into one day. And where would we be without the reader exchanges touched off by the president's columns in 2015? Having decidedly duller watercooler talks, that's where!

In 2015, we generated 270 articles and 426 pages of content. More than half of those pages were written by ASBMB members, participants in our contributors program, or volunteers from the larger biochemistry and molecular biology community, reminding us that the magazine is an inclusive space for member voices and perspectives from all corners of the BMB world.

Late in the year, we use the imperfect metric of website page views to get a sense of our most popular articles. It's unfair to our most recent articles, since they haven't had as much time to accrue hits, but it's still an interesting glimpse at what readers have been seeking.

The 10 most-read online articles (so far) in 2015

1. Cover story | Waiting for the day to come by Rajendrani Mukhopadhyay (June/July)

2. Essay | The reality that dare not speak its name by Andrew D. Hollenbach (April)

3. Feature | Science in sign language by Maggie Kuo (February)

4. Cover story | Breaking dogma? by Rajendrani Mukhopadhyay (February)

5. President's Message | "Funding decisions: the NIH method" by Steven McKnight (April)

6. Defying Stereotypes | "So, a biochemist walks into a comedy club …" by Rajendrani Mukhopadhyay & Geoffrey Hunt (June/July)

7. Defying Stereotypes | "Beyond the finish line" by Geoffrey Hunt & Rajendrani Mukhopadhyay (February)

8. President's Message | "The straightjacket of hypothesis-driven research" by Steven McKnight (June/July)

9. President's Message | "Welcome aboard!" by Steven McKnight (August)

10. President's Message | "Two kinds of grants?" by Steven McKnight (May)

You'll see one member essay in that top-10 list and if we were to dig just a little deeper into our reader favorites, we'd find many more. Your stories are perennial hits.

Whatever year it is, this remains your magazine. Keep in touch in 2016 and be a part of it!

Lauren Dockett (ldockett@asbmb.org) is the managing editor of ASBMB Today.

PRESIDENT'S MESSAGE

Steven McKnight's column will resume next month.

Science policy year in review

By Chris Pickett

It has been a busy year in science policy. Congress debated major legislation in 2015 that could improve research funding, the National Institutes of Health unveiled some long-anticipated projects and the American Society for Biochemistry and Molecular Biology continued to increase its prominence as a leading voice on critical policy issues.

The ASBMB

In July, members of the ASBMB Public Affairs Advisory Committee published a paper in the Proceedings of the National Academy of Sciences that explored the scientific community's recommendations for improving the sustainability of the research enterprise (1). The society now is planning a summit that will bring together experts to develop implementation plans for some of the recommendations.

The ASBMB continued its efforts to provide new ways of understanding research funding and engaging with Congress. The society sponsored a congressional briefing in September that presented the effects of stagnant research budgets on scientists and encouraged a return to a period of budget growth. The society also played a major role in the recent #RaiseTheCaps lobbying push led by the Nondefense Discretionary United coalition. The push resulted in Congress relaxing the spending caps on the federal budget.

Congress

In the spring, the U.S. House of Representatives proposed $1 billion and the U.S. Senate proposed $2 billion in funding increases to the NIH budget for fiscal 2016. Neither of these increases has come to fruition. However, the success of the #RaiseTheCaps campaign means that Congress will have some flexibility to increase the budgets of federal science-funding agencies in the coming year.

In nonappropriations news, after more than a year's worth of work, debates and committee hearings, the House passed the 21st Century Cures Act in June. The bill would increase funding for the NIH by $8.8 billion over five years. While the increased funding would be welcome, the society still had several concerns about funding restrictions and other policy riders in the bill and ultimately neither endorsed nor opposed 21st Century Cures. As the Senate works on its own version of the bill, the ASBMB has been advocating for the Senate to include increased funding for all NIH institutes and centers and sensible policies that promote research. A draft version of the Senate's bill is expected in mid to late autumn.

Federal agencies

In June, the NIH unveiled a set of long-expected rules for grant applications meant to improve rigor and reproducibility in basic research (2). Some of the new guidelines include requiring grant applications to evaluate sex as a biological variable, authentication of cell lines and identification of antibodies (3).

The NIH also began work on its next big-science project, the Precision Medicine Initiative (4). The PMI is meant to sequence the genomes of one million Americans to make personalized medicine more of a reality. However, the federal agency is facing significant competition from Alphabet, the parent company of Google, which has begun working on a similar initiative.

And these were just the highlights! The development of policies around the use of CRISPR/Cas9 and similar technologies, the government avoiding shutdown and default, and the ASBMB's continuing efforts to engage young scientists in advocacy were all major storylines in 2015. We expect 2016 will be just as busy.

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Chris Pickett (cpickett@asbmb.org) is a policy analyst at the ASBMB.

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Hobbs wins Breakthrough Prize

HOBBS

Helen Hobbs, a professor of internal medicine and molecular genetics at the University of Texas Southwestern Medical Center at Dallas and an investigator at the Howard Hughes Medical Institute, has been awarded the Breakthrough Prize in Life Sciences for her innovative contributions to the field of genetics.

A set of international awards recognizing outstanding achievements in the life sciences, fundamental physics and mathematics, the $3 million Breakthrough Prizes were founded by prominent innovators in the fields of science and technology, including Google co-founder Sergey Brin, 23andMe founder Anne Wojcicki, Facebook founder Mark Zuckerberg and his wife Priscilla Chan, Alibaba founder Jack Ma and his wife, Cathy Zhang, and entrepreneur Yuri Milner and his wife, Julia Milner. The prizes are awarded at a celebrity-hosted, televised ceremony designed to promote science and inspire future innovators.

Hobbs holds the Eugene McDermott distinguished chair for the study of human growth and development; the Philip O'Bryan Montgomery Jr., M.D., distinguished chair in developmental biology; and the 1995 Dallas Heart Ball chair in cardiology research at the University of Texas Southwestern Medical Center at Dallas. Since 1999, she has directed the Dallas Heart Study, a multiethnic, population-based study in Dallas County designed to aid in the understanding of cardiovascular disease.

Hobbs, with her collaborator Jonathan Cohen, helped develop new treatments for heart and liver disease by identifying genes involved in lipid metabolism and fatty liver disease. She identified rare genetic variations that change the levels and distribution of cholesterol and other lipids in the body, leading to the development of cholesterol-lowering drugs that won U.S. Food and Drug Administration approval this summer.

Among her many accolades, Hobbs has been elected to the National Academy of Sciences, the American Academy of Arts and Sciences, and the National Academy of Medicine.

Lobel honored with Innovators Award and Edison Patent Award

LOBEL

Peter Lobel, a member of Rutgers University's Center for Advanced Biotechnology and Medicine and a professor in the department of biochemistry and molecular biology at Robert Wood Johnson Medical School, won a 2015 Innovators Award from the New Jersey Inventors Hall of Fame. Lobel and David Sleat at Rutgers were recognized for discovering the cause of Batten disease and for providing groundwork for treatment of the disease. Also known as late infantile neuronal ceroid lipofuscinoses, or LINCL, Batten disease is an inherited disorder of the nervous system that usually begins in early childhood and can cause loss of vision, recurrent seizures and motor problems. Patients ultimately become physically and mentally incapacitated before premature death in late childhood.

Batten disease is caused by mutations in the CLN2 gene and protein tripeptidyl peptidase I, or TPP1. Lobel and Sleat have developed a treatment method that involves administering TPP1 in an amount effective to reduce symptoms. Previously, patients' symptoms have been managed only by anti-epileptic drugs and physical, speech and occupational therapies. Initial clinical evaluation of a TTP1-based treatment shows a delay in the disease's progression.

Lobel and Sleat's treatment method is also being recognized with a 2015 biopharmaceutical Edison Patent Award from the Research and Development Council of New Jersey. The award recognizes scientists and inventors who do outstanding research and development work in the state.

Hanawalt and Pollard receive Wilbur Cross Medals

HANAWALT

POLLARD

Yale University alumni Philip C. Hanawalt and Thomas Pollard are being honored by the Yale Graduate School of Arts and Sciences with Wilbur Cross Medals. Named in honor of Wilbur Lucius Cross, former dean of the Yale Graduate School and governor of the state of Connecticut, the medal recognizes the outstanding achievements of alumni in scholarship, teaching, academic administration and public service.

Hanawalt is the Morris Herzstein professor in biology at Stanford University. A pioneer in the field of DNA repair, he discovered the process of repair replication in DNA in 1963 and subsequently helped develop novel techniques for studying DNA repair. In addition to his research accomplishments, Hanawalt is a celebrated educator and recipient of the Excellence in Teaching Award from the Northern California Chapter of Phi Beta Kappa. He is also a member of the National Academy of Sciences and a fellow of the American Academy of Arts and Sciences.

Pollard is the Sterling professor of molecular, dellular and developmental biology at Yale. An honorary recipient of the Wilbur Cross Medal, Pollard is being recognized for his service to

the Yale Graduate School. He served as dean of the graduate school from 2010 to 2014 and is celebrated for his efforts to develop mentoring strategies and other initiatives for students. Pollard maintains an active lab group, which explores the molecular basis of cellular motility and cytokinesis. He has pioneered investigations into the actin cytoskeleton, which accounts for structure and movement in all cells. Pollard received a Gairdner International Award in 2006.

Schell is a Young Scientist Seminar Series winner


SCHELL

John Schell, an M.D./Ph.D. candidate in the lab of Jared Rutter at the University of Utah, is one of five winners of iBiology's Young Scientist Seminar Series. A vehicle for young scientists, Ph.D. candidates or postdocs to promote their research to a wider audience, the series competition provides winners an all-expense-paid trip to San Francisco, California, where they take part in a science communication workshop and record 30-minute research talks that are posted and advertised on the iBiology website.

Supported by the Lasker Foundation and the Alan Alda Center for Communicating Science, the Young Scientist Seminar Series helps young biologists hone their message, improve communication skills and showcase their work on a larger stage.

Schell is working on cellular metabolic homeostasis and, along with Rutter, helped identify the mitochondrial pyruvate carrier, a gene that plays an important role in cellular metabolism. In his video for the Young Scientist Seminar Series (www.ibiology.org/ibioseminars/john-schell.html), he examined how defects of the mitochondria affect human metabolic function.

Written by Erik Chaulk

Five ASBMB members elected to National Academy of Medicine

Five members of ASBMB were among the 70 new members and 10 foreign associates elected to the National Academy of Medicine. Election to the NAM is considered one of the highest honors in the fields of health and medicine and recognizes individuals who have demonstrated outstanding professional achievement and commitment to service. Below are the newly elected members:


ABEL

Evan Dale Abel, Carver College of Medicine, University of Iowa


CAPECCHI

Mario R. Capecchi, University of Utah School of Medicine


GLASS

Christopher K. Glass, University of California, San Diego


RAMOS

Kenneth S. Ramos, University of Arizona Health Sciences Center


STRUHL

Kevin Struhl, Harvard Medical School

Written by Alexandra Taylor

IN MEMORIAM: Oscar Touster (1921 – 2015)


TOUSTER

Oscar Touster, emeritus professor of molecular biology and biochemistry at Vanderbilt University, passed away in February. He was 93.

Touster grew up in New York City and obtained a bachelor's in chemistry from the College of the City of New York. He recieved his master's from Oberlin College in 1942, but World War II delayed his doctoral work.

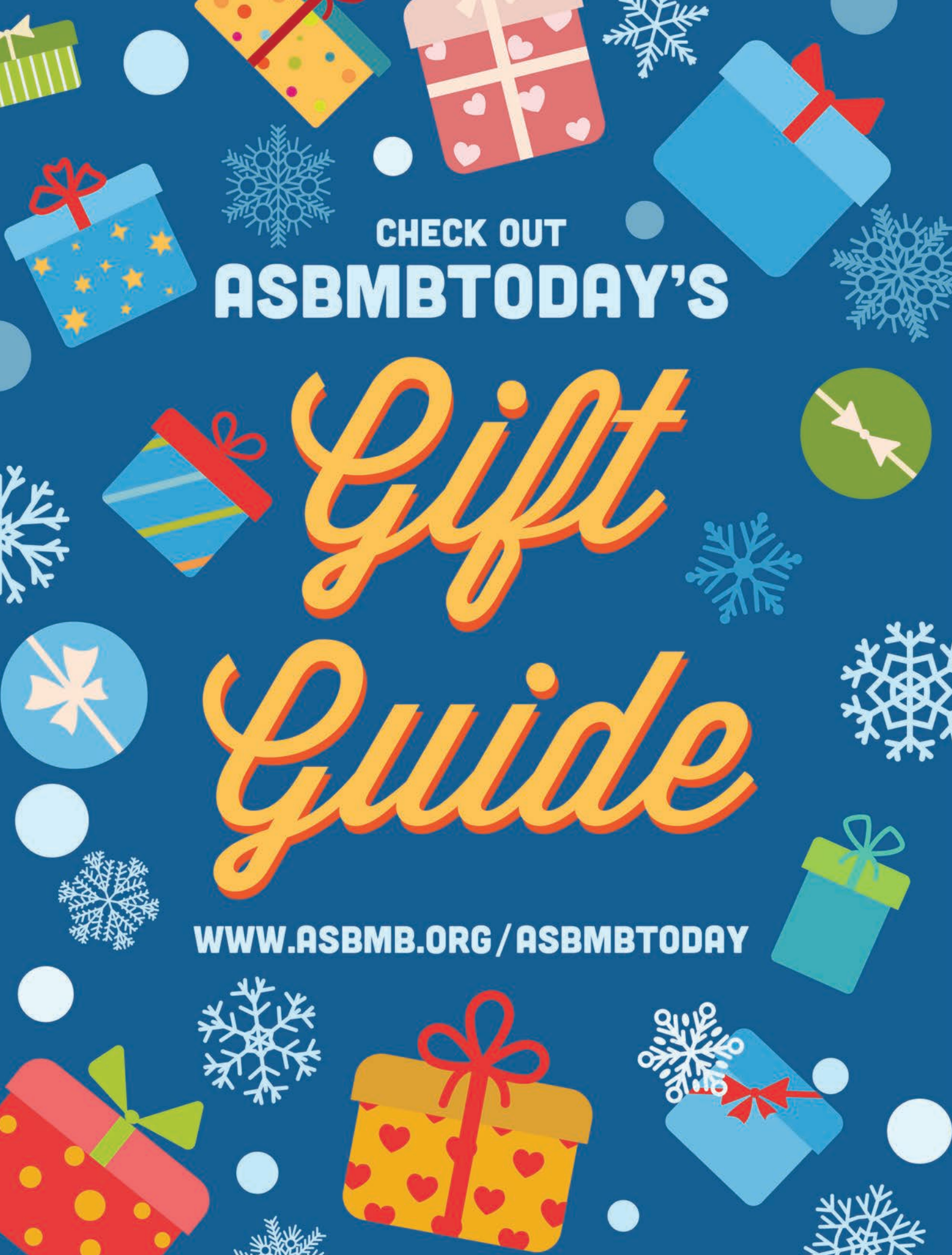
Before returning to his studies, Touster worked for the TNT-producing Atlas Powder Company, training as a lab supervisor. He met his wife Eva, who later became a poet and professor of English at Peabody College in Nashville, in a plant in Kentucky. He subsequently served as a research biochemist at Abbott Laboratories and worked on penicillin research with University of Illinois' Herbert Carter. Touster ultimately would obtain a Ph.D. in biochemistry and continue working with Carter after the war.

In 1947, Touster joined Vanderbilt University and remained at the school for his entire career. Sixteen years after joining, he founded and became the first chairman of the department of molecular biology at Vanderbilt's College of Arts and Science and graduate school. He received the Thomas Jefferson Award and the Harvie Branscomb Award from Vanderbilt for his service.

Touster also served as president of the Oak Ridge Associated Universities, a consortium aimed at promoting and enhancing scientific research and education, from 1976 to 1988.

Preceded in death by his wife of 65 years, Touster is survived by a daughter and two grandchildren.

