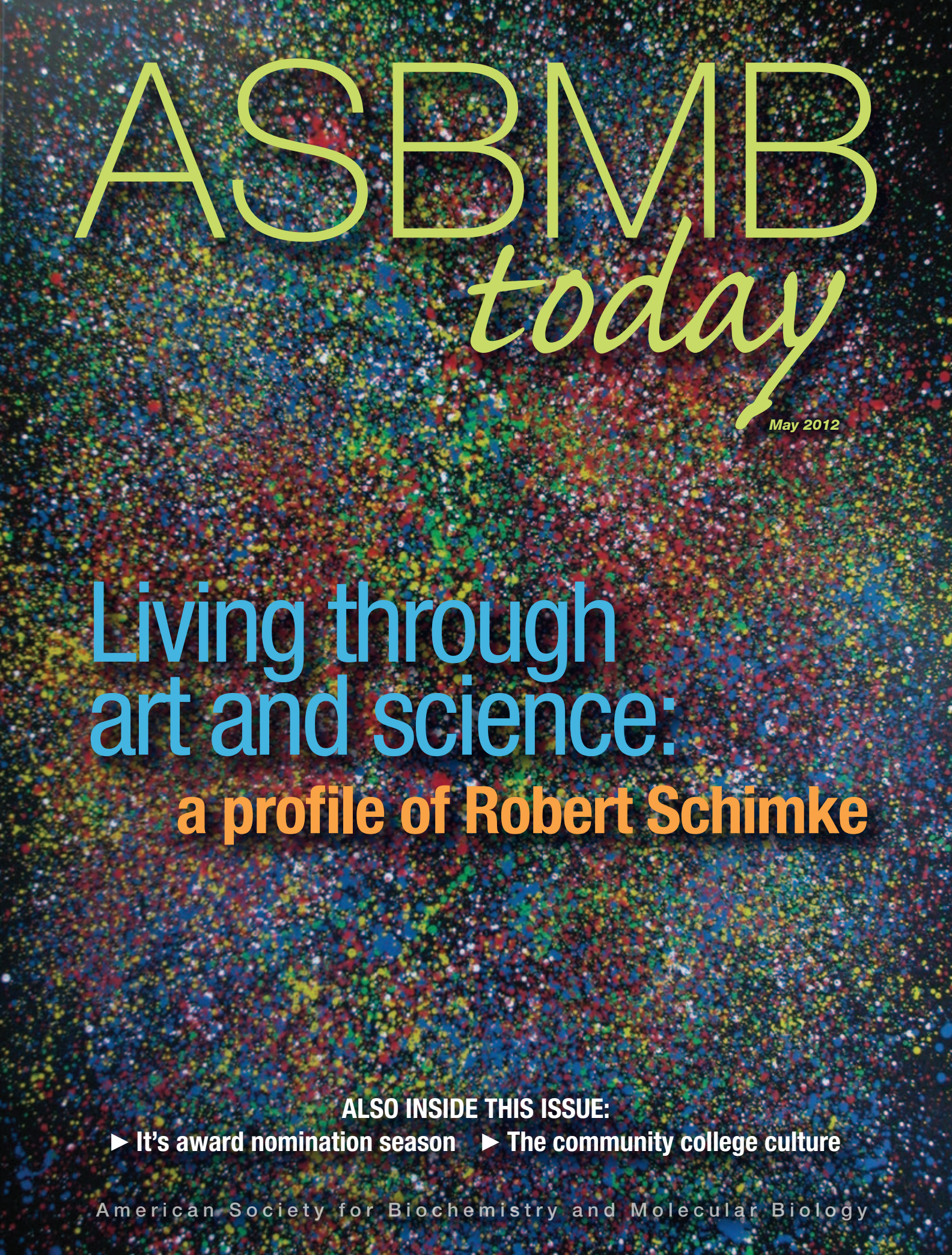

# ASBMB today

May 2012

# Living through art and science:

## a profile of Robert Schimke

**ALSO INSIDE THIS ISSUE:**

► It's award nomination season ► The community college culture

American Society for Biochemistry and Molecular Biology

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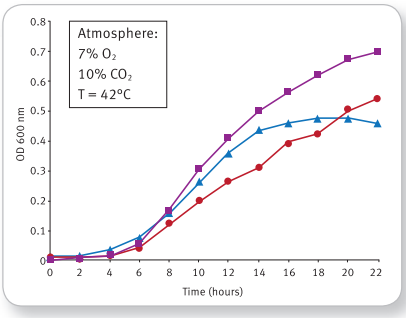


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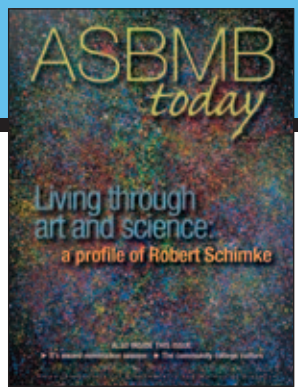
# contents




MAY 2012

On the cover:
ASBMB Today science writer Rajendrani Mukhopadhyay profiles Robert Schimke, whose lab made major contributions to at least four different areas of biology and who is now an artist. 12

## news



Introducing the Mildred Cohn Award. 10

## features

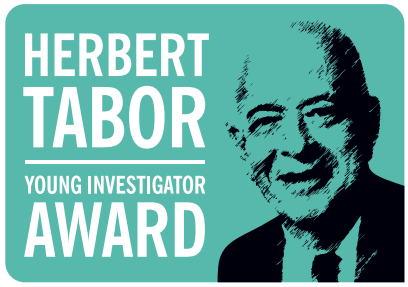


Can't figure out what to buy that new grad in your life? Check out our list of must-have gifts. 20

## departments



Find out about the first two winners in 2012 of JBC/Tabor Young Investigator Awards. 8




### *education*

A community college assistant professor addresses the well-documented repercussions of transfer shock and writes openly about her own experience with it decades ago to persuade others to help create a culture of undergraduate research at community colleges. Page 30

ASBMB today

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who got (temporarily) inked at the society's tattoo parlor booth and a roundup of blogging about symposia and special events.

## Tune in to advocacy

Earlier this spring, Hill Day was a multi-channel, multimedia affair, and we have videos to prove it. Hear from the 2012 cohort of ASBMB members on our website.

## Complementary skills: *What they are and how to develop them*

In the coming months, ASBMB Today contributor Aruni S. Arachchige Don will report on a variety of skills that young scientists should acquire to advance their careers — both inside and outside of the lab. Read her introductory column at www.asbmb.org/asbmbtoday this month, and look for her forthcoming discussions about important skills, such as communication, leadership, management, professionalism, research conduct and professional and social networking. She'll offer insights from professional communicators, leadership and ethics specialists, and those who make a living using social media to advance causes and careers.

# Credos for challenging times

BY SUZANNE PFEFFER

Have biochemists and molecular biologists become more cranky in recent years? I think so. For example, there was a time when manuscript reviews would come back with warm praise and a highly constructive tone. I once received a review in which the referee took the time to make suggestions about grammatical usage that were very much appreciated by this then-assistant professor. That kind of review doesn't need to be rare: Each of us can be the change we wish to see, as the saying goes. Referees should remember that their comments are not just directed at a lab head; reviews have the biggest impact on the students and postdocs who have to respond to each of the points raised with additional data and, certainly, some level of discouragement.

A vicious cycle can start with a critical or seemingly unfair manuscript review. Crankiness can escalate: How we treat each other can mirror how we feel we are treated. Are referees asking for more and more information for a single manuscript each year? Who decided that more was needed? All of us did, as authors, grant applicants, reviewers and editors, somewhere along the line. We calibrate reviews of papers and grants by what we perceive the state of the field to be — which we learn by looking at what other published papers (or funded grants) include and what other reviews look like.

I recently submitted a manuscript to a journal that is expressly designed to publish papers that present new information, requiring only that the conclusions be justified by the data. This story was part of a graduate student's very challenging thesis; the highly significant results were just out of reach, and it was time for this man to graduate. One reviewer thought it was just fine; the other reviewed the work as if it had been submitted to a much fancier journal. There was no appeasing this reviewer, despite my attempt to remind him or her which journal we had selected. So a new lab member did all that was asked; at last, the significance of the findings took a major leap forward, and we resubmitted a fully revised manuscript to a journal of much higher repute. I remind my lab members that I have never seen a paper that is not improved upon revision, no matter how stupid the comments may sometimes seem. Reviewers do help authors improve papers – they just should do this constructively and with sensitivity.

I have heard it said, "A day planning experiments can be more valuable than a week doing experiments." Mike Brown and Joe Goldstein chide their students that it is always "pH before Ph.D." My former colleague Arthur Kornberg was well known for saying, "Don't waste clean thoughts on dirty enzymes." Another credo I like is "Don't be greedy." This one applies when a student complains that half the expressed enzyme is insoluble. I say, focus on the great yield in the soluble fraction!

Gregory A. Petsko and Dagmar Ringe are both professors of biochemistry and chemistry at Brandeis University, where they jointly run a laboratory.

**Greg Petsko and Dagmar Ringe have a set of rules for their jointly run lab that I find useful.**

1. If you think you know the answer, you will get that answer, even if it's the wrong answer.
2. Never confuse an assumption with a fact.
3. One good experiment is worth a thousand expert opinions.

4. The strong shall take from the weak, but the smart shall take from the strong.
5. Take nothing on faith. Things are frequently not what they seem to be or what people tell you they are. Check everything.
6. Excellence is the result of preparation, planning, imagination and tenacity. Neglect any one of these and the result is mediocrity.
7. It's often not that hard to handle a crisis, because usually your course of action is obvious. It's how you deal with day-to-day living that really proves what you're made of.
8. Adversity doesn't build character — it reveals it.
9. You are what you do.
10. Luck is the residue of design.
11. The odds of success are never improved by excessive caution.
12. Never let your sense of morality prevent you from doing what's right.
13. When you fully understand the simpler alternative, it usually will turn out to be as complicated as the complex alternative. Occam's razor is usually a poor reason for making a selection, especially in biology.
14. Only a fool is never afraid, but never let fear make the decisions for you. Do right, and risk the consequences.
15. It's nice to be first, but it's better to be right.
16. Create an environment where people can learn and have fun learning, and the work will take care of itself. The results are just the report card.
17. Be your own toughest referee. Whenever you get a result that you expected or that you think you understand, always ask, "How might nature be trying to fool me?"
18. Be generous to your coworkers, your colleagues and your collaborators. Give more credit rather than less, and err on the side of inclusiveness. It won't cost you a thing, and it will gain you a lot.
19. Underpromise and overdeliver.
20. Fame is a bubble, popularity an accident, and money takes wings. The one thing that endures is character.

Petsko and Ringe's rules reflect another credo that I truly believe in: Life and science are not always fair, but we will all get what we deserve at the end of the day. All of us are part of a community of science, and it is the American Society for Biochemistry and Molecular Biology's role to help bring us together. Let us all treat others as we would wish to be treated. Let us share reagents and share credit and honor each other's accomplishments.

In the spirit of honoring one another, I am delighted to announce two new awards: an enhanced award in honor of Herb Tabor for his more than four decades of service to the Journal of Biological Chemistry, and a new award in honor of Mildred Cohn, the first woman to serve as president of ASBMB. Help us nurture our community by taking time to nominate a colleague for an award. And please share with us your own favorite credos! XXXX

ASBMB President Suzanne Pfeffer (pfeffer@stanford.edu) is the Emma Pfeiffer Merner professor of medical sciences and a biochemistry professor at the Stanford University School of Medicine.

# ASBMB addresses the issue of diversity in the biomedical research work force

BY JULIE MCCLURE

Over the past four decades, the National Institutes of Health has been dedicated to encouraging scientists from underrepresented racial, ethnic and socioeconomic backgrounds to participate and succeed in the biomedical research enterprise. A 2011 report in the journal Science cast an alarming shadow over these efforts. The study showed black researchers were 10 percent less likely to receive NIH funding than white researchers (1). What was perhaps most striking was that the disparity remained even when potentially confounding factors, such as education, training, previous research awards and publication record, were accounted for. Understandably, NIH leaders found the study results both surprising and highly disturbing.

In response, NIH Director Francis S. Collins created a working group charged with developing recommendations to address diversity and focusing on five transition points in the work-force pipeline:

1. entry into graduate-degree programs,
2. the transition from graduate degree to postdoctoral fellowship,
3. the move from a postdoctoral position to the first independent scientific position,
4. the award of the first independent research grant from the NIH or equivalent in industry and
5. the award of tenure in an academic position or equivalent in an industrial setting.

In January, the working group requested input from the research community on several topics, including training, the role of mentorship and role models, access to the application process for NIH grants and fellowships, and ways to address potential biases in the peer-review process. A joint committee composed of several members of the ASBMB Public Affairs Advisory and the Minority Affairs committees put forth a number of recommendations. Several addressed access to resources for minority scientists.

Currently, each institute at the NIH manages its own resources for minority researchers. The ASBMB recommended creating a single, centralized database for all intramural resources for minority scientists, creating a one-stop shop where individuals can easily access information on scholarships, training programs, and mentoring and networking groups.

The ASBMB also addressed the obstacles facing early-career scientists, specifically the lack of training in and exposure to the grant-writing and review process. The ASBMB recommended that the NIH identify and develop new opportunities for early-career scientists to expand their grant-writing skills and gain experience with the peer-review process.

Finally, the ASBMB addressed mentorship. Because many universities still have low numbers of minority students and faculty members, professional societies are uniquely positioned to create networks that can reach across institutions. The ASBMB encouraged societies to develop and foster more opportunities for mentorship among early and established researchers.

"We need to play an active role in providing minority scientists and their research programs more exposure," emphasizes Squire Booker of The Pennsylvania State University and chairman of the ASBMB Minority Affairs Committee. "In this highly competitive game of securing research funds, name recognition goes a long way. Having someone on a study section who can vouch for you and the quality of your work is critical, especially in the absence of a long track record."

The ASBMB strongly supports the efforts of the NIH community as it works toward finding solutions. The ASBMB also has a long history of working for greater inclusion and success of minority scientists, specifically through its Minority Affairs Committee.

The full ASBMB recommendations can be found at www.asbmb.org/Advocacy/advocacyhome.aspx.

Julie McClure (jmcclure@asbmb.org) is the science policy fellow at ASBMB.

REFERENCE

1. D.K. Ginther et al. *Science*, "Race, Ethnicity, and NIH Research Awards" (2011).


BOOKER


YOUNG


RAVETCH


KANG


FUCHS

## Penn State's Booker honored with the Arthur C. Cope Scholar Award from ACS

Squire J. Booker, an associate professor of chemistry and an associate professor of biochemistry and molecular biology at the Pennsylvania State University, was awarded an Arthur C. Cope Scholar Award from the American Chemical Society. Booker, chairman of the ASBMB Minority Affairs Committee and a member of the ASBMB Today editorial advisory board, received a prize of $5,000 and an unrestricted research grant. "This is a completely unexpected blessing," Booker said. Booker's many accolades include the Presidential Early Career Award for Scientists and Engineers, bestowed in 2004 by then-President Bush, and the 2002 National Science Foundation Faculty Early Career Development award. His lab has garnered international attention recently for elucidating a mechanism by which bacteria evade entire classes of commonly used antibiotics.

## 'Modern-day explorers' Young, Ravetch each win $100K from the Gairdner Foundation

The Rockefeller University's Michael W. Young and Jeffrey V. Ravetch were named winners of the Gairdner Foundation's 2012 Canada Gairdner International Awards. Young, head of Rockefeller's Laboratory of Genetics, and Ravetch, head of the Leonard Wagner Laboratory of Molecular Genetics and Immunology, will receive $100,000 each. "The work of these two scientists underscores the ability of basic research to benefit the field of medicine," said Rockefeller University President Marc Tessier-Lavigne in a statement. "Jeff's work with antibodies and immune system and Mike's findings on the molecular mechanisms of circadian rhythms and functioning have increased our understanding of how the human body works. This recognition from the Gairdner Foundation is a well-deserved testament to their dedication to science and medicine." The two will receive their awards this fall in Toronto and will give talks as part of the Gairdner National Program, a month-long series of lectures by award winners at 21 universities. "Our 2012 Canada Gairdner Awardees are a group of modern-day explorers who have dedicated their lives to using basic science to discover answers to puzzling medical challenges," said John Dirks, the president and scientific director of Gairdner. "Because of their tenacity and their dedication, we have a whole new realm of potential medical solutions open to us. It is our hope the awards continue to inspire researchers to conquer unchartered medical territory."

PHOTOS COURTESY ROCKEFELLER UNIVERSITY

## Princeton's Kang recognized at AACR meeting for his metastasis research

Yibin Kang was awarded the 32nd annual American Association for Cancer Research Award for Outstanding Achievement in Cancer Research at the association's annual meeting in Chicago in early April. Kang, a professor of molecular biology at Princeton University and a member of the Cancer Institute of New Jersey, was recognized for his "outstanding work related to the intricate interactions between tumor cells and stromal components during the metastasis of breast cancer to bone and other organs," according to the association. The award, established in 1981, is intended to recognize investigators under the age of 40. Among other pursuits, Kang's lab focuses primarily on the identification and functional characterization of metastasis genes, the preclinical evaluation of antimetastasis therapeutics, and the development of imaging technologies and noninvasive detection of tumor–stroma interaction during metastasis. Upon winning the award, Kang said, "This prestigious award reflects the strong commitment of AACR to the career development of young cancer researchers. It is also a nice recognition of the progress that we have made in the field of metastasis research. I am very hopeful that, by working together with our colleagues, we will achieve the much-needed success in preventing and controlling metastatic cancer."

## March of Dimes Prize in Developmental Biology goes to Rockefeller's Fuchs

Elaine Fuchs of The Rockefeller University has been named a co-winner of the 2012 March of Dimes Prize in Developmental Biology. Fuchs, who will share the prize with longtime colleague Howard Green of Harvard Medical School, was recognized for having contributed significantly to our understanding of skin biology and for advances in treatments for both skin cancer and burn victims. Fuchs' work has revealed the genetic basis of blistering skin diseases and how skin stem cells develop into tissues and organs and how activation mutations can lead to cancer. She is also known as a pioneer in reverse genetics. "Their work has saved the lives of thousands of burn patients, and we hope their work with skin stem cells will lead to new ways to prevent and treat birth defects," Joseph Leigh Simpson, senior vice president for research and global programs at the March of Dimes, said in a statement. The March of Dimes Prize was created in 1996 in honor of Jonas


WANG


OLSON


DE LANGE


KORNBERG

Salk. "Elaine's work has had a significant impact on the lives of those suffering from skin injuries and disorders, and it has the potential to ultimately lead to new regenerative therapies. It is deeply gratifying to see her work recognized with this award," Marc Tessier-Lavigne, president of The Rockefeller University, said in a statement. Fuchs received the $250,000 prize at the Pediatric Academic Societies' annual meeting in Boston in April.

## NIAMS names Wang one of four appointees to advisory council

Xiao-Jing Wang of the University of Colorado, Dever, has been appointed to the advisory board of the National Institute of Arthritis and Musculoskeletal and Skin Diseases. Wang was one of four new appointees selected for their expertise in the mission areas of the institute, which is a component of the National Institutes of Health. Wang, a professor at UC-Denver's department of pathology, is also director of the university's Head, Neck, and Squamous Cell Carcinomas Research Program. Her lab developed multiple genetically engineered mouse models that mimic human head and neck cancers at both genetic and clinical levels. She also identified a gene deletion responsible for 80 percent of mouse head and neck tumors.

## UT-Southwestern's Olson wins the 2012 Passano Award for muscle research

Eric Olson of the University of Texas Southwestern Medical Center at Dallas won the 2012 Passano Award for his research on muscle differentiation, through which he identified major genetic pathways controlling the development of the heart and other muscles. The founding chairman of the molecular biology department at UT-Southwestern, Olson has studied the genes and transcription factors responsible for development of the heart in embryos and defects resulting in congenital heart disease. Announcing the award, Passano Foundation officials said Olson's discoveries "have profoundly influenced our understanding of the mechanisms responsible for development and dysfunction of the heart." Twenty-three past winners of the Passano Award have gone on to win the Nobel Prize. Three have ties to UT-Southwestern, including Michael S. Brown and his co-winner, Joseph L. Goldstein, who emphasized in a statement that Olson's work has "unveiled the molecular underpinnings of congenital and acquired diseases of the heart and established a foundation for the advancement of new cardiovascular therapeutics." Indeed, several drugs based on Olson's findings are under development.

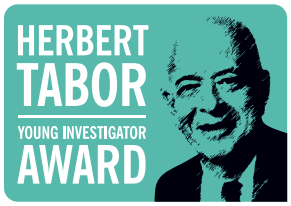
## For her telomere work, de Lange is first woman to win Heineken Prize for biochem, biophysics

Titia de Lange of Rockefeller University won one of this year's H.P. Heineken Prizes from the Royal Netherlands Academy for Arts and Sciences. The first woman to receive the $150,000 award for biochemistry and biophysics, de Lange was recognized for having identified the protein complex shelterin on telomeres and showing how shelterin hides the chromosome end from the cellular machinery that detects and repairs broken DNA ends. Heineken Prizes are awarded biannually to five scientists and one Dutch visual artist for their contributions to science, Dutch art and society. "Titia's research on telomeres has had a significant impact on our understanding of how a cell responds when its DNA is damaged," Marc Tessier-Lavigne, Rockefeller's president, said in a statement. "Her work has shed light on the causes of human cancer and is a prime example of the importance of basic research in the fight against cancer, and I am greatly pleased to see her recognized with this important prize." De Lange's previous honors include the 2011 Vilcek Prize in Biomedical Science, the 2010 American Association for Cancer Research Clowes Memorial Award, the 2008 Massachusetts General Hospital Cancer Center Prize and the 2005 National Institutes of Health Director's Pioneer Award.

PHOTO COURTESY ROCKEFELLER UNIVERSITY

## Kornberg appointed to the advisory board of nonprofit Prize4Life

Nobel laureate Roger Kornberg will join the scientific advisory board of Prize4Life, a nonprofit focused on accelerating the development of treatments and a cure for amyotrophic lateral sclerosis. "Prize4Life is delighted to welcome such an accomplished and talented scientific mind," Avi Kremer, co-founder and chief executive officer of Prize4Life, said. "Roger Kornberg is an excellent addition to our (board), which provides a high level of expert knowledge and wise counsel to Prize4Life and is integral to the success of our important mission." Kornberg, a professor at Stanford University School of Medicine, won the Nobel in 2006 for seminal research on the molecular basis of eukaryotic transcription, and his lab has continued to elucidate the complex processes by which DNA is unraveled, read and transcribed. In a statement, Kornberg called the nonprofit's mission "imperative" and said he was looking forward to joining the board. Prize4Life was founded in 2006 by Kremer, who was diagnosed with ALS at age 29.