Written by Erik Chaulk.
Image courtesy of Vanderbilt University Special Collections and University Archives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Glycobiologists expand symbol nomenclature

By Alexandra Taylor

SHAPE	White	Blue	Green	Yellow	Orange	Pink	Purple	Light Blue	Brown	Red
Filled Circle	Hexose	**Glc**	**Man**	**Gal**	Gul	Alt	All	Tal	Ido	
Filled Square	HexNAc	**GlcNAc**	**ManNAc**	**GalNAc**	GulNAc	AltNAc	AllNAc	TalNAc	IdoNAc	
Crossed Square	Hexosamine	**GlcN**	**ManN**	**GalN**	GulN	AltN	AllN	TalN	IdoN	
Divided Diamond	Hexuronate	**GlcA**	**ManA**	**GalA**	GulA	AltA	AllA	TalA	**IdoA**	
Filled Triangle	Deoxyhexose	Qui	Rha			6dAlt		6dTal		**Fuc**
Divided Triangle	DeoxyhexNAc	QuiNAc	RhaNAc							FucNAc
Flat Rectangle	Di-deoxyhexose	Oli	Tyv		Abe	Par	Dig	Col		
Filled Star	Pentose		Ara	Lyx	**Xyl**	Rib				
Filled Diamond	Nonulosonate		**Kdn**				**Neu5Ac**	**Neu5Gc**	Neu	
Flat Hexagon	Unknown	Bac	LDManHep	Kdo	Dha	DDManHep	MurNAc	MurNGc	Mur	
Pentagon	Assigned	Api	Fruc	Tag	Sor	Psi				

THE CONSORTIUM OF GLYCOBIOLOGY EDITORS, LA JOLLA, CALIFORNIA.ORIGINAL DRAWING BY RICHARD D. CUMMINGS.

A new nomenclature system extends to plants, invertebrates, archaea and bacteria.

Glycans are structurally complex and difficult to represent on paper. This December, editors of a glycobiology textbook introduced an extended nomenclature system that simplifies complicated branching sugar structures into easy-to-use symbols. The new nomenclature will be available for free as an advance online appendix of the third edition of "Essentials of Glycobiology," published by Cold Spring Harbor Press.

The system expands on the widely adopted nomenclature from the textbook's second edition (2005). That version was limited to glycans in vertebrates. The new system has been expanded to include common monosaccharides in plants, invertebrates, archaea and bacteria. "We're trying to address the fact that there are many more monosaccharides in nature than the limited list represented in the current version," says Ajit Varki at the University of California, San Diego. Varki, a member of the American Society for Biochemistry and Molecular Biology, is executive editor of the textbook's third edition.

The goal in developing this system was to make it logical, easy to remember, and easy to use. New symbols have been added, but existing symbols will remain intact, making the system easier to adopt. In an invited publication for the December issue of the journal Glycobiology, the book editors said that they hope the new nomenclature will "help students and researchers to more easily discover and appreciate the relevance and beauty of glycan diversity in living systems, and to communicate this exciting information to others."

There will be one central website available through the National Center for Biotechnology Information as a reference. Each monosaccharide symbol will be linked to its entry in PubChem at NCBI, and pre-drawn symbols will be available to download or copy and paste.

The editors hope that making the system freely available will discourage the introduction of minor variations to the nomenclature. These variations popped up when the second edition's system became widely adopted.

Consistency may help to avoid confusion, but Varki stresses that adoption of this system will be entirely voluntary. "The last thing you want to do is try and push a nomenclature onto other scientists," he says.

No official international body currently governs nomenclature for the symbolic depiction of glycans. The new system is the product of a collaboration between many leaders in the field. The editors of "Essentials of Glycobiology" are coordinating with several databases that may decide to adopt it. The International Union of Pure and Applied Chemistry, for example, is considering using the system in its recommendations for carbohydrate nomenclature.

After the recent National Research Council report on glycosciences, the National Institutes of Health Director's Common Fund awarded $10 million toward a glycoscience program for development of new tools and approaches. These are promising signals of the growing importance of the field. For glycoscience to make unhampered progress, a clear, accessible and ubiquitous nomenclature could provide some much-needed consistency.

Alexandra Taylor (ataylor@asbmb.org) is a science writing intern at ASBMB Today and a master's candidate in science and medical writing at Johns Hopkins University.

How dangerous are holiday plants to pets?

By Indumathi Sridharan

Holiday decorations aren't complete without ornamental plants. But certain seemingly innocuous holiday plants can be poisonous to pets. If ingested, these plants can induce vomiting, diarrhea, abdominal pain and excessive salivation. Seizures, coma or death may occur in severe cases. In 2009, the Animal Poison Control Center at the American Society for Prevention of Cruelty to Animals received 8,000 calls related to poisonous plants during holiday season.

Holly, amaryllis and Christmas rose are some of the most toxic holiday plants, according to Tina Wismer, the medical director of the ASPCA Animal Poison Control Center. The toxic effects of these plants come from specific bioactive compounds.

"Holly contains triterpenoid saponins; these are soaplike substances that irritate the digestive tract and can cause severe vomiting and diarrhea, sometimes with blood. Fortunately, most species of holly have prickly and leathery leaves that are not normally attractive to pets," says Wismer.

Cardiac glycosides in the Christmas rose can cause death by affecting heart rhythm. These compounds affect the contractility of cardiac muscles by binding to Na-K ATPase, an enzyme that modulates intracellular concentrations of sodium and potassium ions. Amaryllis contains alkaloid compounds, such as lycorine. Lycorine inhibits peptide bond formation during protein synthesis by interfering with the peptidyl transferase activity of ribosomes (1, 2). These toxins can lead to depression, convulsions and tremors.

FLORA DE FILIPINAS

Flowers of the amaryllis are less toxic than the bulb.

The severity of the toxic effects depends on many factors. "One important factor is the plant itself. The toxic amounts in a plant will vary with the species and stress the plant was exposed to during growth," says Wismer. "Another factor is the size of the animal and the amount of plant ingested — did the cat just nibble a leaf or eat the entire plant?"

In the case of amaryllis, the toxicity varies according to plant part; the foliage and flowers are less toxic than the bulb. Some plants are deadly only to certain pets. For example, true lilies cause kidney failure in cats, while dogs experience only mild stomach upset. The reason for this species difference is unknown.

Not all holiday plants are a cause for concern. Contrary to popular belief, poinsettias (Euphorbia pulcherrima) are not toxic to pets. Research indicates that the pulcherrima species lacks diterpenes, a key toxic substance generally found in the Euphorbia genus (3).

Despite best efforts to keep pets away from plants, accidental ingestion may happen. In preparation for such an event, Wismer recommends keeping a list of all plants in the household and calling a veterinarian in cases of suspected ingestion.

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Indumathi Sridharan (sridharan.indumathi@gmail.com) earned her bachelor's degree in bioinformatics in India. She holds a Ph.D. in molecular biochemistry from Illinois Institute of Technology, Chicago. She did her postdoctoral work in bionanotechnology at Northwestern University.

Holiday plants dangerous for cats and dogs (except one)

"Since many different plants have the same common name, knowing their Latin names can come in handy."
– *Tina Wismer,* American Society for Prevention of Cruelty to Animals *Animal Poison Control Center*

FLICKR COMMONS USER DREW AVERY

Hippeastrum (amaryllis lily, belladonna lily, Saint Joseph lily, cape belladonna, naked lady)

THE U.S. DEPARTMENT OF AGRICULTURE

Ilex opaca (American holly)

FLORA VON DEUTSCHLAND, ÖSTERREICH UND DER SCHWEIZ (1885)

Ilex aquifolium (English holly)

FLORA VON DEUTSCHLAND, ÖSTERREICH UND DER SCHWEIZ (1885)

Helleborus niger (Christmas rose, hellebore, lenten rose, Easter rose)

WIKIMEDIA COMMONS USER TARAGUI

Solanum pseudocapsicu (Jerusalem cherry)

THE NATIONAL GEOGRAPHIC MAGAZINE (1917)

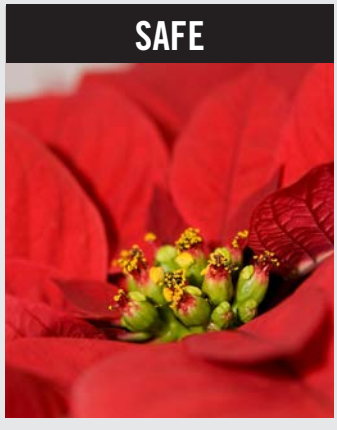
Phoradendron flavescens (American mistletoe)

WIKIMEDIA COMMONS USER VIZU

Viscum album (European mistletoe)

FLORA VON DEUTSCHLAND, ÖSTERREICH UND DER SCHWEIZ (1885)

Solanum dulcamara (bittersweet nightshade)



FREEPIXELS.COM

Euphorbia pulcherrima (poinsettia)

Bioengineering a microbial workforce

By Kathleen McCann

They may not punch timecards, wear protective clothing or gossip around the water cooler, but microorganisms are a vital part of the industrial work force. The metabolic pathways of microorganisms have been harnessed and engineered to produce molecules that are important to the pharmaceutical, food, chemical and alternative-energy industries. In the November issue of the **Journal of Lipid Research**, investigators from the University of Saskatchewan describe how they engineered one particular yeast, Pichia pastoris, to produce ricinoleic acid, a rare fatty acid commonly used in the manufacture of a wide variety of products.

Ricinoleic acid is produced naturally in high amounts by castor beans. But harvesting the acid from the beans can be tricky, since castor beans also produce high levels of the potent toxin ricin. To circumvent this problem, researchers have tried identifying other ways of procuring ricinoleic acid from plants. Initially, tobacco and the commonly used plant model organism Arabidopsis were engineered to express an enzyme of the ricinoleic acid biosynthesis pathway. But both plants produced a comparatively small fraction of ricinoleic acid and proved to be poor replacements for the castor bean.

Xiao Qiu and his colleagues have a long-standing interest in lipid biosynthesis and bioengineering, and they turned to microorganisms to tackle the ricinoleic acid problem. Like the castor bean, the fungus Claviceps purpurea is known to produce high levels of ricinoleic acid. Qiu previously had identified two enzymes, CpFAH and CpDGAT2, that were important for the biosynthesis of ricinoleic acid in C. purpurea and had demonstrated that when these enzymes were expressed in yeast, the yeast produced higher levels of ricinoleic acid.

U.S. DEPARTMENT OF AGRICULTURE

Xiao Qiu and colleagues at the University of Saskatchewan engineered a yeast to produce high yields of ricinoleic acid, which occurs naturally in castor beans.

In the article, Qiu and his colleagues describe how they took this production process one step further by identifying yet another enzyme that plays a critical role in the biosynthesis of ricinoleic acid. When expressed in yeast, the enzyme CpDGAT1 significantly outperformed CpDGAT2. With this new enzymatic ace in hand, they turned to the yeast Pichia pastoris, which is known for producing a high yield of biomass and oil. They incorporated CpFAH and CpDGAT1 into the genome in such a way that they could express these enzymes conditionally. After inducing expression for three days, ricinoleic acid accounted for more than half of the total fatty acids, representing a significant improvement over the production levels seen in engineered plants.

While Qiu's work represents a substantial step forward in bioengineering microorganisms for industrial gains, it does raise some interesting questions. For instance, why was Pichia a more effective organism for ricinoleic acid? Can Pichia be engineered to produce high amounts of other important biomaterials? Furthermore, can we determine what makes Pichia such a robust organism and then engineer a plant to have the same capabilities? However these questions are answered, it has become clear that microorganisms can make powerful contributions to modern industry and society.

Kathleen McCann (kathleen.mccann2@nih.gov) earned her Ph.D. in genetics from Yale University. She is now a postdoctoral fellow at the National Institute of Environmental Health Sciences.

Structural studies of GRK5

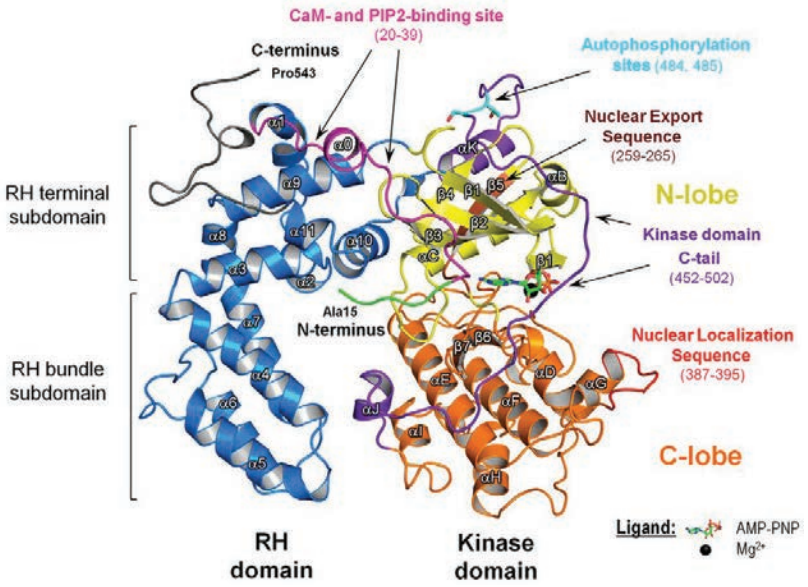
A conversation with two JBC Paper of the Week authors

By Diedre Ribbens

*The **Journal of Biological Chemistry** featured two Papers of the Week in August about structural studies of G-protein-coupled receptor kinase 5, or GRK5. The studies (1, 2) were authored by two groups that conducted their work separately and then later discovered that their structures of GRK5 were in agreement.*

The JBC's podcast host, Diedre Ribbens, interviewed the corresponding authors of the papers, Jeff Benovic of Thomas Jefferson University and John Tesmer at the University of Michigan, to hear more about their work on the GRK5 protein and how these two structures have affected the GRK field. Here, we've reprinted some of their conversation. You can listen to the full podcast or read the full transcript at www.jbc.org.

Benovic and Tesmer both got their start studying GRKs with Robert Lefkowitz, a Howard Hughes Medical Institute investigator at Duke University Medical Center whose group pioneered the GRK field. (Lefkowitz won the Nobel Prize in chemistry in 2012.)



Ribbon representation of GRK5·AMP-PNP crystal structure. Full-length GRK5(1–590) was crystallized, and residues 15–543 are clearly resolved (the first and last residues are labeled).

DIEDRE RIBBENS: G-protein-coupled receptor kinases, or GRKs, are a family of protein kinases that have a role in the desensitization of G-protein-coupled receptors. In particular, GRK5, one of the most widely expressed proteins in the GRK family, has been implicated in several diseases, such as cardiovascular disease, cancer, diabetes and Alzheimer's. Although structures have been solved for other GRKs, such as GRK2 and GRK6, no structure has been solved for the clinically relevant GRK5. The study by Benovic's group was able to resolve the structure of human GRK5 at a resolution of 1.8 Å in complex with either the ATP analog AMP-PNP or the nucleoside sangivamycin. The Tesmer group study also solved the GRK5 structure to a 2.4 Å resolution but complexed with an inhibitor called CCG215022. Importantly, the two groups realized that their structures captured GRK5 in a strikingly similar conformation at its C-terminus that was unique to this enzyme and not found in other GRKs. Ultimately, these structures will enable future studies probing the function of GRK5 and possibly lead to the design of selective inhibitors.

In my interview with Benovic and Tesmer, they shared how they became interested in studying GRKs, how their work on GRK5 addressed previously unknown questions in their field and where each of their research groups would like to go next.

BENOVIC: Well, for me, it actually goes back to my graduate work in the mid-'80s (when) I worked with Bob Lefkowitz, and we were trying to identify the kinase that phosphorylates the $\beta_2$adrenergic receptor in an agonist-dependent manner. And then this … ultimately led to the cloning of cDNAs for what are now called GRK5 and GRK6. We published that in 1993, and then we really spent, not full time, but a good portion of our time over the last 20 years trying to understand how this kinase functioned.

RIBBENS: Tesmer also crossed paths with the Lefkowitz lab during his postdoc. As a collaborator, he worked on GRK2, which eventually led him to start his own research group focused on GRKs.

BENOVIC: (GRK5 is) one of the few kinases that John's group hasn't crystallized, but it's interesting because it's been implicated in a number of human diseases, including various cardiovascular diseases, prostate cancer, diabetes and a number of neurological

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disorders. So I think it's an interesting enzyme and interesting potential therapeutic target.