## A NEW CROP OF AMAZING SCIENTISTS RECOGNIZED BY SERIES

# First winner named at epigenomics meeting

BY ANDREW HARMON

Shalini Oberdoerffer, a tenure-track investigator at the National Cancer Institute, won the Journal of Biological Chemistry/Herbert Tabor Young Investigator Award in January at the Keystone Symposium on epigenomics for her work demonstrating DNA methylation and CTCF mediate reciprocal effects on alternative pre-mRNA splicing.

Oberdoerffer earned her bachelor's in biology from Bryn Mawr College, worked as a technician in Ronald Collman's lab at the University of Pennsylvania and earned her Ph.D. at Harvard University. She was a postdoc in Anjana Rao's lab at Harvard, where she examined the role of RNA binding proteins in alternative splicing regulation of the protein tyrosine kinase CD45, and then joined the NCI's Mouse Cancer Genetics Program in 2010.

**Shalini Oberdoerffer received her award from Joel Gottesfeld, a Journal of Biological Chemistry associate editor, at the Keystone Symposium on epigenomics in January.**

"I developed an interest in alternative splicing as a graduate student when I saw a lecture by Francis Collins after the publication of the human genome. I was amazed by the disconnect between the number of human genes and predicted size of the proteome. With the ability to map expressed sequence tags, evidence quickly mounted for wide-scale diversification of the human transcriptome. Since then, I have focused my research on determining the mechanisms supporting regulated shifts in alternative pre-mRNA splicing during lymphocyte development.

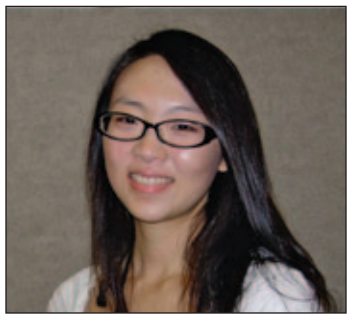
Andrew Harmon (aharmon@asbmb.org) is ASBMB's science and publishing technology manager.

# Second winner named at biophysics meeting

BY ANGELA HOPP

Shannon Yan, a Ph.D. candidate at the University of California, Berkeley, won the Young Investigator Award in February at the 56th annual meeting of the Biophysical Society. She was recognized for her work to resolve how the ribosome dynamically translates during frameshifting along a messenger RNA.

"Universally, across all species, the ribosome long has been known to read three nucleotides as one codon and incorporate one amino acid per translation cycle. Yet there are well-established cases when specific mRNA templates bearing slippery sequence and other frameshift promoting elements effectively induce this high-fidelity machine to switch its translation reading frame and synthesize more than one kind of protein products from a single mRNA. And till this day, the detailed mechanism remains largely unsolved," Yan says.



**Shannon Yan received her award from Norma Allewell, a Journal of Biological Chemistry associate editor, at the Biophysical Society's annual meeting in February.**

Yan earned her bachelor's in chemistry at the National Taiwan University, where she trained as "a hard-core physical chemist" working in gas phase chemical kinetics and reaction dynamics. "I've always found the basic physical principles most intuitive and have enjoyed applying them to explore and explain the unknown systems, in particular the dynamic ones," she explains. "Later, I realized similar manners and strategies of study can be beautifully generalized to seemingly complicated biological systems, as long as one can focus on the most relevant issue and ask the right question with the right tool."

Today, in Ignacio Tinoco's lab, she is working with a reconstituted in vitro translation system and using optical mini-tweezers to monitor real-time translation activity from a single ribosome as it translocates and gradually unwinds an mRNA hairpin. "We hope to visualize exactly how ribosome frameshifts in real time," she says.

Angela Hopp (ahopp@asbmb.org) is editor of ASBMB Today.

# New award in Mildred Cohn's name

Starting in 2013, the American Society for Biochemistry and Molecular Biology will issue an annual Mildred Cohn Award in Biological Chemistry. Named after the first female president of the society, then the American Society of Biological Chemists, the award will be for scientists of all career levels who have made substantial advances using innovative physical approaches.

"Mildred was an exceptional scientist and colleague," says Judith Klinman of the University of California, Berkeley. "Her contributions to science continued unabated over a very long period of time."

After graduating from high school at the age of 14, Cohn earned a bachelor's in chemistry in 1931 at Hunter College and earned a master's in 1932 and a Ph.D. in physical chemistry in 1938, both at Columbia University. She was a postdoc at George Washington University with Vincent du Vigneaud and a research associate at Cornell University's medical school. In 1946, she began her long association with the Carl and Gerty Cori lab at Washington University and was promoted to associate professor in biochemistry in 1958 but left for the University of Pennsylvania School of Medicine, where she became a full professor in 1961. She was the Benjamin Rush Professor Emerita of Physiological Chemistry in the biochemistry and biophysics department.

"Beginning with her Ph.D. studies with Harold Urey at Columbia, Mildred exploited the use of isotopes in her pursuit of understanding both enzyme mechanism and cellular metabolism. One of her most important independent breakthroughs was the development of nuclear magnetic resonance methods for the study of enzyme reactions," Klinman said. "Mildred was able to overcome the primitive, low-sensitivity instrumentation available at that time, together with the need for enormous quantities of biological samples, to map out the geometry of bound substrates in proximity to paramagnetic metal ions."

Cohn was president of ASBC from 1978 to 1979 and the first woman appointed to the Journal of Biological Chemistry editorial board. "Mildred was a true pioneer who was brilliant and whose accomplishments were legion. She was an inspiration to us all," said Mark Lemmon, ASBMB's secretary and department chairman at Penn.

"Mildred was always the consummate professional and devoted considerable energy to numerous scientific societies," Klinman added. Indeed, over the years her efforts were recognized with election to the American Academy of Sciences, the National Academy of Sciences and the American Philosophical Society. She won the National Medal of Science in 1982 and was named to the National Women's Hall of Fame shortly before her death in 2009.

# Updated Tabor research award

Late last year, the American Society for Biochemistry and Molecular Biology governing body voted to rename the Herbert Tabor/Journal of Biological Chemistry Lectureship the Herbert Tabor Research Award and to increase the prize amount to $30,000.

The move came on the heels of the creation in early 2011 of a young investigator award also in Tabor's name and reflects the society's desire to recognize Tabor's contributions to the journal, for which he served as editor and now serves as co-editor. "I cannot think of anyone who has given more to ASBMB than Herb Tabor, and Council was unanimous in its wish to honor him for his more than four decades of leadership of the JBC," Suzanne Pfeffer, ASBMB's president, said.

The lectureship, which recognized lifetime achievements, will be replaced with the research award for excellence in biological chemistry and molecular biology and contributions to the scientific community. For more information about the nomination process, see page 10.

"Herb has been a pillar for the society and the scientific community," Barbara Gordon, ASBMB's executive director, said. "This is one way for us to emphasize how much we appreciate the work he's done — and continues to do on a daily basis. He is, indeed, a living legend, and we expect that those who are selected for this research award in years to come will be of exceptional caliber as well."

# 2013 award nominations

*Do you know someone who has made important contributions to the scientific enterprise? The American Society for Biochemistry and Molecular Biology wants to recognize the very best among us and is now accepting nominations for its 2013 awards. See descriptions of the available awards below. The nomination deadline is June 5.*

## NEW: The Mildred Cohn Award in Biological Chemistry

The Mildred Cohn Award in Biological Chemistry was established to honor the pioneering scientific accomplishments and the spirit of the late Cohn, who was the first female president of the American Society for Biochemistry and Molecular Biology, at the time known as the American Society of Biological Chemists. The award recognizes and honors scientists at all stages of their careers who have made substantial advances in understanding biological chemistry using innovative physical approaches. Nominations must be made by ASBMB members, but the nominees need not be ASBMB members. The award will be given annually and carries a $5,000 prize and travel expenses to the annual meeting to present a lecture.

## UPDATED: The Herbert Tabor Research Award and Lectureship

The Herbert Tabor Research Award and Lectureship was established to recognize the many contributions of Herbert Tabor to the Journal of Biological Chemistry and the society. The award will be given for excellence in biological chemistry and molecular biology and contributions to the community of scientists. The ASBMB seeks to be the first to recognize outstanding accomplishments. Nominations must originate from and nominees must be ASBMB members. The award consists of a $30,000 research prize, a plaque and travel expenses for the annual meeting to present a lecture.

## The Alice and C. C. Wang Award in Molecular Parisitology

The Alice and C. C. Wang Award in Moleuclar Parisitology recognizes established investigators making seminal contributions to the field of molecular parasitology. Novel and significant discoveries on the biology of parasitic organisms are of particular emphasis. The areas of research to be awarded are limited to protozoan parasites but otherwise broadly defined, including but not limited to biochemistry, molecular biology, gene regulation, metabolism, cell biology, development biology and host–pathogen interactions. Nominations must originate from ASBMB members, and self-nominations are acceptable. The recipient should be an internationally recognized scientific leader who already has made important discoveries in the field and continues an active effort at the cutting edge of research. The award consists of $35,000 for use by the recipient's research laboratory, a plaque and travel expenses for the recipient to attend the ASBMB annual meeting to present a lecture. In addition, the winner will organize a half-day symposium on molecular parisitology at the meeting.

## The ASBMB–Merck Award

The ASBMB–Merck Award recognizes outstanding contributions to research in biochemistry and molecular biology. Nominations must originate from ASBMB members, but nominees need not be members. The award consists of a plaque, $5,000 and transportation and expenses to the annual meeting to present a lecture.

## The William C. Rose Award

The William C. Rose Award recognizes outstanding contributions to biochemical and molecular biological research and a demonstrated commitment to the training of younger scientists, as epitomized by the late Rose. Nominations must originate from ASBMB members, but nominees need not be members. The award consists of a plaque, $3,000 and transportation to the annual meeting to present a lecture.

## The Earl and Thressa Stadtman Distinguished Scientist Award

The Earl and Thressa Stadtman Distinguished Scientist Award was established by the couple's friends and colleagues to preserve their legacies as scientists and mentors. It is awarded to an established scientist for his or her outstanding achievement in basic research in the fields encompassed by the ASBMB. The award is given every

# welcome

other year, alternating with The Earl and Thressa Stadtman Young Scholar Award. Nominations must originate from ASBMB members, but nominees need not be members. The award consists of a plaque, a $10,000 cash prize and travel expenses for the annual meeting to present a lecture.

## The DeLano Award for Computational Biosciences

The DeLano Award for Computational Biosciences was established by family, friends and colleagues to honor the legacy of Warren L. DeLano. The award is given to a scientist for the most accessible and innovative development or application of computer technology to enhance research in the life sciences at the molecular level. The contribution should include two key elements — more productive use of computers to accelerate and facilitate research and ready access of these programs for the scientific community. Nominations must originate from ASBMB members, but nominees need not be members. The award consists of a plaque, $3,000 and travel expenses for the recipient to give a lecture at the annual meeting.

## The Avanti Award in Lipids

The Avanti Award in Lipids recognizes outstanding research contributions in the area of lipids. Nominations must be made by ASBMB members, but nominees need not be members. The award consists of a plaque, $3,000 and transportation and expenses to present a lecture at the annual meeting.

## The Avanti Young Investigator Award in Lipid Research

The Avanti Young Investigator Award in Lipid Research, established by the ASBMB's Lipid Research Division, recognizes outstanding lipid research contributions by young investigators with no more than 15 years of experience since receiving their degrees (Ph.D. and/or M.D.). The award consists of a plaque, $2,000, and transportation and expenses to present a lecture at the annual meeting.

## The ASBMB Young Investigator Award

The ASBMB Young Investigator Award (formerly the ASBMB/Schering-Plough Research Institute Award) recognizes outstanding research contributions to biochemistry and molecular biology. The recipient must have no more than 15 years post-postdoctoral experience. Nominations must originate from ASBMB members, but nominees need not be members. The award consists of a plaque, $5,000 and transportation and expenses to present a lecture at the annual meeting.

## The Ruth Kirschstein Diversity in Science Award

The Ruth Kirschstein Diversity in Science Award was established to honor an outstanding scientist who has shown a strong commitment to the encouragement of underrepresented minorities to enter the scientific enterprise and/or to the effective mentorship of those within it. The award consists of a plaque, $3,000 and transportation expenses to present a lecture at the annual meeting. The recipient is chosen by the Minority Affairs Committee. Nominations must be made by ASBMB members, but nominees need not be members.

## The ASBMB Award for Exemplary Contributions to Education

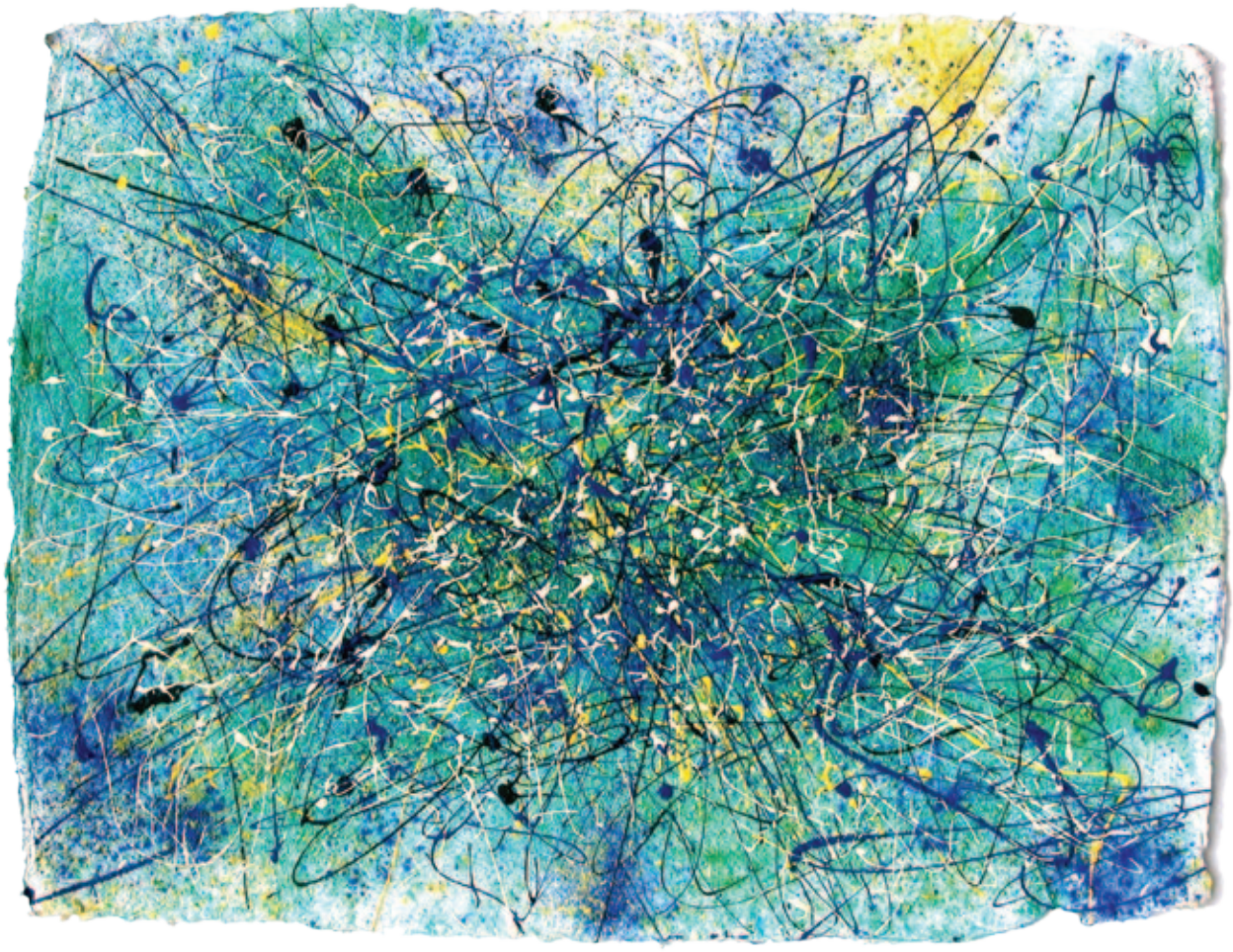
The ASBMB Award for Exemplary Contributions to Education is given annually to a scientist who encourages effective teaching and learning of biochemistry and molecular biology through his or her own teaching, leadership in education, writing, educational research, mentoring or public enlightenment. Nominations must come from ASBMB members, but nominees need not be members. The award consists of $3,000, and the winner presents a plenary symposium lecture at the annual meeting.

**All awards will be given at the 2013 annual meeting in Boston.**

# Living through art and science

## *Robert Schimke embraces the life of an artist after spending decades as a scientist*

BY RAJENDRANI MUKHOPADHYAY



***Robert Schimke has ditched the pipettes and gels for paintbrushes and canvases.*** *An emeritus professor from Stanford University's department of biological sciences, Schimke's scientific portfolio is tremendous.*

From the 1960s to the 1990s, his laboratory made major contributions to at least four different areas of biology. Schimke served on boards for scientific journals and biotechnology companies and was president of the American Society for Biochemistry and Molecular Biology in 1988. But now he has left science behind to spend his time creating art. He also spends his days in a wheelchair.

A quadriplegic for 17 years with limited use of his arms and feet, Schimke has found a way to express movement through art. "I used to be rather physically active. Obviously I can't do that anymore so I take it out on my paintings!" he says. "They are all moving. There's nothing static about them."

Schimke was ready to leave science after the accident that left him mostly paralyzed. "I was 62 at that time and I was ready to retire, which is very different from most scientists. They don't know what else to do. I really wanted to retire so that I could paint and garden," says Schimke.

Schimke hasn't let the accident dash his dreams of painting. These days, he melds his scientific methods with his artistic skills to get different kinds of paint to sweep, skirt, splotch or splatter over canvases. "I'm continually experimenting with new techniques. Many artists over time will paint more or less in the same genre that they've painted all the time," he says. "I try all kinds of different things."

Schimke is focused these days on understanding what happens to latex paints, which he purchases from Home Deport, as he drips and splashes them across canvases. "I'm trying to figure out how to make some interesting shapes by simply pouring dilute, light-colored paint on canvases that are painted black," he says. "The other thing I have been doing very recently is to make relatively small canvases that have drips of undiluted paint that comes right out of the gallon can. That produces some striking three-dimensional patterns. They have a lot of different colors … I must say if you look at them, all you can do is smile."

## EARLY YEARS

There weren't many smiles when Schimke was growing up Spokane, Wash. Born in 1932, "my first eight years were right in the middle of the Depression," he says. "I really didn't have a lot of the fancy accoutrements that all kids have these days."

His father was a dentist and his mother was a homemaker. "They had their own problems," reflects Schimke. "I didn't have too happy a childhood."

A self-described loner, Schimke was most content riding his sister's bicycle (hers was superior to his) around the forests on the outskirts of Spokane and spending Friday afternoons at his grade school when they held art classes. "I loved to paint and muck around with it," he says, recalling when he tried to paint daffodils with oil paints and failed. No one around him, however, was an artist, and he didn't have anyone encouraging him to pursue art. At high school, he abandoned his artistic pursuits.

For his undergraduate degree, Schimke went to Stanford University, where he ended up in the premed program and got married. "My wife was majoring in humanities. One of her courses was on art history," says Schimke. "I learned more about art history than probably anything else at Stanford!"

After getting his undergraduate degree in 1954, Schimke and his wife went hitchhiking in Europe. "We went to all the art galleries," says Schimke. "We didn't go to Spain and Russia, but we saw literally everything else that we possibly could. That was a lot of fun."

After he returned, Schimke went on to get his medical degree in 1958 from Stanford. He interned at the Massachusetts General Hospital until 1960 and then was drafted into the Public Health Service. The draft got him into the National Institute of Arthritis and Metabolic Diseases, where he worked with Herb Tabor, who later became editor-in-chief for the Journal of Biological Chemistry. In 1966, Schimke returned to Stanford as a faculty member.

Over the years, Schimke's group made significant contributions to understanding protein turnover, steroid hormone control of gene expression, the connections between cell division and apoptosis, and gene amplification as a way for cells to resist cancer chemotherapy drugs. Schimke's

**Schimke also was a scientific adviser to Monsanto, DuPont and Amgen and was crucial in helping Amgen launch its first blockbuster drug, Epogen.**

work on protein turnover and gene amplification was featured as a JBC Classic (1). His work on gene amplification is now used for mass production of large quantities of therapeutic proteins, such as erythropoietin and tissue plasminogen activator, in mammalian cells.

Schimke also was a scientific adviser to Monsanto, DuPont and Amgen and was crucial in helping Amgen launch its first blockbuster drug, Epogen, a version of erythropoietin. Schimke was a JBC associate editor from 1975 to 1981 and from 1983 to 2002 and also served on its editorial board. In addition to numerous awards, he was elected to the National Academy of Sciences in 1976 and to the Institute of Medicine in 1983.

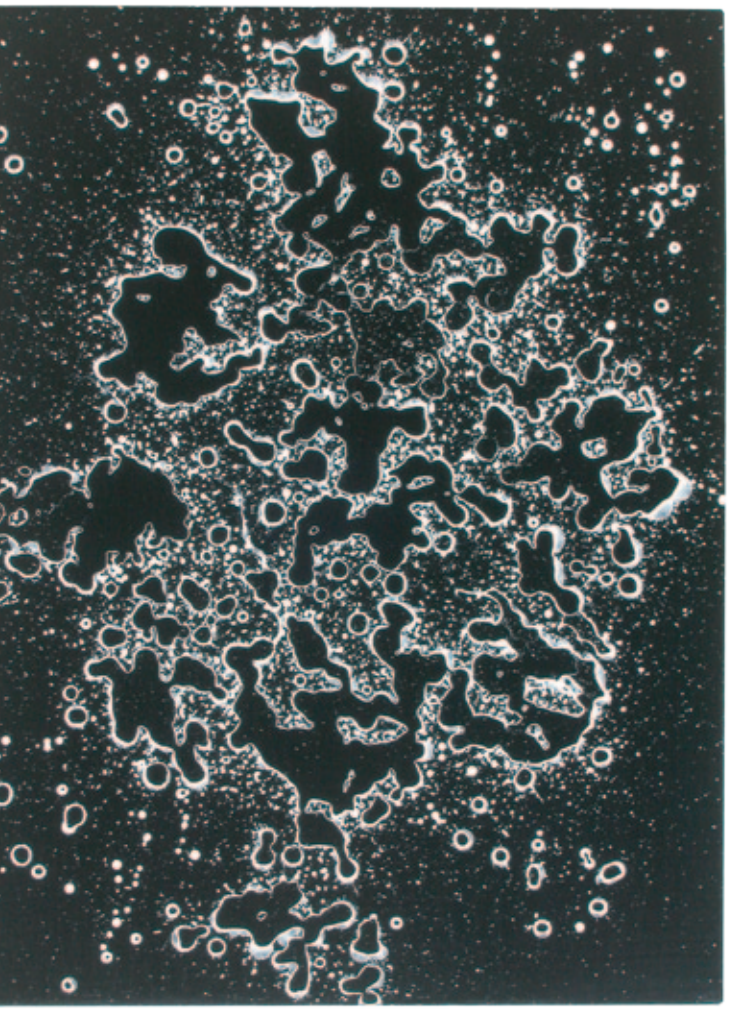
## THE FIRST BURSTS OF SERIOUS PAINTING

But as life went on, tragedies struck. At those times of suffering, Schimke found himself turning to his boyhood passion of painting. In 1976, the woman he was married to at that time, Mary, suddenly died of cerebral hemorrhage. After his wife's death, "I decided I didn't want to do science," says Schimke.