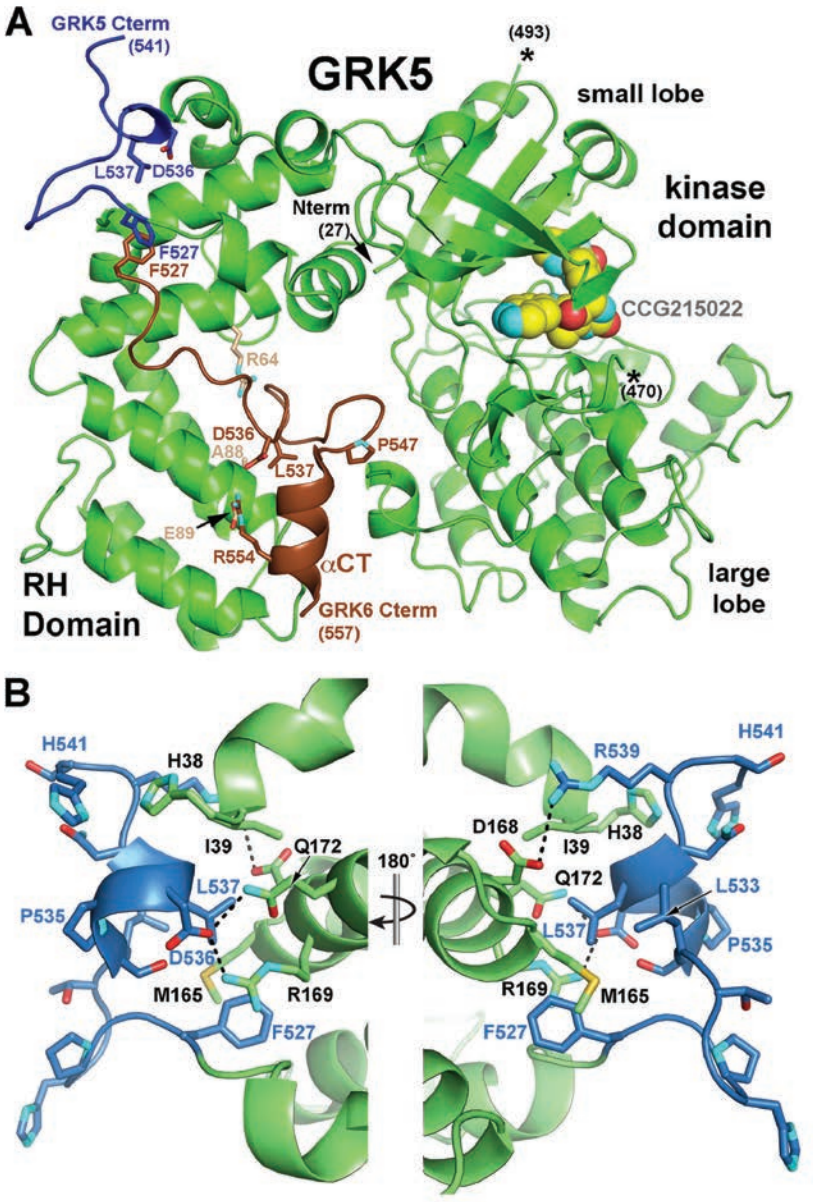
TESMER: When I started my lab in the late '90s, my initial project was to structurally characterize GRK2 … and we were interested in it in principle because it interacted with a lot of G-protein subunits, and that was my specialty as a postdoc. And, since then, I actually collaborated with Jeff to look at other members of the GRK family, and one that we worked together on was GRK6, which we published back in 2006. And GRK5 is a member of that subfamily to which GRK6 also belongs.

More recently, we decided to look at these kinases more in a translational sense because we had a good feel for what they looked like structurally; and of course GRK2 was one of them because of its involvement in heart failure; and then we also turned back to GRK5 because, as Jeff pointed out, it's involved in a host of diseases including cardiac hypertrophy. And so it's been actually something that we've been working on for a number of years and looking for the structure of, which we finally got to be able to publish with Jeff this year.

RIBBENS: Tesmer and Benovic crossed paths often, leading to the occasional collaborative study.

TESMER: I think the people in our field, at least I feel, have a habit of getting together when they need to and going their own ways when they feel like they're able to … Jeff, I think we first started working together in 2003 or so …

BENOVIC: Right. Yeah. We had certainly had our own efforts actually in trying to crystallize GRK2, and they didn't really go anywhere, and then that was a major focus of John's group. And a former trainee of mine, Rachel Sterne-Marr — I kind of linked her up with John to help with some characterization of GRK2. So that was kind of our initial interaction



A, comparison with the GRK6 sangivamycin complex (PDB entry 3NYN) (13). CCG215022 (spheres with yellow carbons) binds in the active site of the GRK5 kinase domain. As in most other GRK structures, the AST region is disordered (last visible residues denoted by asterisks). The C-terminal region of GRK5 (royal blue) has a dramatically different conformation than observed for GRK6 sangivamycin (brown), despite the fact they are closely related enzymes (see C). Key residues in the C terminus are labeled to emphasize how they contribute to packing in each structure. Side chains shown with beige carbons are from the RH domain of GRK6 (same identity and numbering as in GRK5). GRK6-Pro-547 is analogous to GRK5-Pro-546, which was mutated in this study. B, close-up view of the interactions between the C-terminal region (royal blue) and the RH domain (green). Hydrogen bonds/salt bridges are shown as dashed lines.

on the crystallization side of it, and then we worked somewhat on GRK6, but it was really us just providing reagents to John to do the work — to facilitate the work. You know, so we've collaborated over the years. I think we're trying to do some similar things, and a lot of that will be collaborative, and some will kind of be trying to do some other things and publishing on our own too, I'm sure.

TESMER: Mm hmm. It's all good.

RIBBENS: Benovic admitted that his group had never undertaken a solo

effort to solve a GRK crystal structure before, but GRK5 seemed to present the perfect opportunity to make an attempt at doing so.

BENOVIC: Really, the field, at least the GRK crystallography field, which has given tremendous insight — in terms of how these proteins … function, how they fold — was almost completely driven by John's work. He crystallized GRK2, GRK2 in various complexes, GRK1 and GRK6 and has multiple papers and has gained a lot of insight.

For us, the challenge was that we really had never tried to crystallize a GRK alone … But we thought really one of our goals was to better understand how GRKs interact with GPCRs and how this results in activation of the GRK … GRK5 was a very well-behaved protein, so we thought it might be a good model to really pursue that effort. And then when … a senior postdoc joined my lab a few years ago — Konstantin Komolov, who had a lot of experience with GRK1 — we decided that he would focus on trying to crystallize GRK5. And this paper for us is the culmination of … his initial efforts in this area.

And it turns out that he actually got crystals almost immediately once he purified enough protein … Then, once we had that, we really just used John's GRK6 structure to do molecular replacement to solve the structure of GRK5.

RIBBENS: Tesmer's group was going at the problem from a slightly different angle, as they wanted to solve the structure of GRK5 so his group could focus on the design of specific inhibitors of the enzyme.

TESMER: We decided to tackle the problem of developing selected inhibitors for GRKs, and there's a need for this in a couple different camps, one of which is that a lot of electro-pharmacologists would like to know which of these particular kinases are responsible for certain phenotypes in cells, and there's no chemical probes out there that are very good, in my opinion, that are selected for individual members of this family.

And, of course, there are unresolved issues … GRK5 is very closely related to GRK6, and there's a bit of a controversy on what's going on with its C-terminal structure, and its C-terminus is very important for its membrane targeting in cells. In prior structures of GRK6, it appeared to be in a conformation that wouldn't permit it to interact with membranes, and so that was an unanswered question as to what was really going on in the C-terminus of the subfamily of GRKs.

RIBBENS: I asked the two researchers at what point they became aware of their simultaneous efforts to obtain a GRK5 crystal structure and how they came to publish in the same issue of the JBC.

BENOVIC: We certainly discussed it initially at an (American Society for Biochemistry and Molecular Biology) meeting a few years ago. We had had the structure at that point, and I'm not sure how far along John had been on his structure, whether they had their complex or not at that point … And then we've been in a few meetings together and have talked in more detail about it.

TESMER: Yeah, that's exactly right. And I have to thank Jeff. I think his structure was done earlier than mine, and I think he actually delayed his publication so that we could resolve our structure fully and write the paper and publish them together, which I'm very thankful for.

RIBBENS: Working with the human GRK5, Benovic's group seemed to solve the GRK5 without too many roadblocks, but that was not the case for Tesmer's group working with the bovine form of the enzyme.

TESMER: The truth of the matter is we've been working on GRK5 for quite some time, and we had actually given up on it. And, of course, kudos to Jeff for getting it done with the human enzyme. We're working with bovine. And as a consequence of our drug-design efforts, a postdoc in my lab, Kristoff Homan, noticed that one of the inhibitors that we had rationally designed as a GRK2 inhibitor … increased the thermostability of GRK5 enormously …

That worked almost instantly after — I don't know — four years of trying to crystallize it otherwise, and so that led us to the structure. And what the structure enabled us to do is look at how this drug interacts with GRK5. It verified our rational design strategies. We're very pleased with that.

RIBBENS: Ultimately, publishing back-to-back papers allows the work of both groups to garner equal visibility from the field and draws attention to the important similarities between their two structures.

TESMER: The neat thing was that we both resolved the same C-terminal structure, and I believe I speak for both of us in that we both believe that this is the proper confirmation of the C-terminus when this enzyme would be interacting with a membrane. And that's really the power of the two papers, I think. So often in crystal structures, the flexible parts or the movable parts and frankly the interesting parts end up trapped in crystal contacts or in weird conformations, and it's sometimes hard to figure out if it's functional or not. And when you get two independent structures, completely different crystal forms, it's really a powerful confirmation that you're looking at the right thing.

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Engaging with enzymes

Reflections on Ortiz de Montellano's passion for heme and renewal

By Alexandra Pantos

ORTIZ DE MONTELLANO

In a recent issue of the **Journal of Biological Chemistry**, Paul Ortiz de Montellano, a professor in the pharmaceutical chemistry and pharmacology departments at the University of California, San Francisco, looked back on a scientific career that revolved around heme enzymes. Heme enzymes perform a wide array of functions and are involved in biosynthesis, carrying oxygen in the blood and metabolizing drugs. Ortiz de Montellano is best known in scientific circles for his extensive research on the cytochrome P450 family of enzymes and his work with heme oxygenase and heme-modifying peroxidases tied to cytochrome P450.

Born in Mexico City to the distinguished Mexican poet Bernard Ortiz de Montellano and an American mother who was a teacher from Missouri, Ortiz de Montellano grew up with two siblings. His younger sister, Ana, went on to become a writer and professor, and an older brother, Bernard, who studied to be a chemist, is now an emeritus professor of anthropology.

With a bit of help from a biology teacher he calls "phenomenal," Ortiz de Montellano discovered a passion for science as a high schooler in San Antonio, Texas, and went on to the Massachusetts Institute of Technology for his undergraduate degree in chemistry. He says he always knew he belonged in science, but it was his brother enrolling in graduate school at the same time that Ortiz de Montellano started his undergraduate career that sealed his choice of field.

Ortiz de Montellano went on to do his graduate work in bioorganic chemistry at Harvard University under E.J. Corey, who won the 1990 Nobel Prize in Chemistry, and Konrad Bloch, who won the 1964 Nobel Prize in Physiology. After earning his Ph.D., Ortiz de Montellano did a postdoctoral fellowship in bioorganic chemistry at the Swiss Federal Institute of Technology in Zurich, Switzerland.

Ortiz de Montellano has studied a wide array of topics since he joined the University of California, San Francisco, as an independent researcher in 1972. His most notable contributions have been to the study of cytochrome P450, a huge family of more than 21,000 enzymes that have a heme cofactor. That work has included studying porphyria, a rare disease that can cause neurological symptoms and skin problems from the buildup of excess porphyrins. (In normal quantities, porphyrins are used to produce heme.) Ortiz de Montellano also has researched multiple classes of hemoproteins and enzymes found in Mycobacterium tuberculosis, the bacterium which causes most cases of tuberculosis. Since tuberculosis is a leading cause of death in HIV/AIDS patients, this research was done as part of a team studying HIV/AIDS.

Ortiz de Montellano is currently considering following in his father's footsteps and becoming a writer, perhaps of novels. He also enjoys reading about history and historical fiction and notes particular interests in the industrial revolution, military history, and the mid-1600s, during which Louis XIV and Charles II reigned.

Ortiz de Montellano says he believes it is "always important to take time to renew oneself" and has taken five sabbaticals over the years. His advice to young scientists is to keep one foot in the ideal world and one in the practical world. "One has to keep in mind that one has to eventually make a living," he says. But he stresses that once the practicalities are taken care of, it is important to do something you love.

The students and postdoctoral fellows in Paul Ortiz de Montellano's laboratory when they entered the cytochrome P450 and heme world. Seated from left to right, Kathryn Prickett, Paul Ortiz de Montellano, Dianne Jassawalla. Standing from left to right, Wayne Vinson, Kent Kunze, Bruce Mico, Gary Yost and Stephen Dinizo. Kunze, Mico, Yost, and Dinizo were the founding members of the P450 team. Prickett, Jassawalla and Vinson worked on squalene biogenesis.

Alexandra Pantos is an editorial assistant at the ASBMB and a senior biology student at the University of Maryland.

Racca wins Tabor Award for lipid research

By Erik Maradiaga

Ana Racca, a postdoctoral researcher at the National University of Córdoba in Córdoba, Argentina, received the **Journal of Biological Chemistry**/Herbert Tabor Young Investigator Award for her research on two members of the Fos transcription family and their relationship to malignant cell growth in breast tumors.

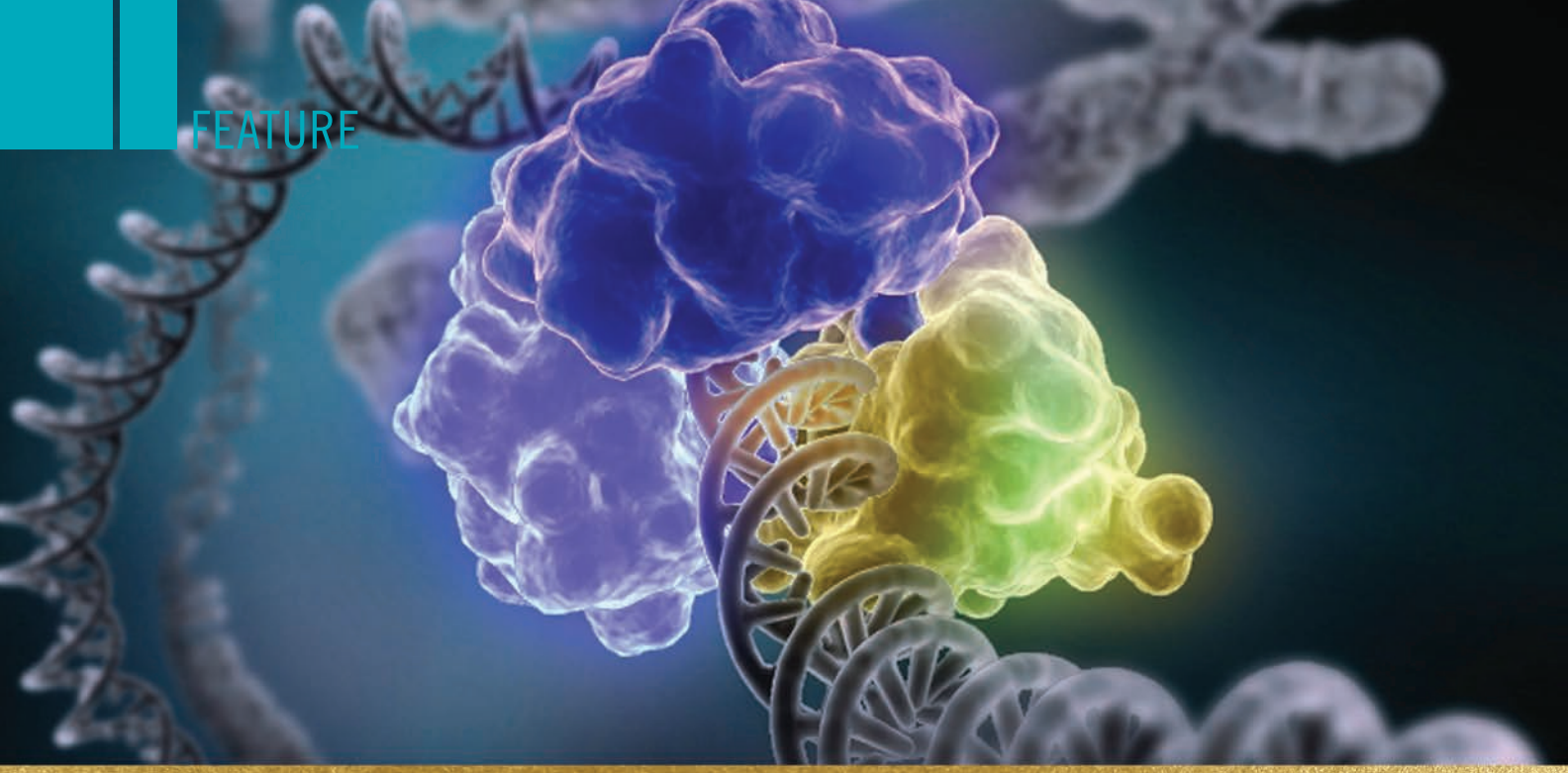
Racca has shown that c-Fos and Fra-1 work in the cytoplasm independent of their nuclear functions as transcription factors. The two molecules interact with and activate key enzymes of the phospholipid synthesis pathway — particularly CDP-DAG synthase — by increasing the rate of membrane biogenesis in the endoplasmic reticulum. This increase helps sustain the proliferation of malignant breast cells.

Raised in the town of Carmen de Patagones in southern Argentina, Racca moved to Córdoba for a biochemistry degree at the National University of Córdoba. She remained for a Ph.D., joining the lab of Graciela Panzetta and working on trophoblast differentiation in normal and diseased human placenta. Her special focus was on the role of Krüppel-like factor 6, and before completing her doctorate, she extended her work on KLF6 and the placenta in Charles H. Graham's laboratory at Queens University in Ontario, Canada. Racca returned to Córdoba to finish her Ph.D. and then joined Beatriz Caputto's lab for a postdoctoral fellowship. Caputto's lab specializes in the molecular mechanisms of c-Fos and Fra-1.

Ana Racca received the Tabor award from JBC Associate Editor George Carman at the 56th International Conference on the Bioscience of Lipids in Argentina.

Racca says that because c-Fos and Fra-1 are expressed at nearly undetectable levels in healthy breast cells, therapeutic strategies targeting their cytoplasmic function shouldn't do secondary harm. She will continue her work on the interactions of c-Fos and Fra-1 and study how negative dominant peptides derived from the proteins they activate can help block phospholipid synthesis and slow tumor growth.

Erik Maradiaga (em3914a@student.american.edu) is a biology major at American University.



Curiosity & Cures

This year's Nobel Prizes in chemistry and medicine will reward fundamental research that illuminated DNA repair mechanisms and helped establish a cure for neglected tropical diseases. In the two articles that follow, Alexandra Taylor gets the story on the science behind the prizes.

Combating parasitic diseases

Nobel in medicine recognizes work that led to treatment for river blindness and lymphatic filariasis

By Alexandra Taylor

After nearly a decade of digging in the dirt, researchers in the 1970s unearthed a novel treatment for parasitic infections. The scientists had sifted through hundreds of thousands of soil samples before coming up with the powerful properties of ivermectin. Ivermectin is potent, cheap to produce and easy to administer. After its success as a veterinary antiparasitic, ivermectin won approval in 1987 for use in humans, bringing hope to the hundreds of millions of people suffering from debilitating, yet neglected, tropical diseases.

On Dec. 10, Satoshi Ōmura, a member of the American Society for Biochemistry and Molecular Biology, will receive part of the Nobel Prize in medicine for his work on ivermectin, which is used to treat river blindness and lymphatic filariasis. Ōmura will split one half of the prize with William C. Campbell of Drew University, who worked on ivermectin as a member of Merck's natural products team. (Ōmura and Campbell will receive the Nobel Prize alongside Tu Youyou, who is recognized for her discovery of artemisinin, an antimalarial drug.)

Origins of disease

River blindness and lymphatic filariasis both are caused by parasitic roundworms and are endemic to some of the world's poorest areas. Rural regions of sub-Saharan Africa are affected most severely by river blindness, although the disease also is found in limited areas in South and Central America and Yemen. Lymphatic filariasis, often referred to as elephantiasis, occurs in tropical and subtropical regions of Asia, Africa, South America, the Western Pacific and the Caribbean.

River blindness is spread among humans by blackflies. The flies become infected with microscopic larvae by feeding on the blood of an affected person and then pass the worms from host to host. Lymphatic filariasis is spread in a similar fashion by certain species of mosquitoes. For both diseases, a person must be bitten many times to become infected, so short-term visitors to these regions typically are unaffected.

In river blindness (also known as onchocerciasis), as the worms mature, they cause nodules in the skin that itch unbearably. Often they permeate the cornea, leading to a loss of vision. Patients with advanced river blindness often are unable to work and may exhibit irrational behavior. Their skin begins to look aged. Lesions caused by scratching leave the skin vulnerable to bacterial infection.

The flies that transmit river blindness live near rivers and streams; fertile

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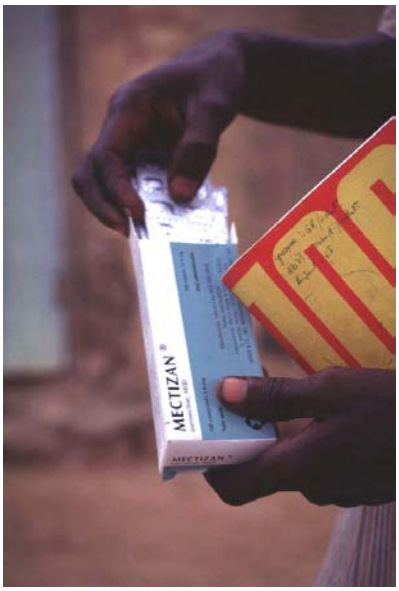

WORLD HEALTH ORGANIZATION

Ivermectin is distributed throughout affected regions under the brand name Mectizan

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farmland sometimes is abandoned as a result. In addition to being economically crippled by a loss of able-bodied workers, villages afflicted with river blindness often are shunned by neighboring communities for being unclean.

In lymphatic filariasis, worms infiltrate and damage the lymphatic system, sometimes with no external symptoms. Rarely, a victim will develop lymphedema, a swelling in the limbs, breasts or genitals. Damage to the lymphatic system leaves the patient with a decreased ability to fight off infection, and the swelling associated with lymphedema can be physically impeding.

According to the World Health Organization, more than 25 million people have river blindness worldwide. The Centers for Disease Control and Prevention estimates that lymphatic filariasis affects more than 120 million people.

Origins of ivermectin

ŌMURA

In the 1970s, there was a great interest in medicines derived from natural products. Conducting research at the Kitasato Institute in Japan, Ōmura collected thousands of soil samples from all over the country in hopes of discovering microbes with medicinal applications. He isolated strains of Streptomyces bacteria from the samples and cultured them in his laboratory.

In 1974, he found a particular strain of Streptomyces bacteria in a soil sample that he had collected from a nearby golf course. He sent it, along with 49 other of the most promising soil samples, for testing at the U.S. pharmaceutical company Merck. Working as a visiting professor at Wesleyan University a few years prior, Ōmura had made connections with the American pharmaceutical industry; upon his return to Japan, he established a partnership with Merck with the aim of developing new veterinary drugs.

Rather than hunting for a cure to a particular disease, researchers in Merck's natural product isolation unit were tasked with identifying any compounds that might have activity against pathogenic microorganisms. At the company's New Jersey location, the scientists sifted through samples from Ōmura and others over the course of a decade.

The researchers fermented the soil sample containing the Streptomyces and found that the bacteria were producing avermectins. Avermectins are thought to be part of the bacteria's natural self-defense system. Bacteria likely produce avermectins to paralyze the soil worms who feed on them.

While at Merck, Campbell and his colleagues demonstrated that avermectins were particularly effective against parasitic worms. Researchers isolated and purified 16 avermectin derivatives. They selected the most potent one and chemically modified it to make it less toxic. The result was ivermectin.

Ivermectin originally was used as a veterinary antiparasitic therapy. It rapidly became the market leader in antiparasitic veterinary treatment and has generated an average of $1 billion in annual sales. Ivermectin is perhaps most recognizable in the U.S. as the active ingredient in the heartworm preventative Heartgard. It also combats mites, ticks and insects.

In 1981, clinical trials of ivermectin in humans began in Senegal. Before ivermectin, the only available treatments for river blindness either caused severe side effects or were impossible to administer to patients on a large scale.

How ivermectin works

Ivermectin is extremely effective at

paralyzing parasitic worms.

Ching Chung "C.C." Wang worked at Merck in the 1970s and discovered the mechanism of action for ivermectin. (Every year, the ASBMB issues the Alice and C.C. Wang Award in Molecular Parasitology, which was established by Wang and his wife.)

Ivermectin works "by opening the GABA receptor-controlled chloride ion channel," says Wang. "It keeps the chloride ion channel open, so there is no response signal from the central nerve to the motor neuron."

With no neurotransmission between the central nervous system and the motor neurons, larval nematodes are paralyzed, making them unable to reproduce. Once the adult parasites have died off, the population within the human host declines.

Ivermectin is unique in that it does not cross the blood-brain barrier, so it does not have the same harmful effect on humans as it does on parasites.

Treatment once a year is enough to control the river blindness parasite, but a patient must receive ivermectin every six months for several years to be cured. When administered annually, a combination of ivermectin and albendazole, another antiparasitic that is made by GlaxosmithKline, can prevent the spread of lymphatic filariasis.

Public–private partnership

Executives at Merck in the 1980s were faced with a quandary: Their scientists had unearthed one of the most powerful human antiparasitic treatments ever discovered. It had the potential to cure hundreds of millions of people suffering from neglected tropical diseases. However, they were unable to market the drug in the affected areas without being accused of exploitation. What happened next was a humanitarian triumph that has served as a model for drug distribution in the developing world.

In 1987, P. Roy Vagelos, then the chief executive officer of Merck, decided to give the drug away for free for as long as necessary to eradicate river blindness. Merck partnered with the World Health Organization, the World Bank and several nongovernmental organizations to distribute the drug to nations where the disease was rampant.

CENTERS FOR DISEASE CONTROL AND PREVENTION

A technician in Tanzania tests school-age children for lymphatic filariasis.

"If you think about public-private partnerships, this is the model, particularly for neglected tropical diseases, where there isn't a lot of market-driven incentive to make these types of drugs," says Zachary Mackey, a parasitologist at Virginia Polytechnic Institute and State University. The partnership has served as a model for drug donations by other pharmaceutical companies, such as albendazole by GlaxoSmithKline, which is used in combination with ivermectin to treat lymphatic filariasis.

The Nobel announcement noted that ivermectin has "radically lowered the incidence of river blindness and lymphatic filariasis." Ōmura and Campbell's discovery has "provided humankind with a powerful new means to combat these debilitating diseases that affect hundreds of millions of people annually," it said.

Using ivermectin coupled with an insecticide program, the United Nations' Onchocerciasis Control Programme cured 30 million people of river blindness in West Africa between 1974 and 2002. The Carter Center, a nongovernmental organization working to fight river blindness, is campaigning to increase treatment to two times a year in parts of the world that remain affected. It hopes to eliminate the disease worldwide by 2025.

Alexandra Taylor (ataylor@asbmb.org) is a science writing intern at ASBMB Today and a master's candidate in science and medical writing at Johns Hopkins University.

Guardians of the genome

Nobel Prize in chemistry recognizes three DNA repair mechanisms

By Alexandra Taylor

In the very act of being alive, we humans expose our DNA to a constant onslaught of damage. Every time it replicates, our genetic code amasses mutations. Ultraviolet rays from the sun, oxygen in our lungs, and exposure to natural and synthetic chemicals cause us to accumulate about 200 mutations per day. If not for certain repair mechanisms present in the human genome, our lives would be very short.

We now know that more than 100 genes are involved in the efficient correction of DNA damage. Problems with DNA repair mechanisms can have serious consequences, in some cases leading to cancer and other conditions, such as neurological damage and developmental defects. Changes to the infamous BRCA1 tumor suppressor gene, for example, can reduce the cell's ability to repair DNA, leading to breast or ovarian cancer.

There was a time when scientists assumed DNA was immutable, but that time has passed. "Damage is all over the genome," says F. Peter Guengerich of Vanderbilt University. "Even if you lead a relatively clean life, you're still going to get certain amounts of damage."

Guengerich is the interim editor-in-chief of the Journal of Biological Chemistry, which has published papers by the three biochemists who will be awarded Nobel Prizes this month for describing some of the chemistry of DNA repair. (The JBC is published by the American Society for Biochemistry and Molecular Biology.)

On Dec. 10, 2015, Tomas Lindahl, Paul Modrich and Aziz Sancar will receive the Nobel Prize in chemistry. All three are members of the ASBMB and contributors to a field of DNA repair that dates back to the late 1920s. (Scientists were studying the effects of radiation on the genome long before comprehending its structure.) And while none of this year's laureates discovered DNA repair per se, each has made major contributions to the molecular understanding of how various repair pathways fix different types of DNA damage.

Therapeutic applications are beginning to emerge from our understanding of DNA repair mechanisms. This year's Nobel Prize in chemistry highlights the value of fundamental research done at a time before translational applications were on scientists' radar. Modrich appreciates the Nobel committee underlining the importance of basic research. "My personal view is that most major biomedical advances can be directly traced to advances in basic science," he says.

Sancar will receive the Bert and Natalie Vallee Award in Biomedical Science, which recognizes established scientists for outstanding accomplishments in basic biomedical research, at the ASBMB 2016 Annual Meeting in San Diego next April.

Base excision

LINDAHL

Tomas Lindahl, now at the Clare Hall laboratory of the Francis Crick Institute in the U.K., carried out his prize-winning research at the Karolinska Institute in Stockholm. In the 1970s, he and his team demonstrated that DNA decays over time. This work eventually led Lindahl to identify the DNA repair mechanism known as base excision repair.

Base excision repair targets routine chemical damage that would otherwise cause breaks or mutations in the DNA — problems that could potentially lead to disease. This pathway seeks out and removes damaged bases in DNA strands and then patches the strands with new nucleotides.

Patrick Sung, a DNA repair expert at Yale University and a JBC associate editor, finds the Nobel committee's acknowledgement "a major morale booster for people who study DNA repair," and says, "Lindahl's work has brought to the forefront of our awareness that DNA repair is critically important. He's been a very powerful spokesperson for the field over several decades."

Indeed, from 1986 to 2005, Lindahl served as the director for Clare Hall, the principal research laboratory of the Imperial Cancer Research Fund (now a part of Cancer Research UK). "My time at Clare Hall has been very stimulating," he says. "We tried to get together a number of people who were top-class in the field of DNA repair, which wasn't as fashionable at that time as it is now. In that way, the Clare Hall laboratory became a world leader in this area."

Mismatch

Paul Modrich, at the Howard Hughes Medical Institute and the Duke University School of Medicine, has worked extensively on DNA mismatch repair. The copying mechanism for DNA is imperfect: Each time a cell duplicates its DNA, incorrect bases sneak in, known as mismatches. Rather than allow these mistakes to perpetuate, the mismatch repair pathway acts as a copyeditor, seeking out the errors and fixing them. Errors are 1,000 times less likely with a functional mismatch repair system.

MODRICH

Modrich and colleagues determined the pathways for mismatch repair in both E. coli and human cells. They also demonstrated that tumor cells from patients with Lynch syndrome, one of the most common forms of hereditary cancer, are deficient in mismatch repair. They showed that such cancers have insufficient levels of certain proteins required for the initiation of mismatch repair.

In addition to his work on mismatch repair's role in Lynch syndrome and related cancers, Modrich is interested in the expansion of triplet repeat sequences, which underlies a number of neurodegenerative diseases. In the case of Huntington's disease, for example, the proliferation of a specific three-base DNA sequence leads to the production of toxic proteins in the brain. Work by others in mouse models has shown that triplet expansion depends upon a functional mismatch repair system.

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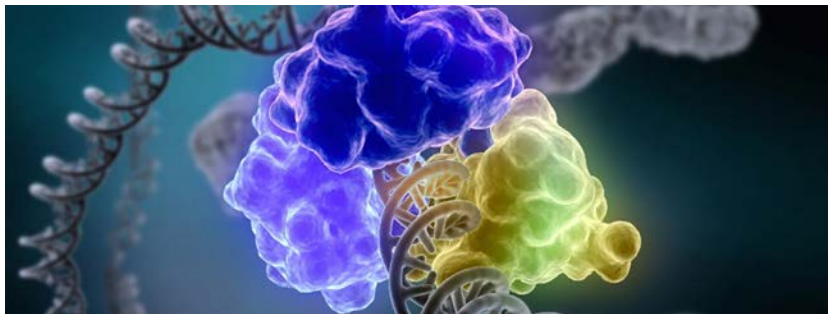

TOM ELLENBERGER, WASHINGTON UNIVERSITY SCHOOL OF MEDICINE IN ST. LOUIS, AND DAVE GOHARA, SAINT LOUIS UNIVERSITY SCHOOL OF MEDICINE (NATIONAL INSTITUTES OF HEALTH)

An enzyme encircles and repairs a broken DNA strand.

About the Nobel festivities

The Nobel Prizes are handed out annually on Dec. 10, the anniversary of Alfred Nobel's death. In the days leading up to the ceremony, the laureates deliver lectures about their work. The ceremony itself takes place at the Stockholm Concert Hall, where the laureates are honored with a speech and endowed with a diploma and a medal. The celebration then moves to Stockholm City Hall, where members of the Swedish royal family join 1,300 guests for a Scandinavian-inspired banquet. On the same day, the Nobel Peace Prize is awarded separately in Oslo, Norway.