One day, while in England, where he had gone to do a sabbatical, Schimke walked down to a Camden Town flea market. There, Schimke discovered a set of pastels priced at 50 pence, "undoubtedly stolen from somewhere." With these pastels in his hands, he felt he ought to do something with them. So he bought some good-quality paper and began to ease back into art.

When it came time for him to return to the U.S., Schimke realized the pastels were powdery and would brush off during the course of the journey. At this point, he decided to switch to oil paints because they lasted better and also because he had always loved to use them. He worked with oil paints for a while back in the U.S., but his laboratory got involved in work that would lead to the discovery of gene amplification. "That was something that brought me back into science in a big way," he says. He returned to the laboratory in 1977.

But in the mid-1980s, he experienced another artistic burst and left the laboratory. This time, he focused on placing natural products, such as eucalyptus and bamboo, on canvas so that their three-



dimensional shapes played with light and shadow.

But then his research group got involved in studying how mistakes in regulating the cell cycle caused gene amplification or cell death. Schimke returned to the laboratory to devote his time to the research.

## THE ACCIDENT

In February 1995, on a Saturday afternoon, Schimke mounted his bike to cycle back home from the lab. Palo Alto, where Stanford University is, has mountains on its borders that reach up at least 3,000 feet, and Schimke often biked them. That day, he decided to go up halfway and take the long way home.

Around 2 p.m., Schimke was in a bike lane on Sand Hill Road in Woodside, a small town filled with redwood, oak and eucalyptus trees. The road had a T-intersection. "I was going to go straight in the T, but some bicyclists in front of me were going very slowly and were turning right," says Schimke. "There was a car behind me whose driver thought I was part of that group and was going to turn as well. She started to make a turn, and her tire hit me."

Schimke has a few hazy memories of the next few moments. "I remember vaguely, very vaguely, somebody talking to me and putting me on a stretcher. The next thing I remember was the doors to the emergency ward at Stanford University opening up," he says. "The next thing I remember somebody saying, 'Do you know somebody to call?'" Schimke was aware enough to tell them to call his current wife, Patricia Jones, Stanford's vice provost for faculty development and diversity.

Schimke stayed at the local county hospital for three days. Because he had served in the Public Health Service, he was considered a veteran. With Tabor's contacts at the U.S. Department of Veteran Affairs, Jones got the necessary paperwork to have

Schimke quickly transferred to the Palo Alto veteran's hospital, which had a better spinal cord injury center.

In the second week after the accident, as a slow recovery loomed, Schimke says, "I remember thinking, 'All right, Bob, what the hell are you going to do now? You better start doing something!' I was determined I was going to get better."

The accident left Schimke's spinal cord damaged but not completely severed, so he has some sensory and motor capabilities in his arms and feet. "My hands are like claws. I can grab a pencil and write my name badly," he says. "I can hold a brush."

## HAVING FUN

On his property in Palo Alto, which is almost an acre in size, Schimke does his art in a garage that has been converted into a gallery. He also makes beaded necklaces. The place is filled with his work, which includes drip paintings in the style of Jackson Pollack and a series done with masks mounted on foam boards. "I've painted over 400 different things in my lifetime," says Schimke. Some of his work is on display at ASBMB headquarters in Rockville, Md.

Schimke says the artists he admires are Vincent van Gogh, Pablo Picasso and, up to a point, Pollack. "Other than the drip paintings that he did, [Pollack] was not a very good artist," he says. "If Jackson Pollack's paintings are worth millions and millions of dollars, hell, I can do that stuff just as well as he could. Indeed, I can."

An assistant helps him open up paint cans, stretch out canvases and clean up. Because of his limited movement, Schimke works on canvases stretched out on plywood and no more than four feet wide. He attaches sticks, the kind used to mix paint, to his paintbrushes so he can reach two feet across the canvas. Then he wheels himself around to the other side to get the remaining two feet. At noon sharp each day, a shrill, 19-year-old Siamese cat makes Schimke stop his work because it insists on having its lunch of turkey breast. "It eats basically what I have for lunch," chuckles Schimke.

Despite all he has accomplished as a scientist, Schimke says he doesn't miss science. He tried to stay in touch with his areas of expertise after his accident by continuing to serve as a JBC associate editor but "it became obvious that I was not keeping up," he says. "I resigned."

He is not sure what kind of artist he would have been had the accident not happened. But he is sure of one thing: The art he would have produced would not have been "nearly as interesting and as much fun!"

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## Lilly-NIH partnership aims to revolutionize drug-development pipeline

BY CONNOR BAMFORD

The National Institutes of Health and Eli Lilly and Co. last month announced a joint venture to develop a public resource to create a more effective drug-discovery program. Spurred by various challenges in getting an experimental candidate approved and to the clinic, those heading up this public–private partnership say they hope the results will help in the development of novel treatments for some of our most common diseases.

This collaboration— which will run over the next 18 months— will involve teams from NIH's recently established National Center for Advancing Translational Sciences and Lilly Research Laboratories. It will open the doors of the NIH Chemical Genomics Center's Pharmaceutical Collection of 3,800 approved and investigational compounds suitable for high-throughput screening. Access to this collection will allow the Lilly group to profile comprehensively the compounds' biological activities through its Phenotypic Drug Discovery panel of assays constructed to model complex pathways of various human diseases.

For example, the anti-angiogenesis assay module is used to investigate the potential for compounds to inhibit the growth of new blood vessels. This automated test utilizes a co-culture of endothelial and adipose stem cells. The addition of a compound that inhibits growth of the endothelial progenitor cells while not harming the adipose-derived adult stem cells would be considered a drug of interest and would form the starting point for further experiments, collaborations and clinical trials.

If the partnership finds an approved medicine could be a possible treatment for a different disease, it will reach out to whoever owns the compound to pursue additional studies. Alternatively, results with investigational drugs from high-throughput screens might inspire generatation of new drug candidates. "This initiative is a great example of how we can collectively leverage unique capabilities from the public and private sectors toward our shared goal of advancing science and improving patients' lives," said Alan D. Palkowitz, Lilly's vice president of discovery chemistry research and technologies. Those interested in the progress of the venture can check in on the results for free at http://tripod.nih.gov/npc/.

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## Data from 1000 Genomes Project now accessible on Amazon Cloud

BY RAJENDRANI MUKHOPADHYAY

Data from the 1000 Genomes Project, the world's biggest resource on human genetic variation, are now available on the Amazon Web Services cloud. The collaboration between the National Institutes of Health and AWS to store the data will let any researcher obtain and study them at a fraction of the cost that it would be for his or her institution to host the information.

"The explosion of biomedical data has already significantly advanced our understanding of health and disease. Now we want to find new and better ways to make the most of these data to speed discovery, innovation and improvements in the nation's health and economy," said NIH Director Francis S. Collins at an event at the White House to announce the collaboration.

The four-year-old 1000 Genomes Project now stands at 200 terabytes of data. That's the same amount of information in more than 30,000 DVDs. Because of the massive size, few researchers have sufficient computing power to mine the data, so AWS is hosting the information as a free public data set. The data can be accessed through high-performance computing services such as Amazon Elastic Compute Cloud and Amazon Elastic MapReduce. Researchers pay only for additional AWS resources if they need to further process or analyze the data.

"Improving access to data from this important project will accelerate the ability of researchers to understand human genetic variation and its contribution to health and disease," said National Human Genome Research Institute Director Eric D. Green. NHGRI is a major funder of the 1000 Genomes Project, along with Wellcome Trust and BGI-Shenzhen. Having the data on the cloud also means users can analyze them much more quickly. They need not be downloaded, and analyses can be run over many servers simultaneously.

### THERE ARE MULTIPLE WAYS TO ACCESS THE 1000 GENOMES PROJECT DATA

- **Amazon site, http://s3.amazonaws.com/1000genomes/**
- **1000 Genomes site, www.1000genomes.org**
- **NCBI site, ftp://ftp-trace.ncbi.nlm.nih.gov/1000genomes**
- **EBI site, ftp://ftp.1000genomes.ebi.ac.uk**

Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the senior science writer for ASBMB Today and the technical editor for the Journal of Biological Chemistry.

# Top 10 gradua

BY CONNOR BAMFORD

**Graduation season is upon us, which means it's time get on with gift buying. Here are 10 recommendations for thoughtful and fun gifts for the science student in your life.**

Up first is the crowd-sourcing website **PetriDish**, which specializes in raising funds for science projects across the world. Log in and browse the collection of potentially fundable investigations. You can pick your favorite and pledge any amount of money to the cause. Who knows, you may even receive a free gift for your help. **www.petridish.org/**

Next is a **genetic testing kit by 23andMe**. Here you buy the chance to send off a saliva sample and get it screened for a range of genetic variants, and a few weeks later you will receive a summary of what your genome can say about your health, particular traits and, best of all, where your ancestors most likely came from. **www.23andme.com**

Artologica is a U.S.-based artist who focuses on creating science-inspired (and in particular biology-inspired) pieces of artwork. One exceptional creation you could give is a **painting of the cell cycle**, an ideal gift for a budding molecular biologist. The artist has many, many others that come with a wide range of price tags. **http://etsy.me/n9ggrK**

With the widespread use of biochemical techniques outside of the lab, molecular gastronomy – the application of chemistry and molecular biology to cooking – has caused a revolution in how we prepare and cook our food. This book, **"Molecular Gastronomy: Exploring the Science of Flavor,"** written by Hervé This, a leader in the field, teaches readers in theory and practice of applying the last couple of years of science training to making the most delicious and interesting food. **http://amzn.to/luKXHv**

Do you know a graduate who has a love of all things micro? Somebody who would really like the chance to explore the world in its finer details? If so, then this **minimicroscope for the iPhone 4** will be right up their alley. Attach this implement to the front of a smartphone and get ready to see how nature really looks. Don't forget to share the pictures with the rest of us! **http://bit.ly/IzKFAI**

The last half a decade or so has seen a massive increase in the interest in online science blogging. To document, highlight and organize this massive amount of journalism and commentary, one group has set about creating a **collection of the best blog posts** from a wealth of bloggers and science fields. Give the gift of knowledge or even inspire someone to take up blogging by buying your graduate the very best in science blogging from 2006 to 2011. **www.lulu.com/spotlight/coturnix1**

**Cafepress** is a U.K.-based company that lets you browse a range of specialty clothes and accessories. The great thing is that if you don't like anything, you can design your own! So if you have an idea for, say, a molecular-biology-themed mug, give it a go and make one for your grad. If you have no ideas, check out the DNA electrophoresis gel-inspired T-shirt. **http://bit.ly/IIFVKf**