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Nucleotide excision

SANCAR

Aziz Sancar, at the University of North Carolina, Chapel Hill, started studying how UV light can cause DNA damage in 1974. UV exposure causes lesions, such as the thymine dimer, which induce a kink in the DNA. During UV light exposure, a photon causes a covalent bond to form between two bases where none should exist.

Sancar and colleagues mapped out a pathway similar to Lindahl's, known as nucleotide excision repair. Sancar's research was based on the work he was doing with photolyase, an enzyme that repairs UV damage to DNA in certain organisms. He improved our understanding of the nucleotide excision repair pathway, which corrects lesions resulting from UV light exposure by detecting the damage, cutting it from the DNA, and rejoining the strands. This research has been instrumental to our understanding of skin cancer, which can be caused by UV light damage.

This year, Sancar and colleagues completed a map of the nucleotide excision repair pathway for the entire human genome. This map can be used to determine the ways in which each specific nucleotide in the genome is repaired. Sancar is gratified to have finished the project: "I went to Peru to give a couple lectures. I told my wife that if my plane hits the Andes and I die, I'll die a happy man because I have the map."

Cancer and clocks

As seen in the work of Modrich and others over the past 20 years, DNA repair is not always positive. Cancer cells with increased DNA repair activity can develop resistance to radiation or chemotherapy. For this reason, fundamental research into the various repair pathways is starting to make inroads toward clinical applications. Drugs that hinder DNA repair are currently undergoing clinical trials.

However, many aspects of DNA repair are highly complex and not yet fully understood. One example is the role of the circadian clock. In mammals, the circadian clock turns genes on and off depending on the time of day. Sancar and his colleagues found that DNA repair activity in mice is at its highest around 4 p.m. and at its lowest around 4 a.m. In cases where DNA repair can diminish the efficacy of chemotherapy, this fluctuation potentially could be exploited to time the delivery of anticancer drugs, optimizing their impact with minimal side effects.

Stimulating the field

There are many DNA repair mechanisms beyond the three acknowledged by the 2015 Nobel Prize in chemistry, such as chromosomal breakage repair. Many who made important contributions were not recognized due to the interpretation of specific stipulations in Alfred Nobel's will by the prize committee (1). For example, Sancar's mentor Claud Rupert discovered the enzyme photolyase in 1958. Sancar considers him to be the father of the field.

Nevertheless, experts in DNA repair are thrilled with the recognition bestowed by the prize. As Lindahl says, "I hope that it will stimulate the field a great deal. My colleagues are very positive and enthusiastic about drawing attention to the field."

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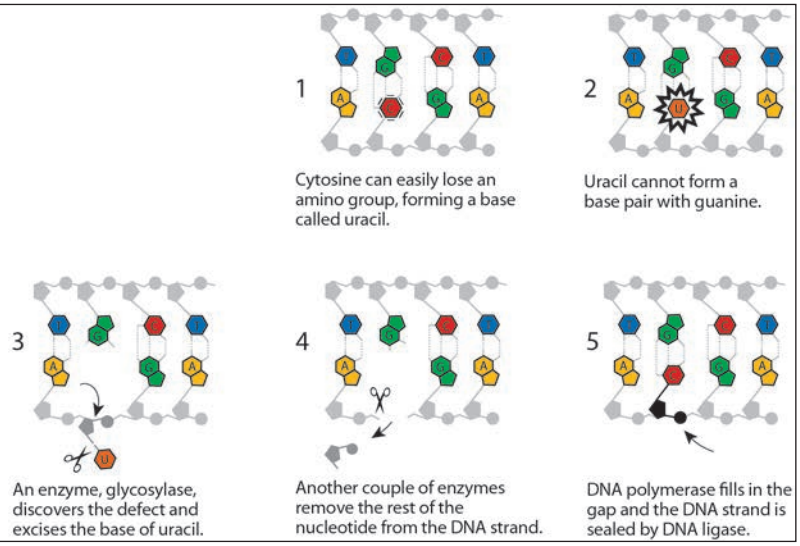
1. http://pubs.acs.org/doi/full/10.1021/ac9018457

Royal Swedish Academy of Sciences' explains Nobel Prize in chemistry 2015.

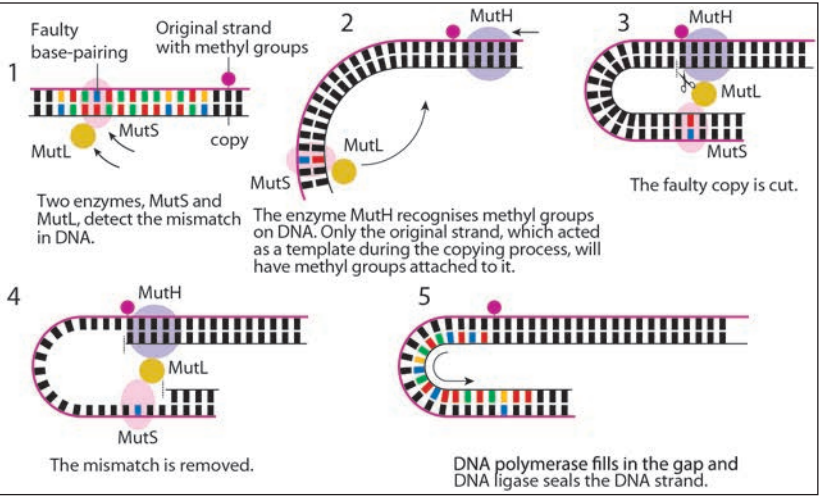
Base excision repair

Base excision repairs DNA when a base of a nucleotide is damaged, for example, cytosine.



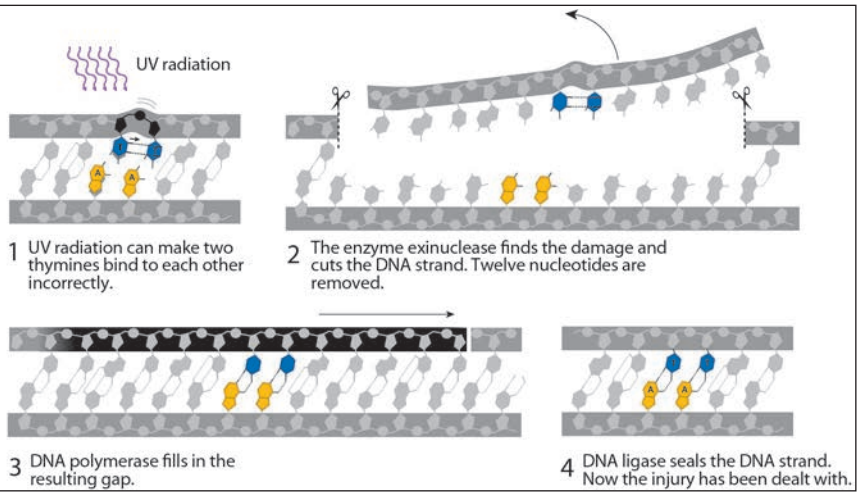
Mismatch repair

When DNA is copied during cell division, mismatching nucleotides are sometimes incorporated into the new strand. Out of a thousand such mistakes, mismatch repair fixes all but one.



Nucleotide excision repair

Nucleotide excision repairs DNA injuries caused by UV radiation or carcinogenic substances like those found in cigarette smoke.



FROM THE ROYAL SWEDISH ACADEMY OF SCIENCES NOBEL PRIZE IN CHEMISTRY 2015 POPULAR SCIENCE BACKGROUND, ILLUSTRATIONS BY JOHAN JARNESTAD/THE ROYAL SWEDISH ACADEMY OF SCIENCES

Pairing science with the paso doble

By Natalya Gertsik

The Spanish Gypsy dance resounds aggressively, almost menacingly, at 120 beats per minute from every unattended corner of the polished but visibly beaten space. The sound slices through a sweat-induced dew. Layers of net, stretch satin, chiffon and organza adhere to tiny, curve-embracing bodysuits through which every taut, elegantly sculpted muscle can be seen moving in rhythm with the reverberations. Neons, rhinestones, cheetah prints and fringe flash swiftly in human whirlpools of sweat and sparkle. Figures appear in many places at once, the changes in speed and direction making it impossible to discern between object and image reflected in floor-to-ceiling, wall-to-wall mirrors and in the reflections of the reflections. Heels click sharply against the floor in step with the flamenco rhythm. Bodies drop or fly with every buildup and crash of the music. Wrists and ankles writhe and whirl. Fingers curl. Pelvises thrust vigorously toward one another and then recoil. The breath surrounds, mounts and attacks, saturating the music with its greedy inhales and loud, urgent, carnal exhales. These are professional ballroom dancers. This is the paso doble.

The paso doble, or paso, is one of five dances in the international Latin division of competitive dancesport. The others are cha-cha, samba, rumba and jive. Together with the waltz, foxtrot, tango, Viennese waltz and quickstep, the Latin dances fall under the umbrella term "ballroom dance." Paso is a pair dance set to march music that was played at popular and gruesome

The writer's discarded dance shoes, worn down by hours of practice and competition.

Spanish bullfights, marking the bullfighter's entrance into the ring and the final kill. Today, paso is performed at dance competitions worldwide, most frequently to the song "España Cañi," a piece of music so complex that it must be choreographed bar for bar. In addition to being the most choreographically demanding, the paso also requires a strong dose of acting skills, as the man plays the combative matador and the woman his swift, sinuous cape. It is the fiercest of the five international Latin dances.

I spent years watching the paso and decades mastering it. In that time I went from high school to college to graduate school, lived in three of five boroughs of New York City, and traded in bell-bottoms for skinny jeans, all the while working on my chasses cape (a classic figure of the paso). Lest you think this is a perspective on classical dance, allow me to add that I was simultaneously pursuing a career in biochemistry and am now finishing my Ph.D. in biomedical research at Weill Cornell Graduate School for Medical Sciences. This is not to list my accomplishments, but to explain that in recent years I've learned quite a bit about learning and the way in which efficient learning differs across disciplines, and to lay

the foundation for the topics I'd like to explore, which are the somewhat unexpected similarities and differences between learning the science of dance and learning the art of science.

The talent dupe

To begin with, common misconceptions abound about both dance and science. The first is the pervasive and inaccurate idea that dance, along with most other art forms, is primarily an innate, talent-based vocation. In reality, the 10,000-hour rule applies as much to dance as it does to astrophysics. This has been demonstrated time after time by ballerinas like Misty Copeland, who was told repeatedly that she did not have the natural form characteristic of a principal dancer but prevailed despite these alleged genetic disadvantages.

The importance of the 10,000-hour rule also has become overwhelmingly apparent in my own experience, as many dancers that the industry deemed untalented have risen to the American and world ballroom finals as a result of raw, unadulterated dedication. One friend who was deemed average as a young dancer was so motivated and exhibited such a vehement work ethic that he landed both on the big screen with Jennifer Lawrence and Bradley Cooper in "Silver Linings Playbook" and in the national final, far above many others who were considered inherently gifted.

Talent may help you get noticed, but hot, sweaty, calloused labor takes the prize.

Spacey artists in white coats

The reverse stereotype, that the best scientists are those who work the hardest and study the most, is similarly false, as it masks the equally important qualities of creativity and vision, words often reserved for artists. I am not saying that science is an innate talent — it certainly follows the same

The writer as a young ballroom dance competitor.

10,000-hour rule that dance does. But the best scientists are not necessarily the ones who can recite every product and intermediate of the citric acid cycle and calculate molarities in their heads. Nor are they those who can pipette the fastest and perform tail vein injections with atomic precision. The best scientists are the ones who get curious, creative and emotional. They realize that in order to do something new, you may need to get a little chancy, a little uncomfortable, and deviate from much of what you learned in those 10,000 hours.

Just as great choreography is often a result of mistakes and digressions from the director's vision, so are some of the most pivotal discoveries the offspring of fortuitous accidents. Penicillin was discovered when Alexander Fleming's poor sterile technique resulted in an infestation of mold on his Petri dish, leading to the realization that some molecule released by the fungus has antibacterial properties. Viagra was discovered as a result of a failed clinical trial meant to alleviate hypertension. Accidents are the driving force of groundbreaking innovation, and it takes an open mind to perceive fortune in the misfortune of these costly and often demoralizing events.

Studying, memorizing and knowing will make a good scientist. Wondering, daydreaming and stumbling will make a great one. The best scientists are just spacey artists in white coats.

Knowing by trying

For better or worse, my own scientific career has been a hodgepodge of blunders, some of which led to discoveries, others to day drinking. One of my more fortuitous accidents occurred when I was trying to purify one protein but ended up purifying another, far more interesting candidate. I had been purifying a behemoth of a transmembrane enzyme (protein A) for six months, and the purification appeared to be working; that is to say, the protein complex and its activity were intact after purification. However, while the purified protein exhibited activity, the crude protein did not. Now, even an elementary understanding of protein purification is enough to recognize the peculiarity of this observation. After a month of titrating every reagent under the sun but still obtaining the same strange and inexplicable result, I finally presented the data (or lack thereof) to my boss, who chuckled and said I had two

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left hands and could not do an activity assay to save my life. I, however, had a more optimistic view of the situation — it seemed to me that there was an endogenous inhibitor of protein A in our system. Purification of this inhibitor would be a higher-impact project than the one I was pursuing. My boss declared, "I don't believe it."

In spite of his skepticism, I proceeded to test the hypothesis. Several weeks later, glowing and elated, I presented him with the evidence that confirmed that I do not, in fact, have two left hands. Only then did I become aware of the fact that his earlier challenge had been a clever attempt at reverse psychology. He had wanted me to pursue the unlikely theory.

"You never know until you try," he proclaimed.

New thoughts

Actually, you often do not know even after you try, and between the trying and the succeeding there will be many hazy detours, discouraging obstacles and cryptic clues. Some would say that the best way to solve such problems of scientific ambivalence is to plow forward, work harder and generate more data. I would say that it is to go on vacation and drink a margarita. The endogenous inhibitor idea came to me at a friend's destination wedding on a beach in Mexico. A colleague of mine solved all her cloning problems while speeding down a slope in Whistler. The key is to give ourselves time to think in a new way, with a different geographical or psychological perspective aiding in the process. Thinking, as it turns out, is a difficult commodity to come by when the protein column is leaking, the building fire alarm is wailing, three timers are beeping and the rotation student is bleeding after having cut himself with a scalpel intended for mouse surgery. But in the turmoil of going after that singular experimental endpoint and cleaning up the student's wound, we may be overlooking some of the most interesting biological phenomena hidden in the data.

As a dancer and scientist, the writer has benefited from trusting in technique.

No thoughts

While analyzing and ruminating are critical in science, they are often detrimental in dance. Certainly, daily training requires a great deal of thought, but a great dancer is one who does not need to think when the moment comes to perform. My own meditative breakthrough came when I trained with a coach who taught me to disconnect my ego from my body. After two hours with him, I was able to improve more than I had

ROSS DEN PHOTOGRAPHY

in the previous two years. Learning how to go on autopilot is one of the best things that can happen to a dancer. On the other hand, prolonged autopilot can be one of the most detrimental qualities for a scientist. As my yoga teacher likes to say, "We are so busy as human doings that we forget to be human beings." Believe it or not, doing too many experiments at the expense of being a scientist may actually impede scientific progress. A scientist who gets too comfortable in her techniques and routines risks not only missing what could have been a groundbreaking observation but also interpreting ambiguous data in a way that supports her desired hypothesis.

Trusting in technique

Thinking makes our science interesting and our dancing dull. If the goal for a scientist is to take a step away from pipetting and toward pondering, then the goal for a dancer is to train a body so capable that he no longer needs to ponder.

As a student of both science and dance, I discovered that there is one necessary but not sufficient prerequisite for achieving both hyper- and hypo-consciousness in these very different disciplines: technique. Sound technical training is the reason a dancer can trust his body to take over his mind and a scientist can trust his creativity to surpass his dogma. Technique allows us to execute all the banal tasks like pirouetting and pipetting so that we can cultivate the creativity, energy and artistry essential to moving from the studio to the lead role in a professional production or from the task-based experiments to the major discoveries. Inspiration can happen in an instant, but technique takes 10,000 hours to learn.

To this day I cannot tell you whether or not it was worth it — practicing the same rumba walks day after day, running the repetitive Western blots and PCRs. It was neither noticed nor applauded, neither glamorous nor sexy. But it was damn liberating: The constraint of technical training gave me the freedom of artistic expression. It is in those hyper- and hypo-conscious, post-10,000 hour moments of euphoric abandon that the real discoveries and the tremendous, hair-raising moves are made. To learn something until it is instinctual is to give yourself the ability to forget it all consciously and selectively in order to change your view and discover something new.