We all know that getting education requires a lot of reading; some people enjoy this, while others grow to loathe it. Forget about the latter and embrace

# tion gift ideas

the former by giving someone you know Amazon's **Kindle Touch**. Your grad can read science books or even recently published papers, and when he or she is sick of science, there are plenty more relaxing novels from which to choose. **http://amzn.to/ILaGvL**

Scientific American has been publishing its amazing take on science for decades now. Full of news, features, analysis and commentary on all the latest happenings in science, a ***Scientific American* subscription** will not fail to please any recent graduate in the biological sciences. Pick an online or print version. **www.sciamdigital.com/index.cfm?fa=Products.ViewGiftPromo&sc =sadigital_gift_BL**

As you know, there is a growing body of people with smartphones and tablet computers. This is especially true for recent graduates, and it is becoming more common for universities and institutions to develop tools targeted at these smartphone-wielding young graduates. So help your graduate get on the bandwagon and give an **iTunes store voucher** to download any one of the incredible educational and entertaining applications. **http://bit.ly/2WGtiy**

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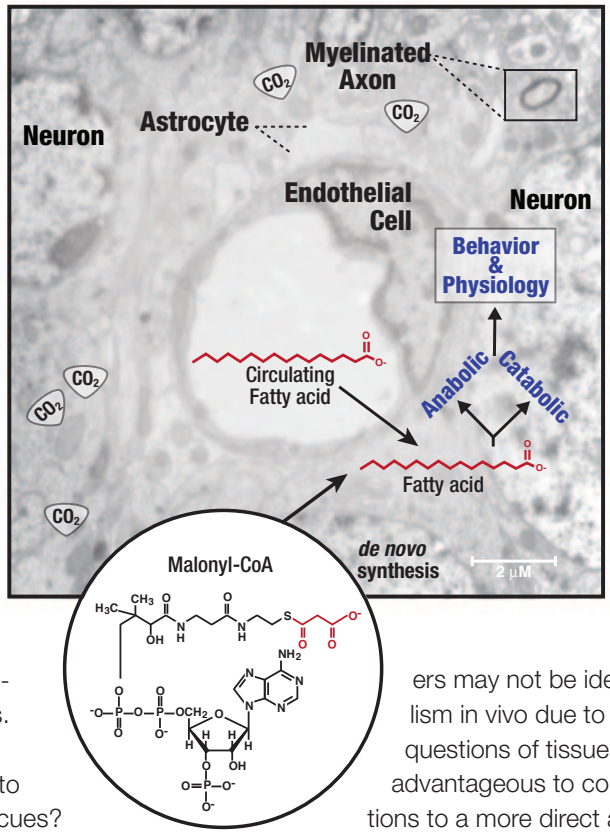
# Reimagining neurometabolism

## *Unraveling the unique biochemistry of brain metabolism*

BY JESSICA M. ELLIS AND MICHAEL J. WOLFGANG

Some of the most interesting, enigmatic and understudied cells in metabolic biochemistry are those of the nervous system. The brain has unique metabolic requirements and expresses unique metabolic enzymes, many of which remain poorly characterized (1). Given that neurons have an exceedingly limited capacity for renewal, understanding neuronal metabolic responses to environmental, nutritional and pharmacological interventions is made all the more important. Determining the basic metabolic biochemistry of the nervous system has the potential to affect translational medicine directly.

Experimental manipulation of fatty acid metabolism in the brain has led to some of the most surprising recent work in neurometabolism. Genetic or pharmacological manipulation of brain fatty acid and lipoprotein metabolism causes dramatic changes in energy balance-related behavior and physiology (2 – 5). Although these are important foundational experiments, they highlight our need to understand more fully lipid metabolism in the nervous system. Predicting the results from these experiments would have been difficult or impossible given our current understanding of the interaction between the brain and circulating or de novo produced lipids. Do a subset of neurons or glia require exogenous fatty acids to sense and respond to dietary cues? Surprisingly, some of the basic dogmas in neurometabolism are not based on strong direct experimental evidence, which hampers our ability to build detailed biochemical models. Biochemistry textbooks state "fatty acids do not serve as fuel for the brain," (6) but what is meant by "brain" is quite subjective, as some cell types in the brain can use fatty acids for fuel. Also, does a subset of neurons or glia require fatty acid beta-oxidation? To date, experimental data cannot stringently answer the question, largely due to the lack of tools.




The lack of strong metabolic data for the mammalian brain is mainly because of significant experimental challenges to metabolic biochemists that require innovative new methodology to overcome. A formidable obstacle to understanding neurometabolism is the heterogeneous nature of cells in the brain coupled with the diversity of neurons themselves. Heterogeneity is a significant confounder for even the most advanced targeted or lipidomic analysis, and, unfortunately, sorting or culturing cells irrevocably alters their metabolism. Genetically encoded metabolite sensors, based largely on fluorescence resonance energy transfer reporters, are useful in revealing cellular and subcellular metabolite changes in situ. Several mammalian reporters, which are adapted largely from bacterial proteins, now exist for various metabolites (7 – 9). However, there are no genetically encoded biosensors for lipid metabolites, and FRET reporters may not be ideal for analyzing brain metabolism in vivo due to their limited dynamic range. For questions of tissue heterogeneity, it would be more advantageous to couple lipid metabolite concentrations to a more direct and dynamic measurement of reporter activity (e.g., short-lived GFP fluorescence).

The challenges of studying brain lipid metabolism are compounded by the relative lack of experimental tools and by the use of inadequate and often nonspecific pharmacologic inhibitors. Although knockout mice are

invaluable for determining the requirements of enzymes in vivo, they are not able to tell the whole story. Ideally, one would combine the quick kinetics, dose responsiveness and reversibility of small-molecule pharmacology with the specificity of targeted knockouts. There has been considerable progress in the development of small stabilizing or destabilizing protein domains that interact with well-defined inert small molecules (10, 11). To manipulate fatty-acid metabolism acutely in vivo, we combined small-molecule inducible protein stabilization with genetically tractable recombination-mediated transgene expression (12). This technique allowed us to manipulate fatty-acid metabolism in a tissue-specific, dose-dependent and reversible manner in live mice. Since the small molecule interacts only with a user-engineered protein, wildtype mice can be used to control for off-target effects. In this way, one can annotate the function of metabolic pathways in a cell-specific manner in vivo while mitigating changes in compensatory pathways.

Despite significant challenges, the study of lipid metabolism in the nervous system is an area ripe for discovery. Combining molecular genetics and biochemistry, we can answer some fundamental mechanistic questions that are relevant for human health and disease. The specialized nature of the nervous system suggests that there are sure to be many unique and surprising roles for lipid metabolism that have yet to be uncovered.

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IN CASE YOU MISSED IT

# Important career lessons from Carolyn Cohen's reflections on seeing and knowing in structural biology

BY KAREN MUINDI

Carolyn Cohen begins her first Journal of Biological Chemistry "Reflections" article by stating a truth well known to those with years of experience but perhaps not fully appreciated by those starting out in their careers: "Chance often determines how a young person finds her calling." While she was an undergraduate at Bryn Mawr College, what she thought was going to be just another summer ended up determining the direction of her career. Feeling hopeless after a waitressing job in a disagreeable environment, she called a college friend, who talked her into spending the rest of the summer at Woods Hole, Mass., and helped her find a summer job at the Marine Biological Laboratory. It was there that Cohen heard a lecture by the English crystallographer Dorothy Wrinch on the atomic structures of proteins. The lecture and what Cohen describes as "strikingly beautiful slides" made such a profound impression on her that she decided to work on the structure of proteins.

Cohen went on to graduate school at the Massachusetts Institute of Technology, where she studied under the mentorship of Richard Bear, a pioneer in the X-ray diffraction of fibrous proteins. From this beginning, she went on to pioneer the determination of the structure of proteins at the atomic level in motile systems such as muscle. Her work has built the experimental foundations and concepts that form the basis of our understanding of the structure and function of these proteins. Today, she is a professor emerita of biology at Brandeis University and a member of the National Academy of Sciences.

In her 2007 article, which she recently followed up with a supplement, Cohen reflects on the many relationships that have shaped her career. The college friend who introduced her to the MBL is one in a long list of friends who played pivotal roles in Cohen's career. Matchmaking efforts by a close friend at Bryn Mawr resulted in a successful match; however, instead of a romantic relationship, Cohen and Don Caspar became collaborators, and eventually the two established a laboratory together at the Jimmy Fund (now part of the Dana-Farber Cancer Institute in Boston).

In the scientific research enterprise, theories are proposed and, after intense scrutiny, remain intact or are disproved. Cohen's "Reflections" article is filled with many anecdotes highlighting this fact. In discussing the ambiguity involved in seeing and interpreting an image, she likens it to the Delphic oracle from Greek mythology whose riddles were interpreted rightly or wrongly by supplicants, sometimes with fatal results. The advantage in structural biology is that one risks only embarrassment. Drawing from the example of Hugh Huxley and Jean Hanson's work that led them to the sliding-filament theory as a mechanism for muscle contraction, Cohen states that "trying to disprove one's own ideas is a common strategy for how to do good science!"

Cohen's "Reflections" highlights some of the ways research has changed over the years. In 1958, having identified the Lotmar-Picken substance, which was thought to be crystalline myosin, as the amino acid taurine, she published the finding in a one-paragraph, one-figure paper! She also describes a very different research-funding climate, stating that in the 1950s, "National Institutes of Health research grants were relatively easy to obtain."

With respect to recent advances in genomics and the dramatic increase in the speed with which simple structures are determined using nuclear magnetic resonance and crystallographic methods, she cautions against assuming that "an understanding of structure leads to an understanding of function" and warns that "too much information, without adequate comprehension, may not really clarify general concepts." She uses the sliding-filament theory of muscle contraction and the packing of icosahedral virus particles as examples of proposals that did not require atomic structures.

Throughout her original JBC "Reflections," Cohen pays homage to mentors and collaborators. In the 2011 supplementary article, she focuses on those who involved in her early education. Chance played a big role in Cohen's career, but it did not act alone; Louis Pasteur put it well when he said "Dans les champs de l'observation le hasard ne favorise que les esprits préparés," or, "In the field of observation, chance only favors the prepared mind."

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THE JOURNAL OF LIPID RESEARCH

# Cutting the fat: potential new drug target for treating lipid accumulation in fatty liver

BY MARY L. CHANG

Obese people often have significant lipid accumulation in the liver, which is associated with the development of insulin resistance and diabetes. One form of lipid that may accumulate, diacylglycerol, is predominately synthesized through an acylation pathway. But it has been hypothesized that an alternative pathway of synthesizing diacylglycerol from monoacylglycerol, utilizing a class of enzymes known as monoacylglycerol acyltransferases, may contribute to these accumulating amounts of lipids in the liver.

In an article titled "Evidence for regulated monoacylglycerol acyltransferase expression and activity in human liver" by Angela M. Hall at the Center for Human Nutrition at Washington University at St. Louis and colleagues, MGAT activity and the expression of three genes known to encode MGATs (MOGAT1, MOGAT2 and MOGAT3) were examined from liver biopsy samples obtained from obese study participants before and after they underwent gastric bypass surgery (1). The results of this study are published in the May issue of the Journal of Lipid Research.

All three MOGAT genes were shown to be readily expressed in the liver. However, only MOGAT3's expression was correlated with MGAT activity, while the expression of the other two genes were not. MOGAT expression also was compared in patients before and a year after gastric bypass surgery: Expression of MOGAT2 and MOGAT3 were significantly lower after surgery than before.