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When science runs in the family

By Rajendrani Mukhopadhyay

Some scientists credit certain schoolteachers or graduate-school and postdoctoral advisers as role models. Henrik Dohlman at the University of North Carolina at Chapel Hill stays within his family. He credits his father.

"I really look up to him," he says of Claes Dohlman. "He's not only done great things professionally, he's a very kind man."

"Great things professionally" is a succinct way to put it. Claes Dohlman, who has been affiliated with Harvard University since 1958, is a well-known figure in vision research. Inducted into the American Society of Cataract and Refractive Surgery's Hall of Fame in 2004 and the recipient in 2007 of the American Academy of Ophthalmology's highest honor, the Laureate's Award, the elder Dohlman is considered the founder of modern corneal science. His research into corneal physiology established the basis for current clinical practice with dry eye disease, corneal burns, wound healing and corneal transplantation.

Although he retired from university administration in 1989, Claes Dohlman has stayed on as a scientist. He is the director of Boston Keratoprosthesis Research and Development, which is part of Massachusetts Eye and Ear, where he has created a device he's most famous for: an artificial cornea known as the "Boston keratoprosthesis."

Claes Dohlman first conceptualized the device in the 1960s. But he turned his full attention to the device in the 1990s, once he retired from being the chair of Harvard's ophthalmology department, director of an ophthalmology laboratory, and a chief at Massachusetts Eye and Ear. At a time when most retirees take life easier, Claes Dohlman has been in the laboratory, perfecting the device. "It's work that really blossomed in his 70s and 80s," says his son.

Henrik Dohlman and his parents after a ceremony at the University of North Carolina at Chapel Hill.

The artificial cornea can be used on patients who can't rely on standard human corneal transplants, such as chemical-burn victims.The prosthetic, which resembles a collar button and is made of medical-grade plastic and titanium, won clearance from the U.S. Food and Drug Administration in 1992. To date, over 10,000 patients have had the device inserted in their eyes.

The younger Dohlman says of his 93-year-old father with a hint of understatement: "He has a lot of energy."

From Sweden to the U.S.

Science and medicine surrounded Claes Dohlman as he grew up in Sweden. His father was the chairman of the ear-nose-throat department at the University of Lund. "It was hinted

Claes and Henrik Dohlman

that there was only one worthwhile profession to consider and that was academic medicine," remembers Dohlman. "All my friends were heading for medicine so I followed the path of least resistance."

After completing an obligatory yearlong stint with the Swedish navy ("To be a naval officer was out of the question. I'm a weakling"), Dohlman got an M.D. and finished a residency in ophthalmology at the University of Lund's Eye Clinic.

The chemistry of proteoglycans, which are proteins bound to glycosaminoglycans and plentiful in the cornea, intrigued him. Jonas Friedenwald was working at Johns Hopkins University on the histochemistry and biochemistry of corneal wound healing. Drawn by his work, Dohlman did a fellowship with Friedenwald in the early 1950s in Baltimore, Md., and then returned to Sweden to get a Ph.D. in biochemistry from the Karolinska Institute.

His work caught the attention of Charles Schepens, who was a famous retina surgeon at The Retina Institute of Boston. Schepens offered Dohlman a fellowship at Harvard University. Having been in the U.S. for the Hopkins fellowship, Dohlman says, he knew that "the possibilities, professionally, were so much greater."

So in 1958, Dohlman and his wife, Carin, moved to the U.S. with three children. Two years later, Henrik became their fourth child and the first to be born in the U.S. Two more children followed.

The little professor

Henrik Dohlman displayed traits of an academic at a young age. "He was a little professor from the start," says his father. "He was always very curious, always eager to lecture people on how things really are and copiously read all kinds of literature."

He also had a willingness to experiment. Claes Dohlman describes a moment in 1968 when he and Carin opened the front door of their home to a sales representative from a hearing-aid company. All of the adults were confused. The sales representative insisted that a Henrik Dohlman had contacted the company. The parents couldn't figure out why a hearing-aid sales representative wanted to see an 8-year-old boy.

The confusion cleared when the child admitted to finding an advertisement that offered free testing of a hearing aid. "I had this image that it would give me super powers, and I would hear what people were saying at great distances," says Henrik Dohlman, still sounding sheepish almost

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five decades after the incident. "So I filled out the card, and then the salesman showed up. When he discovered that the person he was about to try to sell a hearing aid to was an 8-year-old boy with perfect hearing, he stomped off."

The younger Dohlman recalls his childhood home in Arlington, Mass., as filled with joyful chaos of a large and close-knit family. "When my father came from work, we all swarmed to greet him and he would be tackled by his kids," he says. "Dinnertime was masses of spaghetti and conversation."

But Henrik Dohlman got hints from a young age that his father was a well-known figure in the community. "Every time I would pass the principal of my elementary school, he'd tousle my hair and say, 'How's the son of the famous Dr. Dohlman?' I figured if my principal knew who he was, then my father must be prominent."

Education was critical in the Dohlman family. Among the six, two are M.D.s and the rest are Ph.D.s. "My father is very proud of the fact" that all his children hold advanced degrees, says Henrik Dohlman. "If I can say one thing about my parents, is that they were exceedingly generous financially. They put six kids through college and then graduate or medical school. It's something I took for granted when I was growing up. But once I got to college and grad school, I realized what a gift that was, to have no financial barriers to completing my education. That's my inheritance."

Henrik Dohlman was the only one to go into the life sciences. His other Ph.D.-toting siblings are economists. He credits his mother for turning him onto biology even though she holds a degree in political science. Carin Dohlman also grew up in Sweden, where, as her son notes, all schoolchildren are taught to appreciate the natural world and revere the 18th-century botanist and zoologist Carl Linnaes who laid the foundations for modern species nomenclature and ecology. Carin Dohlman shared her love and wonder of nature with Henrik.

Identity of his own

Like his father, Henrik Dohlman earned a Ph.D. in biochemistry. But he is quick to point out that he always was intent on making his way through science as independently as possible. His research portfolio at UNC focuses on understanding the fundamental properties of yeast G protein-coupled receptors, a far cry from clinical corneal research.

But the first project Henrik Dohlman was involved in as a graduate student dropped him into his father's territory. The younger Dohlman was in the laboratory of Robert Lefkowitz at Duke University in the 1980s. At the time, the laboratory was focused on cloning the ß-adrenergic receptor, the first hormone-based G protein-coupled receptor identified and cloned. The work later led to Lefkowitz's Nobel Prize in chemistry in 2012 along with Brian Kobilka at Stanford University.

"I thought I was working in an area that had nothing to do with vision research," says Henrik Dohlman. "But the first thing we noticed about this receptor was it was clearly homologous to rhodopsin, the light receptor."

Because of the striking similarities between the two systems, Henrik Dohlman's first scientific conference was the annual meeting of the Association for Research in Vision and Ophthalmology. "It was not only one of my first public presentations, but it was a public presentation in front of about 500 of my father's friends and colleagues, with my father in the front row," recounts the younger Dohlman.

Perhaps realizing how unprepared his son was for his first presentation at a national scientific meeting, the older Dohlman pulled him aside and asked to see the slides and hear the talk before the event. "It was a very painful experience for both of us," recalls Henrik Dohlman. "The talk that came out in the end bore no resemblance to what I'd prepared. It was the first and last time I've given a scientific presentation with my father in the audience."

But Henrik Dohlman acknowledges that the pain of having his father redo his first public presentation for him was well worth it. "I'm a much better public speaker because of it!" he says with a laugh.

'Just shrug it off'

Besides teaching his son the value of a good talk, Claes Dohlman has influenced Henrik in two other critical ways. "Probably the most important one was that I saw from an early age that he really loved his work," says his son. "That's not a bad way to go through life."

The other way Claes Dohlman has helped Henrik is to be a model for a good laboratory manager: "He's always had a positive outlook. He rarely loses his temper. He tries to be generous in assigning credit. He does not get distracted by office politics or idle gossip."

When it comes to research, Claes Dohlman knows how to roll with the punches. That's something his son says he's still working on. "There are many failures in this business. There are a lot of setbacks, and there's no escaping that. You can drive yourself crazy if you let it get under your skin. The best that you can do is brush it off and move onto the next challenge," says Henrik Dohlman, who is also an associate editor for the Journal of Biological Chemistry. "I hear my father's voice in my head saying, 'Just shrug it off.'"

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The Chemophilately Museum

By Aditi Dubey

When letters were still the only form of long-distance communication, the stamps that carried them to their destinations were miniature works of art with special meanings and identities. The collecting of stamps became a popular hobby soon after the first stamps were issued in the mid-19th century.

Originally the purview of children and teenagers, stamp collecting was elevated when a French stamp enthusiast who was president of the first stamp collectors' society coined the term "philately." It connoted not only collecting but the serious study of stamps and postal history. The American Philatelic Society estimates that around 5 million people in the U.S. alone collect stamps. Several famous personalities including Franklin D. Roosevelt and Charlie Chaplin were enthusiastic stamp collectors.

Stamps have long celebrated a wide range of subjects including science and scientists like Americans Barbara McClintock, Linus Pauling, Melvin Calvin, Edwin Hubble, Josiah Willard Gibbs, Czech-American nobelists Carl and Gerty Cori, and Spanish-American biochemist Severo Ochoa. Several scientific events of importance have found their place on postage. Mercury Project and Messenger Mission stamps were released in 2011 at the Kennedy Space Center in Florida to commemorate NASA's Mercury exploration efforts. More recently, a stamp depicting global sea-surface temperatures based on NASA's satellite images was released in 2014 in Washington, D.C.

CHANG

Gu-Gang Chang, professor emeritus at National Yang-Ming University in Taiwan, is a biochemist and a passionate stamp collector. Chang owns a comprehensive set of chemistry-themed stamps that has taken 30 years to amass. Chang's collection revolves around "chemophilately" and features an array of chemistry-themed subjects, such as chemical concepts, chemical history and notable chemists.

Chang has made his set available online through a website called the Chemophilately Museum (chemophil.blogspot.com). This virtual museum features his collection in both English and Taiwanese, indexed by topics such as atomic energy and X-ray crystallography. Some stamps date back to as early as 1888, and others refer to current events. Chang says the crystallography section of stamps was added to the exhibition when the United Nations proclaimed 2014 the International Year of Crystallography.

There are several sections in the Chemophilately Museum on DNA-themed stamps and famous scientists, such as Charles Darwin and the Nobel laureate Marie Curie. Unusual aspects of the collection include items like Philippine Science Tax Stamps, which served as documentary revenue stamps from 1969 to 1978. In addition to stamps, the site also features antique advertising cards, collectible revenue labels and perfins.

Chang describes perfins as stamps that have "punched holes as a security device to protect against pilferage. Perfins are historical philatelic materials." Chang says perfins are seldom used today, as postage meters have replaced them. The perfins in the exhibition contain symbols or abbreviations for elements, compounds including methane, and biological molecules like hemoglobin. "It is fun to find out that so many biological terms are embedded in perfins," says Chang.

GU-GANG CHANG

Sample stamps from The Chemophilately Museum.

With this site, Chang hopes to bring themed stamp collecting to a wider and newer audience — one that's not deterred by the drop-off in stamped mail. He says, "In this electronic era, it is increasingly less common to receive stamped mail. However, stamp collecting remains one of the most common hobbies in many societies."

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The maestro's weaving art

By Emir Avilés-Pagán

Break time
For coffee and paper,
Saw my professor
With keyboard in hand,
Her eyes in synchrony,
The melody to start.
Swift movements, rapid beats.
Sounds of rising harmony,
Gazing at the screen,
Grazing the keys,
Clear the air,
Calm all down.

The maestro, the professor —
One into another turned.
Surrounded now
By the concert hall,
The maestro, the grand pianist,
Weaving his art.
Such music, such magic,
No comparison,
None alike.
No more a draft
But now
A finished grant.

Emir Avilés-Pagán (emir.aviles@gmail.com) is a Ph.D. student at the Massachusetts Institute of Technology studying fly developmental genetics.

A mock PI works out

By Vivian Tang

A major task that's ever so grueling,
The endeavor of completing my Ph.D.
Perhaps a new hobby to make it more interesting,
One that I came upon through my own study.

When there's a published article to be read,
I'll dive straight into the introduction.
Then, there's a challenge to be met,
Although in a hypothetical situation.

With just the introduction and nothing else covered
But the aims of the published study clear in mind,
With the scientific knowledge and skills I've acquired,
What methods would I have used that are fine?

Assuming the role as a principal investigator,
Obtaining novel data is what I'm geared toward.
Techniques and strategies that make me a prolific researcher,
Published results needed to put my best foot forward.

To have the gene encoding it amplified and identified,
Its catalytic mechanism unraveled by structural biology,
Site-directed mutagenesis to get its active site verified.
I think I have got a good grasp of enzymology.

The composition of the microbiota be subject to analysis,
The bronchoalveolar lavage fluid be collected for proteomic profiling,
Assays be performed to detect changes in lipid synthesis.
Getting it all right is a confidence booster so overwhelming.

Flow cytometry to investigate possible T-cell polarization,
RNA silencing experiments to elucidate the cell signaling pathway,
Immunohistochemistry to visualize the cellular localization.
My reasoning is all sound, but I won't be carried away.

Getting the techniques and approaches right
Does not mean that I would be experimentally productive.
Therefore, let's turn to my mentors for their insight
That has enabled me to thrive and be innovative.

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Science is great but addictive and sedentary.
May also bring harm insidiously —
Bad postures, aches and pains are cautionary;
I need to be humbled constantly.

A second hobby I've cultivated,
A need to counter my sedentary lifestyle.
Before my academic pursuit is vindicated
I just need to go the extra mile.

A hobby that kills two birds with one stone
To destress and slim down with benefits I'll always emphasize,
A rigorous workout regime of my own —
Nothing will ever beat regular physical exercise.

Confronted with stressful and demanding commitment,
With a constant need for high brain power and mental agility,
Our physical health and fitness always an essential requirement,
Although it's too easy for us to see exercise as frivolity.

When the stress of my Ph.D. takes a toll on me,
Just taking a walk helps me put things into perspective,
But a full rigorous workout is better than one can see.
It's a fountain of youth that keeps my mind productive.

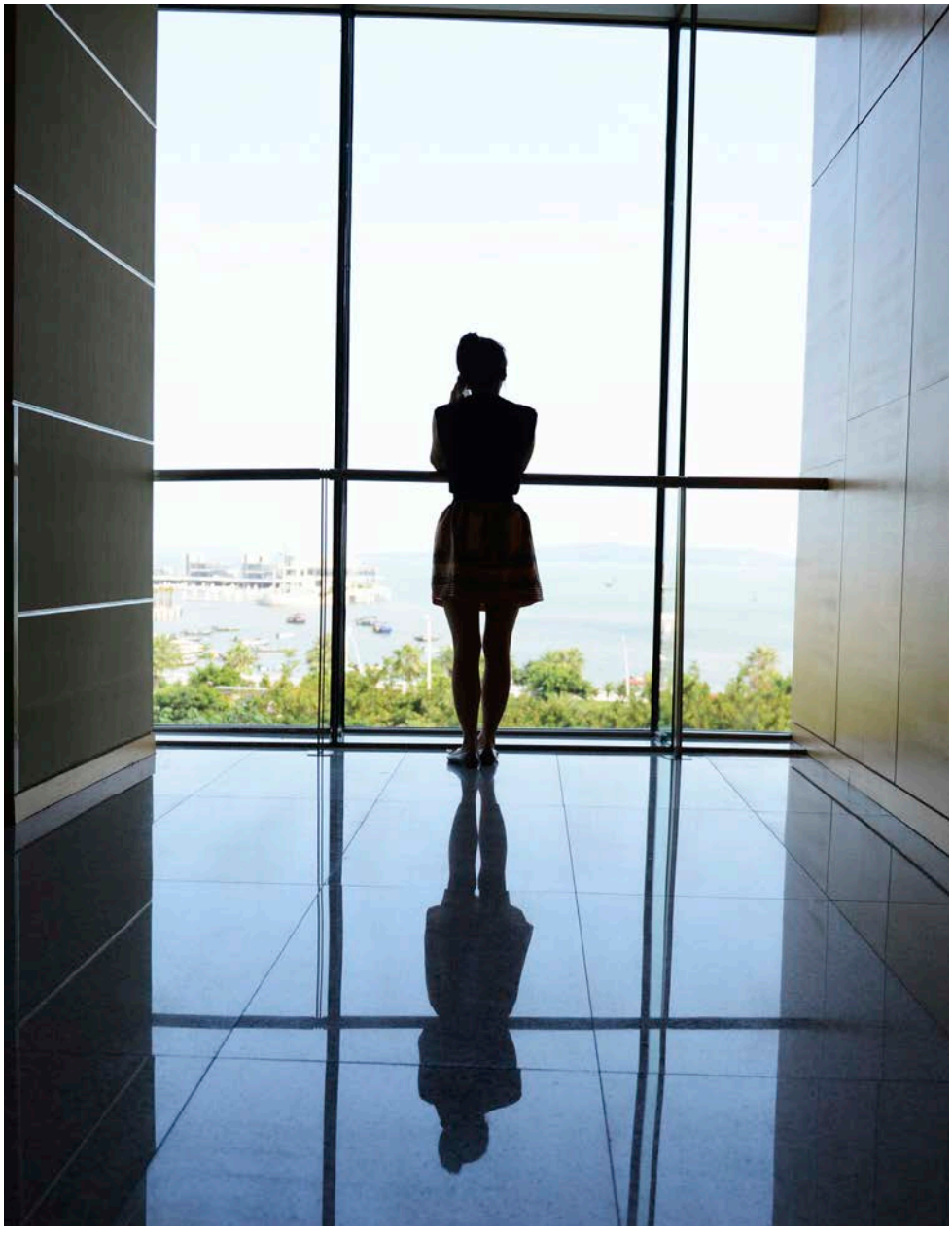
Is the thought of adding to my regime something new
Or becoming a part-time certified personal trainer plausible?
Rock climbing, scuba diving, fencing, just to name a few,
Either way will render my life as a scientist even more sustainable.