These results were compared with MOGAT expression in people with nonalcoholic fatty liver disease, who had significantly higher MOGAT2 and MOGAT3 expression when stacked up against control participants. Their data suggest that when a person has fatty liver disease, MOGAT2 and MOGAT3 expression is upregulated. But when a patient experiences marked weight loss, the body corrects this increased expression effectively to lower it. This up- and downregulation appears to be dynamic, so the increased or decreased activity of these MGATS is expected to depend on an individual's health status.


Taken together, the research presented in this study indicates drugs that specifically target MOGAT3 have the potential to provide therapeutic treatment for obese people with insulin resistance, diabetes and other lipid abnormalities related to fatty liver. Targeting this one gene could head off or prevent lipid accumulation in the liver altogether.

Mary L. Chang (mchang@asbmb.org) is managing editor of the Journal of Lipid Research and coordinating journal manager of Molecular and Cellular Proteomics.

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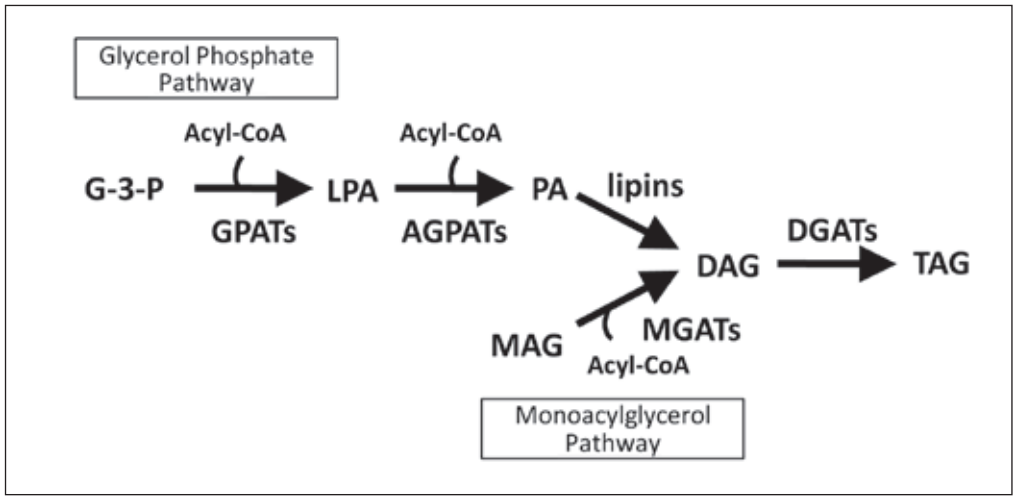


**Two convergent pathways for triacylglycerol biosynthesis. The stepwise acylation of glycerol through the two pathways for triacylglycerol synthesis are shown. Abbreviations: fatty acid (FA), glycerol-3-phosphate (G-3-P), G-3-P acyltransferase (GPAT), lysophosphatidic acid (LPA), acylglycerol-3-phosphate acyltransferase (AGPAT), phosphatidic acid (PA), monoacylglycerol (MAG), MAG acyltransferase (MGAT), diacylglycerol (DAG), DAG acyltransferase (DGAT) and triacylglycerol (TAG).**

jbc THE JOURNAL OF BIOLOGICAL CHEMISTRY

MCP MOLECULAR & CELLULAR PROTEOMICS

# Eicosanoid research of yesteryear and now

BY RAJENDRANI MUKHOPADHYAY

Eicosanoids are signaling molecules involved in a number of major biochemical pathways, such as inflammation and immunity. Two recent articles, one in the Journal of Biological Chemistry and the other in Molecular & Cellular Proteomics, focus on these molecules from different angles and together give a comprehensive view of how research in this field started and has grown over time.

Prostaglandins, prostacyclins, thromboxanes and leukotrienes are types of eicosanoids. They are produced from the oxidation of essential omega-3 or omega-6 fatty acids.

In his JBC Reflections article, Bengt Samuelsson at the Karolinska Institute in Sweden describes the journey his laboratory embarked on in the 1960s to understand the fundamental biochemistry of eicosanoids (1). At least 10 drugs currently on the market are based on initial findings made by Samuelsson's group and its collaborators. The work also garnered Samuelsson the Nobel Prize in physiology or medicine in 1982 along with Sune Bergström at Karolinska and John Vane at the William Harvey Research Institute at St. Bartholomew's Hospital Medical College.

Samuelsson's group discovered an enzyme that catalyzed the conversion of arachidonic acid into a molecule called PGG2. The team named the enzyme cyclooxygenase. Researchers later discovered that a variant of cyclooxygenase called COX-2 was expressed during inflammation. The pharmaceutical industry developed COX-2 inhibitors to fight inflammation, such as Celebra and Vioxx (although Vioxx had to be taken off the market.

Samuelsson's group also discovered thromboxane $A_2$ and found that it plays a role in blood vessel injury by causing platelet aggregation and constriction of smooth vascular muscle. Later, researchers found that low doses of aspirin inhibited the formation of thromboxane $A_2$. Based on that finding, millions of people now take daily doses of baby aspirin to prevent heart attacks and strokes. The discovery of leukotrienes by Samuelsson's group led to the development of several drugs for treatment of asthma and rhinitis. One of these, Singulair, has been Merck´s bestselling product for several years, with sales around $5 billion.

Samuelsson's body of work clearly shows how basic research can have a tremendous impact on public health. But, as Samuelsson concludes in his article, his contributions demonstrate "the power of research that is not targeted to a specific disease but rather focuses on understanding the structures and functions of the molecules constituting the human body."

**E. J. Corey (left) and Robert B. Woodward (right) with Samuelsson at a conference in Uppsala, Sweden.**

The MCP article highlights how modern -omics technologies can reveal connections between different molecular pathways. The laboratory of Edward Dennis at the University of California, San Diego, has studied the activation of phospholipase A2, which causes the release of arachidonic acid. Arachidonic acid then leads to the production of eicosanoids, which are metabolites. Dennis' group previously had quantified these metabolites and correlated their levels with transcriptomic changes of 28 genes. "However, it was clear that the missing link between the transcript and the metabolite was the protein," says Dennis.

To get a handle on the proteins, the Dennis group teamed up with the group of Ruedi Aebersold at the Swiss Federal Institute of Technology in Zurich. They applied multiple reaction monitoring mass spectrometry, a quantitative method that let them measure the amounts of the proteins involved in eicosanoid production (2). For example, Dennis says they were able to show that the protein expression of COX-2 closely follows the same trajectory as its transcript expression.

The work by Dennis and colleagues is one of the first integrations of various -omic analyses, which allow researchers to better understand how seemingly isolated biochemical pathways are connected. Dennis explains -omics techniques have advanced to the point at which researchers can carry out an integrated study of genomics, proteomics and metabolomics. Dennis says, "This has been a long time in coming but is essential to fully understand the complex interplay between the genes, the proteins and the metabolites that the proteins make."

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# U.S. health disparities at a glance

BY FRANK TALAMANTES

## What are health disparities?

Sex, sexual identity, age, disability, socioeconomic status, geographic location, race and ethnicity all influence health (1). If a health outcome is seen to a greater or lesser extent in certain populations, there is a disparity. Biological, genetic, environmental and cultural factors and access to medical care all play a role. Compelling evidence indicates race and ethnicity correlate with increasing health disparities between U.S. subpopulations.

### HEART DISEASE

Heart disease is the leading cause of death for people of most races and ethnicities. For American Indians, Alaska Natives, Asians and Pacific Islanders, it is second only to cancer. Heart disease death rates are more than 40 percent higher for blacks than for whites (2). Blacks who receive drug-coated stents have more than double the rate of clotting compared with those of other races despite taking anti-clotting medications (3).

### DIABETES

The risk of being diagnosed with diabetes is 77 percent higher among non-Hispanic blacks, 66 percent higher among Hispanics and 18 percent higher among Asian-Americans compared with non-Hispanic white adults. Interestingly, Mexican-Americans show a blunted response to insulin (4), which may be one of the causes. Furthermore, Hispanics are almost twice as likely to die from diabetes as are non-Hispanic whites (5, 6). The diabetes rate for American Indians and Alaska Natives is more than twice that for whites.

### KIDNEY DISEASE

Blacks, Hispanics and American Indians are at high risk for developing kidney failure. This risk is due in part to high rates of diabetes and high blood pressure in these communities. Blacks make up about 13 percent of the U.S. population, but they account for 32 percent of kidney failure cases. Since 2000, the number of Hispanics with kidney failure has increased by more than 70 percent (7). American Indians also are disproportionately affected. Compared with whites, they are 1.8 times more likely to be diagnosed with it.

### INFANT BIRTH WEIGHTS AND DEATH RATES

Whereas the rate of low-birth-weight infants is generally lower for Hispanics than for whites, Puerto Ricans have a low-birth-weight rate that is 50 percent higher than the rate for whites. American Indians and Alaska Natives have an infant death rate almost double that for whites.

### CANCER

The death rate for all cancers is 30 percent higher for blacks than for whites; for prostate cancer, for example, the death rate for blacks is more than double that for whites. Black women have a higher death rate from breast cancer despite having a mammography screening rate nearly on par with that of white women (8). Of the cities where black women were more likely to die of breast cancer, that disparity ranged from a 24 percent higher risk of death in New York to more than twice the risk of death in Memphis between 2005 and 2007. Other cities with racial disparities included Los Angeles; Chicago; Houston; Philadelphia; San Diego; Dallas; Jacksonville, Miss.; Columbus, Ohio; Milwaukee; Boston; and Denver. Meanwhile, there was no difference in black and white women's chances of dying from breast cancer in Phoenix; San Antonio; San Jose, Calif.; Detroit; San Francisco; Austin, Texas; Baltimore; Fort Worth, Texas; Charlotte, N.C.; El Paso, Texas; and Seattle (9).

### ALZHEIMER'S DISEASE

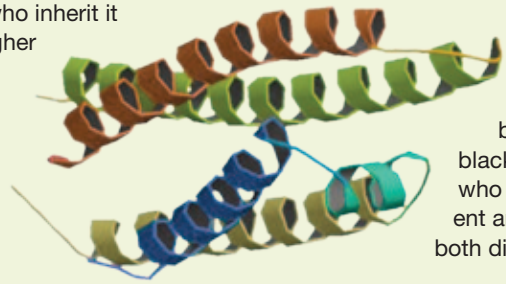
Older blacks in America are about two times more likely than older whites to have Alzheimer's disease and other forms of dementia (see sidebar). Older Hispanics are 1.5 times more likely than older whites to have these conditions (10). High blood pressure and diabetes, both risk factors for Alzheimer's and dementia, are more common in older blacks and Hispanics than in older whites and probably account for some of the differences.

## Final thoughts

While scientific advances have increased longevity and improved quality of life for Americans, racial and ethnic minorities have not experienced these gains equally. Advancing scientific knowledge and technology can improve patient-centered research in the areas of prevention, screening, diagnostics and treatment, and it can

## A closer look at the genetic roots of Alzheimer's disease

A genetic factor associated with late-onset Alzheimer's disease is apolipoprotein E. People inherit one form of the ApoE gene from each parent. Those who inherit the e4 form of the gene from one parent have an increased risk of developing Alzheimer's. Those who inherit it from both parents have an even higher risk. The relationship between ApoE-e4 and Alzheimer's has been studied in populations around the world. A widely cited meta-analysis of 5,930 people with Alzheimer's and 8,607 without showed whites who inherited the e4 form from one parent had a 3.2 times greater risk of developing Alzheimer's than whites who did not. Hispanics who inherited the e4 form from one parent had a 2.2 times greater risk of developing Alzheimer's than Hispanics who did not. The risk of Alzheimer's was 14.9 times higher for whites who inherited the e4 form of the ApoE gene from both parents and 5.7 times higher for blacks who inherited it from both. Blacks who inherited the e4 form from one parent and Hispanics who inherited it from both did not have increased risks.



strengthen existing information systems to improve the quality of health, public health and biomedical research. It makes a big difference when breast cancer is diagnosed early; when a patient having a heart attack is given the correct treatment quickly; when medications are correctly administered; and when doctors listen to their patients and their families, show them respect and answer their questions in a culturally and linguistically skilled manner.