If only my efforts to complete my Ph.D.
Endure as well as running on a treadmill.
The need to listen to my mind and body —
They're set to push me uphill.

The world of academia is relentless.
With the two hobbies, I hope to stay resourceful.
Despite my faith, I'm not entirely fearless —
Time and opportunities are not plentiful.

Overcoming impostor syndrome

By Marion Sewer



A friend and colleague shared with me a recent experience she had at a faculty awards ceremony. Her institution was awarding one of its highest honors, and while the citation was being read and the accomplishments of the winner listed, my friend's colleagues were pointing at her and whispering, "This has got to be you." Despite their reassurances and the plain facts of her extensive academic and service activities being read aloud, she refused to believe the award was for her. Later, she would reveal that not only did she feel that the award couldn't have been for her but, perhaps more troubling, she felt that she didn't deserve it.

This sense of not being worthy plagues many, particularly high achievers with CVs that tell a clear story of exceptional qualifications and accomplishments. The sense of unworthiness has a name — impostor syndrome — and is defined as a complex array of feelings characterized by a belief that one is incompetent and any achievements are in fact undeserved strokes of luck or other external factors. Although members of underrepresented minorities and women suffer from impostor syndrome in high proportions, the syndrome is pervasive and can affect anyone whose life experiences, including socioeconomic status, sexual orientation, religious beliefs, or other factors, make them feel like an outsider.

Since a seminal paper on impostor syndrome was first published by Pauline Rose Clance and Suzanne Imes (1) in 1978, many books and articles have chronicled the struggles

of successful, high-achieving individuals from professional spheres. Joyce Roché described her struggles with imposter syndrome in her book The Empress Has No Clothes: Conquering Self-Doubt to Embrace Success (2). Roché shared her journey as an African-American woman growing up in New Orleans who went on to become vice president of Avon and CEO of Girls Inc. In the book, she describes the deep-seated fear that she would fail and be revealed as undeserving of her achievements. Eventually, she developed coping strategies to dampen the inner voice that undermined her confidence, and she finally accepted that she had earned a seat at the table.

Roché's story resonates with many minority professionals in STEM, particularly those in academia. While there have been gains in the number of underrepresented minorities that pursue undergraduate and doctoral degrees in STEM disciplines, the number of these graduates that matriculate into tenure-track faculty positions has not changed significantly in decades. The proportion of tenured full professors from underrepresented minorities still hovers around 5 percent (3). Similarly, while female graduate students outnumber their male counterparts in the biological sciences, their numbers lag behind when it comes to tenured professorships.

For underrepresented minorities, impostor syndrome can complicate an already challenging career path in which isolation and the pressure of representing an entire race or gender are already in play.

Further seeds of doubt can be planted by seemingly well-meaning individuals. I often reflect back on a graduate school interview during which a faculty member told me that despite my strong academic record I would have to work twice as hard as other students because "all of the other black students" have to work harder. Similarly, after being awarded a Howard Hughes Medical Institute predoctoral fellowship, I was told by a mentor that "they always pick one black student," so I should feel lucky to have been picked. Statements like these can trigger periods of self-doubt and isolation, particularly during challenging times like preparing for a qualifying examination, revising a grant application, reviewing student evaluations, or navigating the promotion and tenure process.

All of this can be compounded further by stereotype threat, a phenomenon studied extensively by Claude M. Steele, profesor of psychology and executive vice chancellor and provost at the University of California, Berkeley. Steel found people feel at risk of confirming negative stereotypes about their social groups, such as the stereotypes that women are bad at math and that African-Americans are less intelligent (4).

So how does one develop mechanisms to cope with the feelings of impostor syndrome? There is no one-size-fits-all answer, but the following strategies may help (3, 5):

Develop a network of colleagues and friends — take a page out of the book Every Other Thursday: Stories and Strategies from Successful Women Scientists by Ellen Daniell, which describes the instrumental role a support group can play in career trajectories.

Speak about your fears with a mentor, partner or therapist or in a journal. Voicing your fears, doubts and concerns with a trusted individual may provide objective clarity.

Share your achievements and accomplishments — celebrate publications, funded grants, defenses and awards.

Accept compliments and accolades. Don't diminish the impact of well-wishes from friends and colleagues by dismissing them as luck.

Don't give power to assumptions others make about you. Stereotypes are pervasive and applied to every population. Try not to let the opinions of others undermine your goals.

Seek out low-risk opportunities to act like you are more confident than you feel — a course lecture or departmental research seminar can be the motivational spark needed to allay self-doubt.

Give yourself the right to make mistakes and to say no. Avoid saying yes to committee service merely to diversify the group.

Keep a healthy sense of humor and perspective. Sometimes the hoop you have to jump through is moving … and on fire.

Assess your strengths and challenges holistically. Ponder the source of your feelings of inadequacy. Perhaps they are rooted in a need for a more fulfilling existence.

Reframe failures as opportunities for growth — "unscored" simply means that the leap to "funded" will be greater.

Don't lose touch with your authentic self — regularly reflect on your personal definition of success and seize opportunities to change your path.

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Who the heck is David Baltimore?

By Eleftherios P. Diamandis

My research lab consists of 12 Ph.D. students and 12 postdoctoral fellows and associates. At a weekly lab meeting last spring, someone asked, "Who is Vladimir Ilyich Lenin?" I was rather astonished to discover that other than me, no one in the room recognized Lenin's name.

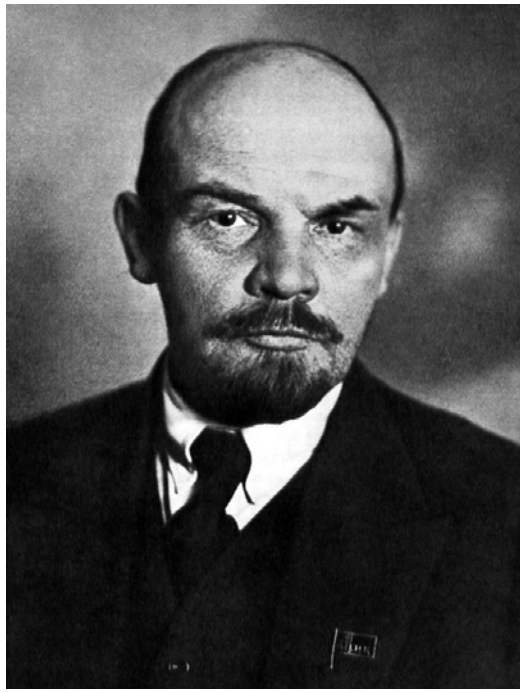
Perhaps being able to name the first leader of the Soviet Union is of little concern to today's young scientists. After all, the man was not in their field. But it is also the case that several of my own and other graduate students and postdocs are not familiar with many of the giants of modern science.

For instance, a student of mine once complained about an unfair question that was asked during the final examination of a Ph.D. thesis containing a series of reverse transcription-polymerase chain reaction experiments. The unfair question was simply, "Who discovered reverse transcriptase?" At another lab meeting, a guest speaker showed a quote attributed to David Baltimore, leaving my staff to ponder, "Who the heck is David Baltimore?" (See box.) Not too long ago, at a final Ph.D. examination on regenerative medicine, I asked who discovered inducible pluripotent stem cells. The candidate responded that the discovery was made by a Japanese group but he failed to name the Nobel Prize winner.

These kinds of knowledge gaps are not limited to North America. When I presented to a group of medical students in Spain recently, I asked if anybody knew of Spaniards who had won Nobels, and again there was silence.

Perhaps when you are starting out these days, reciting the names of distinguished predecessors in your field can seem like a trivial exercise in view of the mountains of material you need to learn for a competitive specialty. When I ask younger scientists why they don't recognize the greats, the answers I receive range from "How would I ever know?" to "I really know a lot about my specialty, but I am not good with names."

But it's not only the names that concern me. This generation, encouraged to focus on current technologies, is also not trained, as previous generations were, in essential math and measurement techniques. Many students are unable to prepare a buffer unless following a recipe, do not understand basic measurement principles — such as those of pH, absorbance and fluorescence — and cannot define the difference between a molar concentration and an absolute amount (i.e., 1 pmol/L vs. 1 pmol). When performing simple calculations, such as verifying the ratio of 99/10, they often turn to a computer or calculator. And when it comes to statistics, they sometimes do not understand the difference between a t-test and a Mann-Whitney U-test or ANOVA. They can, however, use a computer to calculate them.



Vladimir Ilyich Lenin

During a lab meeting, I asked my students, "Which measured signal is larger: 99 or 100?" and they thought it was a bad joke. But they appreciated it when I explained that if the uncertainty of the two numbers is 2 percent or higher, then the two signals are the same (or, more accurately, not statistically different). Finally, some of my students can explain how a mass spectrometer works, an instrument that is used daily in my lab, but are generally stuck when you ask them the difference between a C-8 and a C-18 column used for the up-front chromatography step.

Why is this happening? Although there might not be one particular reason, it appears that the dissemination of ready-made reagents and purchased

services is exacerbating the issue. In my opinion, these allow for a faster research pace at the expense of the educational component of in-depth technical knowledge.

A related observation is that our wet lab, which was very crowded 15 years ago, is now usually empty. I find most of my graduate students sitting at their desks performing complicated bioinformatics analyses of their own or using publicly available databases to delineate mechanisms of disease and hunt for new biomarkers.

I suspect that not knowing the old folks, the old math, and the old techniques is common in many other research labs. But beyond an old guy like myself getting worked up about it, is it really a bad or worrisome development?

Scientific knowledge is expanding at an exponential pace, and our new scientists in training have little time to learn the fundamentals of basic techniques or to remember names of legends. Most likely, this situation will get worse with time.

Don't get me wrong — the younger generation is not only brilliant at using and adapting to newer technologies but also very resourceful and well equipped to solve meaningful scientific questions in the years to come.

Still, I strongly believe that having a solid foundation in basic principles will matter for young students who aspire to true relevance in their field. In a global, competitive world, the people most likely to succeed are those with both deep and broad knowledge and good communication skills.

Let us go back to Lenin for a minute. Imagine sitting at a table with another five or ten speakers at a conference you organized, and each speaker is specialized in one thing. How will you ever sustain a discussion for two or three hours if the only thing you know (even if perfectly) is very narrow?

Scientists are expected to have knowledge and opinions about other peoples' work — especially timely topics like climate change, pollution, renewable energy, stem cells, new cancer therapies, epidemics, animal and human cloning, and so forth. Even politics, sports, music and movies have a place for discussion in such settings.

But how can we remain generally informed while pursuing our more narrow questions?

One way to sustain a well-rounded phenotype is by reading broadly, including leading general and specialty journals, magazines, and newspapers, even if you seem to have no free time. You likely will be a far more memorable individual if you show off multiple interests beyond your specialty. And if, during a discussion, you name one or two Nobel Prize winners from decades ago, you may get an interview for a job at one of your invitees' institutions.

Regarding names of Nobel laureates, here are my suggestions:

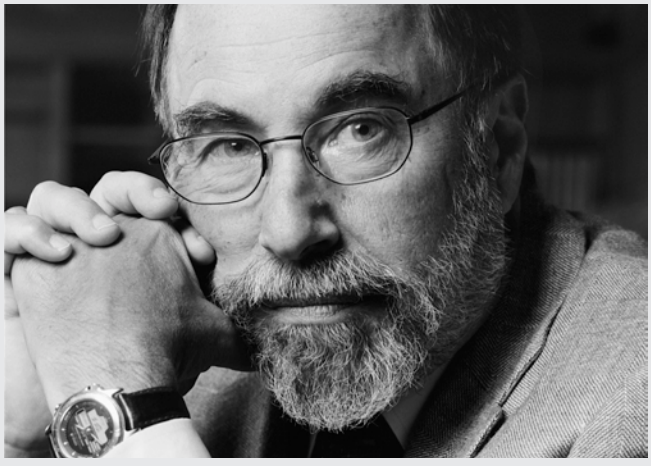
We have 20-plus freezers in the lab, and I propose naming each after a Nobel laureate. It's tough to miss the name when you are opening the freezer!

When Nobels are awarded in early October each year, we could hold a special lab meeting with three presentations: one on the new winners and two on previous ones, starting, let's say, in 1950.

We could also have a hall of fame in the corridor or lab displaying some Nobel winners and their work.

Regarding analytical knowledge, we senior scientists and mentors should advise, remind and expect our students to know the principles of fundamental techniques and their limitations so that data are interpreted properly. After all, we bear responsibility for the validity of such data, especially when published.

Eleftherios P. Diamandis (ediamandis@mtsinai.on.ca) is a professor and head of the clinical biochemistry division at the University of Toronto and holds an endowed chair in prostate cancer biomarkers at Mount Sinai Hospital and University Health Network.



CALIFORNIA INSTITUTE OF TECHNOLOGY

David Baltimore

- An American biologist, university administrator, and 1975 Nobel laureate in physiology or medicine for discovering the enzyme reverse transcriptase
- Served as president of the California Institute of Technology (Caltech) from 1997 to 2006
- Currently president emeritus and professor of biology at Caltech
- Served as president of The Rockefeller University from 1990 to 1991
- Served as president of the American Association for the Advancement of Science in 2007
- Won the U.S. National Medal of Science in 1999

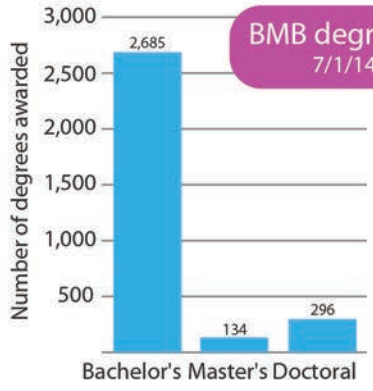
Results of the 2015 ASBMB annual graduation survey

By Erica Siebrasse

The American Society for Biochemistry and Molecular Biology has surveyed programs in biochemistry and molecular biology since 1999. Several changes were made to this year's survey, including revised questions to improve accuracy and the addition of new questions about faculty demographics. The 2015 survey went to departments across the U.S., and 158 institutions submitted complete surveys, for a response rate of 18.3 percent. This was a significant improvement over the 2014 response rate of 13.8 percent.

Of note, the 2015 respondents represented a greater variety of institutional types (No. 4 below) than in 2014, when the majority of respondents were from primarily undergraduate institutions. Very few degrees of any type were awarded to students from under-represented races and ethnicities. This trend was also observed in the percentages of biochemistry and molecular biology faculty, over half of whom were reported to be white men.

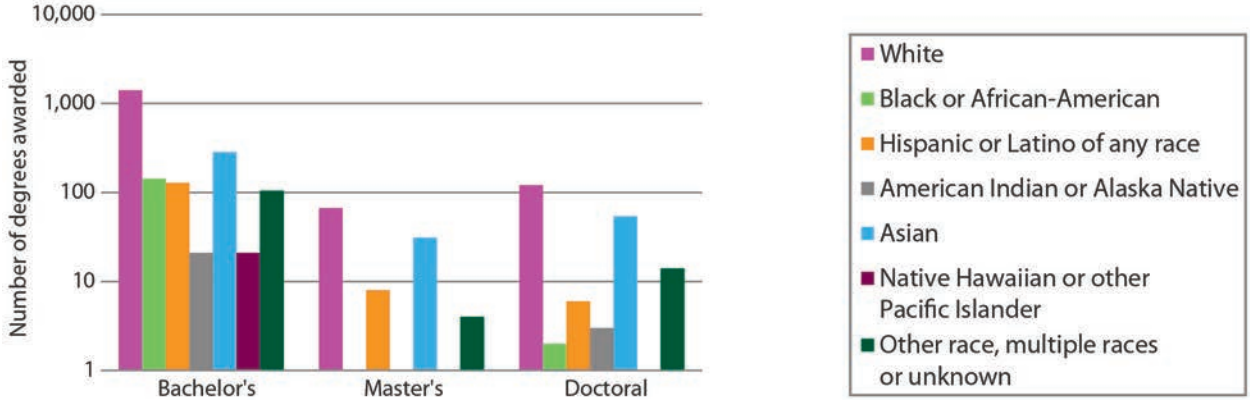
1 BMB degrees awarded
7/1/14 – 6/30/15



2 Genders of degree recipients

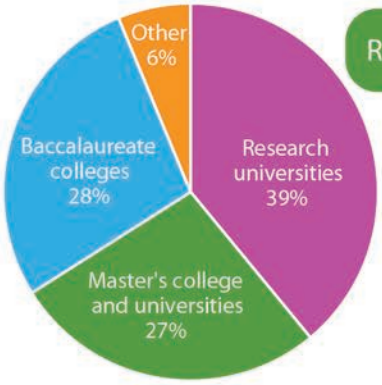
	Female	Male
Bachelor's	48%	52%
Master's	54%	46%
Doctoral	44%	56%

3 Races and ethnicities of degree recipients



4 Respondents' Carnegie classifications

carnegieclassifications.iu.edu



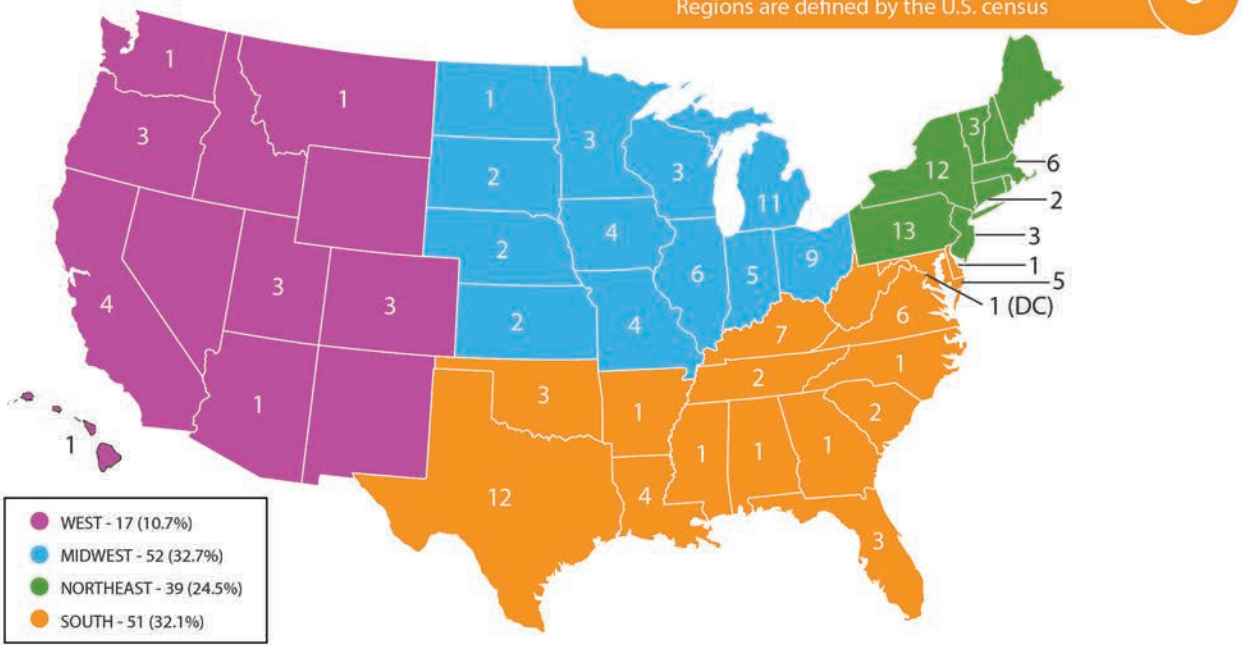
5 Demographics of BMB faculty

	Female	Male	Total	Percent of total
White	674	1,502	2,176	82%
Black or African-American	25	39	64	2%
Hispanic or Latino of any race	23	34	57	2%
American Indian or Alaska Native	2	5	7	<1%
Asian	90	216	306	12%
Native Hawaiian or other Pacific Islander	1	2	3	<1%
Other race, multiple races or unknown	7	31	38	1%
Total	822	1,829	2,651	
Percent of total	31%	69%		

*Total percentages may not equal 100 due to rounding.

6 Map of 2015 survey respondents by state

Regions are defined by the U.S. census



Cracking open the lab doors

Do-it-yourself biologists band together in Baltimore

By Lisa Z. Scheifele

For most Americans, exposure to science laboratories ended in high school or college. In those early science classes, students were led through standard, cookbook protocols and arrived at expected outcomes. Few were able to perform authentic research or pursue open-ended questions. The joy of actual discovery was reserved for those who went to graduate school and gained professional-level laboratory access. But what if there were a venue that allowed the public to engage in the scientific process, encouraged nonscientists to ask questions that professional scientists ask, and offered equipment and guidance that made open-ended science experiments a reality for everyone?

Access and community

Do-it-yourself biology is a movement of citizen and professional scientists who believe everyone should have an opportunity to engage in the scientific process. While the phrase might call to mind nefarious hackers toiling alone in garages, the reality is that most DIY biologists work openly and collectively. Many have banded together to create community labs where members can share space, material and equipment. These spaces allow them to work in a community, develop project ideas, share expertise and make unexpected interdisciplinary connections.

Baltimore UnderGround Science Space, or BUGSS, is a place for just this kind of creative biology. We are a community laboratory with a mission: to enable those interested in biotechnology to learn and do science in a fun, safe and socially responsible manner. BUGGS offers community lectures, lab classes, workshops and meet-ups for member projects in a newly revitalized neighborhood of east Baltimore. We want the public to engage in science at a variety of levels, so for novices we offer highly mentored courses and instruction; for those who want to learn about the latest technologies and discoveries we offer lectures from eminent local scientists; and for those who want to engage fully and use biological technology we offer access to the technology and guidance to bring their research ideas to fruition.

LISA Z. SCHEIFELE

Marissa Sumathipala, shown setting up PCR reactions, mentored other high school students in the 2015 Build-a-Gene course.

Authentic research

Citizen scientists who seek out community labs often are highly educated and keep up with the latest scientific developments. With an Outreach Seed Grant from the American Society for Biochemistry and Molecular Biology, BUGSS has been able to offer these citizen scientists a Build-a-Gene course. For the past three summers, the course has brought together patent attorneys, librarians, computer programmers, high school students and artists who have spent their Saturday mornings in the lab

learning gene-synthesis protocols. Since gene synthesis uses polymerase chain reaction and molecular cloning to assemble a gene from oligonucleotides, teaching the protocols allows us to expose learners to cutting-edge concepts of synthetic biology while helping them master fundamental skills in molecular biology. Offering the class as a five-week series allows students to repeat fundamental techniques, such as micropipetting, PCR and gel electrophoresis; this allows enough independence to build proficiency with enough instruction to complete the tasks accurately.

Over the past three years, participants have synthesized genes for fluorescent proteins, yeast chromosome fragments and bacteriophages. While the protocol is standardized, each gene may differ in how well it assembles, allowing students to experience the various outcomes of real research — including failure. John Torcivia-Rodriguez, a Ph.D. candidate in bioinformatics at George Washington University, says, "The course helped reaffirm in my mind that biology doesn't have 100 percent success, but I was surprised by the level of success we did have!"

Students often take the class to get hands-on training with current materials and methods and as a way to spark future research ideas. Krystal Dodd, a recipient of an Outreach Seed Grant scholarship, came to BUGSS as a student recently out of school who was looking for "lab space and peers interested in pursuing their own projects. I find this refreshing and a much needed outlet for my biological passion," she says. Build-a-Gene participants have gone on to design their own projects. A group of high school students engineered yeast cells to degrade excess starch, solving a real-world industrial problem, which won them a silver medal in the International Genetically Engineered Machines competition.

Build-a-Gene participant and BUGSS board member Ryan Hoover selecting bacterial colonies for PCR screening.

An inclusive and ethical scientific enterprise

BUGSS sees its role as one of creating informed citizens who are engaged with research science, increasing knowledge of cutting-edge techniques in biochemistry and molecular biology, and promoting discussion between scientists and the voting public. Synthetic biology, including the Build-a-Gene course, has yet to enter the broad public consciousness, and we hope to dispel the myths, fears and concerns about this promising technology. We also assume the responsibility of introducing this technology to the broader public by requiring safety training and engaging actively in ethical discussions. In conjunction with our course, we held a public lecture in bioethics with Debra Matthews, a researcher from the Johns Hopkins Berman Institute of Bioethics who led a discussion about gene editing technology.

Opening the doors of the lab to citizen scientists offers unprecedented opportunities for engagement and invites broader participation in the scientific enterprise. These new researchers bring diverse perspectives and engage in exciting interdisciplinary dialogue. The work of citizen scientists does not seek to compete in depth or rigor with that of professional scientists but instead can stimulate new insights into how science can address the needs and visions of our communities.

Lisa Z. Scheifele lzcheifele@loyola.edu is an associate professor of biology at Loyola University Maryland and a member of the board of directors of BUGSS.

Reader comments

Below are two threads of reader comments about the November President's Message

First thread

What nuggets of information can we learn from this story? Well for one, this sentence is rather worrying: "Koshland was so impressed with the application that she and her colleagues recruited Allison from Texas to the University of California, Berkeley." What we can learn is that 30 years ago it was perfectly OK for a reviewer to break confidentiality and headhunt a grant applicant on the basis of exciting (presumably unpublished) data in a proposal. Thankfully today's NIH guidelines forbidding contact between reviewers and grantees, even post hoc, ensure that such unethical practices are rare.

– BamaSS

I think your inability to see past Steve's provocative prose and point out a "breach of protocol" is unfortunate. You seem to have missed the whole point of this article. Science has turned into a game today where people try and sell trendy ideas rather than try to undertake rigorous, unbiased scientific inquiry. There isn't any room for bold science today — just timid, safe and mediocre work coming from scientists desperately trying to preserve their research programs. So many papers, so little impact. It is no wonder that the public is losing faith in science. I wager even scientists are losing faith in the scientific enterprise.

– Shaq Jones

Second thread

Dr. McKnight,

I hope you actually read this message and consider what the community has to say, since we as scientists should be willing to listen to debate and adjust our hypothesis if stronger arguments are presented. As a working biomedical researcher, I hope that you would use your position and this forum to address the real issues in the biomedical research enterprise rather than constantly castigating reviewers who are doing a tough job for little credit. Some of the real issues are

1) flat NIH budgets allocated by Congress for the last 12 years that have not tracked with inflation, decreasing the purchasing power of each grant dollar and increasing the need for more grants to get research done;

2) public and private academic research institutions that have viewed NIH funding as revenue and have consistently increased indirect costs, reducing the amounts of direct cost dollars available for research;

3) academic institutions that have required their faculty/staff to recover some or most of their salaries from extramural funding rather than putting more skin in the game and paying faculty/staff for their work through base dollars;

4) reduced public support for research that helps the entire community due to the politicization of the biomedical research enterprise and caricature of scientists and the scientific process;

5) loss of early- and midcareer scientists that have struggled to establish and maintain their research programs in the worst funding environment in memory. All of these things are very real issues that affect most if not all of biomedical scientists and are the root of the problem, not merely a symptom like reviewer behavior.

Dr. McKnight, you said in one of your first messages as president of ASBMB that you wanted to have a serious debate (President's Message: "Wow!" November, 2014), but we have not seen any such debate yet. What we've seen is a superficial treatment of the problem by attacking some of our own (i.e., reviewers) and using anecdotes rather than data instead of trying to address the real problems. Please use this forum and what remains of your time in this position to try to tackle real problems that can help the entire ASBMB membership (and all other scientists as well), rather than beating up the people in the trenches. If you cannot do this, I implore (incoming president Natalie) Ahn to start to addressing these issues in a real, constructive way when she takes over as ASBMB president. This is what we saw when (Jeremy) Berg was president of ASBMB and is what we would hope to see from future leaders of this organization.

– Philapodia

My contention is that more money won't solve the problem. Higher quality scientists are the solution. This requires that the great scientists of today take their responsibility of training young scientists more seriously. In other words, they need to invest in the training of their students beyond just offering cursory/high-level

Second thread

scientific feedback. We need to bring back the master-apprentice relationship that once pervaded science. Feeding more money to a system of scientific training that turns out poorly trained, ill-equipped scientists won't improve anything. I suspect Steve McKnight trained in an era where the biomedical research enterprise was much smaller, and students had much more meaningful mentoring relationships. This is largely lost now, and this may account for the supposed mediocrity that is plaguing science. Nowadays, most top PIs are more interested in selling their science and attaining visibility rather than actually doing science. How can you honestly claim to run a world-class lab when you travel 25 weeks of the year? When scientists quit being scientists to become administrators and figureheads, it is a loss for trainees and ultimately a loss for science. Stop pumping more money and feeding universities an endless supply of cheap graduate student and postdoc labor. Ask established scientists to take a more active role in driving scientific projects and increase the efficiency of their research groups rather than simply throwing more money at them. Demand high-quality scientific training to be the norm rather than the exception. This is the adrenaline shot that science needs. Once we get this right, then we can talk about more money. But as it stands, we as scientists are failing the public.

– Shaq Jones

I strongly disagree. I think this idea that scientists today are substandard compared to past scientists (aka McKnight's riffraff) is a red herring distracting from the real issues listed above and has little basis in actual fact. Just because you want to understand a system in more than superficial detail does not mean you are a low-quality scientist; it means that you think that the system is important enough to spend a significant proportion of your life (which we each only have one) studying and is a sign of intense focus and scientific curiosity. Try to develop a new therapeutic approach with CRISPR/Cas9 without doing the detail work to understand how the system actually works and what potential pitfalls may occur, and you risk causing great harm to patients and their families. There is a place for both grand innovation and detail work in modern science, and both need to be funded. In terms of publications, there is limited space in the glamour journals that everyone wants to get into (Science/Cell/Nature), and using publication in those type of journals as a surrogate for actually critically analyzing the quality of data in so-called lower tier journals has become a lazy way of looking at the quality of science. We're supposed to critically review data — not only our own but also data of others.

Doing research takes money. You can't do research without money, and control and distribution of money is unfortunately at the heart of how science functions these days. Those with money (i.e., those "great scientists") can come up with innovative ideas because they have the luxury of time to think and try new things without putting their careers in jeopardy. Those supposed substandard scientists who don't have much or any money (probably 85-plus percent of working scientists these days) can't support staff or afford to do experiments to get money to do more experiments unless they constantly submit grants and hope to get lucky. Just like with rich people, money begets money, and those who don't have money have a much harder time achieving the same level of success than those who have it. Merit only plays a part in who gets NIH money; there is a significant role of who you are and what you have done in the past.

The constant attack on young scientists (riffraff) by certain "elite" older scientists is analogous to every other societal situation where a privileged population is threatened by a new population and does what it can to retain control. Women getting the vote, civil rights, gay rights, etc. Perhaps it's human nature, but this type of discrimination is not healthy and generally fails in the long run.

– Philapodia

Correction

In "Eyes everywhere! Funny illustrations bring biology to life" (Hobbies, November) we reported about how Giek Far Chan, a lecturer at the School of Applied Science at Temasek Polytechnic in Singapore, uses drawings to enliven the classroom. Chan is a woman. We regret the error.

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5 – 8: ASBMB Special Symposium Kinases and Pseudokinases: Spines, Scaffolds and Molecular Switches, San Diego

JAN.

9: ASBMB workshop Developing and Sharing Best Practices: From Concept to Classroom, Melbourne, Fla.
23: ASBMB workshop Developing and Sharing Best Practices: From Concept to Classroom, Hattiesburg, Miss.
23: ASBMB workshop Developing and Sharing Best Practices: From Concept to Classroom, New York City
28: Late-breaking abstract deadline for the ASBMB 2016 Annual Meeting, San Diego

FEB.

Feb. 23: Discounted housing closes for the ASBMB 2016 Annual Meeting, San Diego
Feb. 27: ASBMB workshop Developing and Sharing Best Practices: From Concept to Classroom, Westerville, Ohio

MAR.

March 1: Early discounted registration closes for the ASBMB 2016 Annual Meeting, San Diego

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