To better reach out to all the different ethnic groups, it pays for the medical community to develop cultural and linguistic skills. Strategies include expanding the use of interpreters, improving the quality of patient-provider interactions in clinical settings, improving cultural-competence education and training for health-care professionals, and increasing racial and ethnic diversity in the health-care work force.

It is necessary to educate physicians about pervasive racial and ethnic health disparities and to assist them in developing strategies to deliver quality care to underserved populations. In addition, we must foster the training of scientists with the best biochemical and molecular technologies to investigate the causes of many the diseases prevalent among minorities.

Frank Talamantes (lactogen@mouseplacenta.com) is a professor emeritus at the University of California, Santa Cruz.

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# Reach out to your community college colleagues and students

## *Your participation will help develop a culture of undergraduate research*

BY DEBORAH L. NEELY-FISHER

I have been teaching at a Virginia community college for about 16 years, which is not surprising, because I began my academic journey at a junior college. In between, I attended two different universities in Virginia and somehow managed to earn bachelor's and master's degrees in biology, which enabled me to move into the teaching position I now hold.

First and foremost, I attended a junior college due to an insufficient high-school record — through no fault of my high school teachers, I should add. Like so many other students who attend community college, I needed the extra time to mature, the smaller class sizes for academic support and the cheaper tuition.

With the help of professors whose primary focus was teaching, I was able to succeed in developmental and introductory-level science courses. Because the professors had no requirement to do research, they often were available to answer questions and were willing to tutor me. During my two years at junior college, I excelled beyond my parents' wildest dreams and was inducted into Phi Theta Kappa. Afterward, I applied to and was accepted by the university of my choosing.

Unfortunately, my transfer experience was typical: With 300 to 500 students per class, my first year proved extremely frustrating. Professors were polite but distant, and even the graduate-student teaching assistants were pretty aloof. I struggled for a quarter or two, my grade point average took a nosedive and then, toward the end of the year, I began to recover. Although I had survived the year academically, I moved home when the year was up and applied to a university within commuting distance. Later, as a community-college professor, I would learn that I had suffered from what is known as transfer shock.

### A common experience

Transfer shock is well documented. Transfer students' GPAs commonly drop several tenths of a point or more, causing those students to doubt their abilities to be successful at the new institution (1). Although some studies indicate that transfer shock for math and science majors results in statistically significant declines in GPAs (2), you might be surprised to learn that, in general, transfer students do outperform incoming freshmen and native juniors, and they also achieve higher graduation rates (3). Studies by Keeley and House, in fact, indicate that students who earn associate degrees before transferring show continued improvements in GPA and graduate in higher proportions than those who transfer before completing their degrees (4).

The science courses I took through my junior year were not that much different at any of the colleges I attended. They were almost all focused on memorizing content and utilizing cookbook laboratories. (And please remember that this was 38 years ago.) The connection between content knowledge in science and research was not introduced until I started taking upper-level courses. After spending three-and-a-half years studying biology, I knew nothing of the process of scientific research or the career paths of scientists. I know that in the past two decades attitudes and policies have improved concerning undergraduate research, but, unfortunately, the trend continues to be slower in community college science departments.

### A small and quiet revolution

Community colleges serve diverse student bodies and include large pools of nontraditional students with the desire and talent to succeed in science. To increase the likelihood that these students will succeed in science, technology, engineering and math disciplines, opportunities to participate in undergraduate research early in their academic careers must be made available. These students should not have to wait until their junior and senior years to make the research connection.

Fortunately, there is a small and quiet revolution going on at community colleges across the country. Supported by a grant from the National Science Foundation, the Council for Undergraduate Research and the National Council of Institutional Administrators are conducting

workshops at community colleges to develop a culture of undergraduate scientific research (5). There are many documented benefits for students who participate in undergraduate research, including enhanced abilities for critical thinking and problem solving as well as a deeper understanding of science (6).

The report, titled "Undergraduate Research at Community Colleges," characterizes four categories of research activities conducted in STEM at community colleges (8):

1. incorporating research into the curriculum, which might include requiring students to conduct literature reviews or build hypotheses;
2. eliminating cookbook labs and replacing them with research activities;
3. conducting applied research at the community college; and
4. conducting basic research at the community college or partnering with four-year faculty members and conducting research at those institutions.

## A mixed bag of results

Several years ago, I was the recipient of a Bridges to the Future grant from the National Institutes of Health. Students partnered with faculty mentors from a four-year university, and each student conducted a yearlong research project. Their projects culminated in poster presentations at the annual meeting of the Virginia Academy of Science.

While all of the students who participated ended up transferring to four-year instituitions upon completion of their associate's degrees, not all of them were successful. As others have discovered, there are many barriers to student success in STEM, and this is particularly true for community-college students (7). They tend to be older, have strong personal commitments outside of college and often have to work full-time jobs to sustain their families. Often community-college students are not ready or able to make the time commitment required for full-blown research projects (7). Success can be measured on different levels, however, and several of the participants in my program went on to work in research laboratories. One was accepted into medical school, and still another became a teacher.

The U.S. Bureau of Labor Statistics projects that the science and engineering work force's growth will exceed the growth of all other sectors (8). Meanwhile, the National Center for Public Policy and Higher Education reported that community college enrollment increased 375 percent in 30 years and is quickly becoming the single largest segment in higher education due to increases in tuition and stricter admission requirements at four-year institutions, increasing numbers of high-school graduates, and increasing enrollments of low-income and minority students (9).

Community college is the logical recruiting ground for new talent, especially among individuals underrepresented in the STEM disciplines. These students are going to transfer into your classes. I urge you to reach out to community-college science faculty members and potential transfer students; help them develop a culture for undergraduate research.

## What do you really know about your local community college and transfer students?

**1. How many community colleges are in the United States?**
A. 980 B. 500 C. 1,167 D. 250

Answer: C. There are 993 public community colleges, 143 private schools and 31 tribal colleges.

**2. As of fall 2008, how many students were enrolled in community colleges nationwide?**
A. 5 million B. 12.5 million C. 1 million D. 3 million

Answer: B. Note that 40 percent of those were enrolled full time, and that number continues to grow.

**3. What is the average age of your local community college student?**
A. 28 years old B. 21 years old C. 40 years old D. 18 years old

Answer: A. Although students of all ages attend community colleges each year, the average age of students during the 2007-2008 academic year was 28; 39 percent were 23 or younger, and 58 percent were women.

**4. What percentage of college graduates attended community colleges?**
A. 44 % B. 20 % C. 15 % D. 65 %

Answer: A.

**5. What percentage of community college students are minorities?**
A. 25% B. 45% C. 33% D. 75%

Answer: B. In 2008, 13 percent were black, 16 percent were Hispanic, 6 percent were Asian/Pacific Islander and 1 percent were Native American.

*Source: American Association of Community Colleges: Community College Fast Facts. http://www.aacc.nche.edu/AboutCC/Documents/FactSheet2011.pdf.*

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## READER COMMENTS ONLINE

### Lipid News, April 2012

*A grand idea (that I have been pushing for years) that should not be limited to the teaching of lipid biochemistry. All science should be taught from a historical perspective. Otherwise, as I fear often occurs, science appears as an ever-increasing and unapproachable body of facts. We would all be better served to teach science as method, as an ever-simplifying body of explanations. Teach how scientists practically got from knowing a little to knowing a little more. Emphasize that they did not know the answer before they actually designed and performed the experiment!* —TIM CLAIR, BIOCHEMIST, NIH, RETIRED

*There being only 24 hours in our days, there is a first-things-first outlook that says history is very nice, but sorry, I have experiments to do and grants to write. However, there are still enormous lessons of great practical importance to be learned from biohistory, which currently, like war history, tends to get written by the victors, with corresponding bias. Occasionally, the victors admit their errors. Here, the tell-all account by Klaus Eichmann (Birkhauser 2008) is insightful. It is entitled, "The Network Collective: The Rise and Fall of a Scientific Paradigm." Unfortunately, professional biohistorians are thin on the ground. We need to encourage both the agencies to fund biohistory research and our students to consider it as an early career option.* —DONALD FORSDYKE, QUEEN'S UNIVERSITY, CANADA

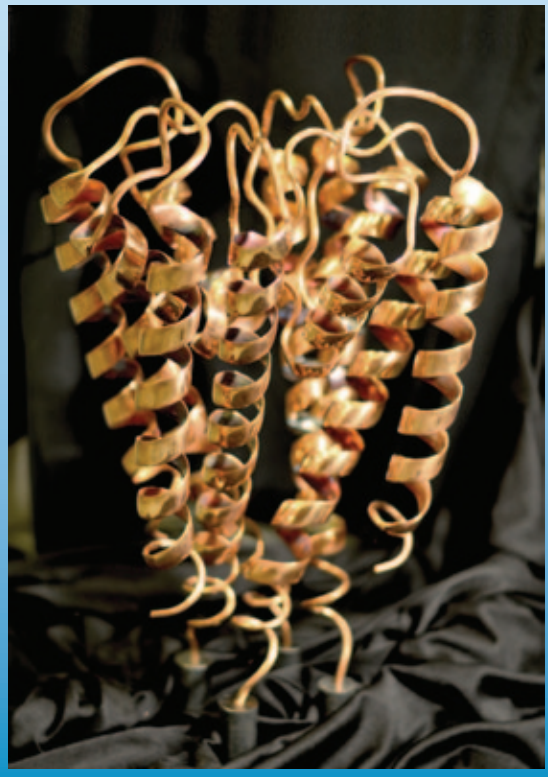
*It is unfortunate that there seems to be little time to relate what we know to how we got to know what we know. Students get stuffed with facts and abstractions that they have difficulty relating to living cells and organisms. As James Bryant Conant said, we need to stimulate curiosity, and students will learn on their own. Stories can do that. When Nathan Kaplan was chair of biochemistry at Brandeis in the 1960s, "History of Biochemistry" was a required course. As his students learned, many classic experiments and stories lie hidden in the literature and never make it to the textbook or lecture. Having worked as a postdoc in Konrad Bloch's lab, I have many stories about KB. (That is not kilobases.)* —HAL WHITE, UNIVERSITY OF DELAWARE

*P.S. Even Linus Pauling is a name students don't recognize anymore. [BAMBED 34(4), 305 (2006)]*

## What's new on Wild Types

**Here's a snapshot of ASBMB Today science writer Rajendrani Mukhopadhyay's blog. Follow it at wildtypes.wordpress.com.**

- **IOM report tackles -omics validation for clinical studies after Duke scandal**
- **Proteomic data validation: a closer look**
- **Protein structure caught in sculpture: the art of Mike Tyka**



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## Next month in ASBMB Today

As the 2012 Summer Olympic Games in London approach, ASBMB Today science writer Rajendrani Mukhopadhyay explores how cheating athletes exploit molecular biology, pharmacology and medicine to win.

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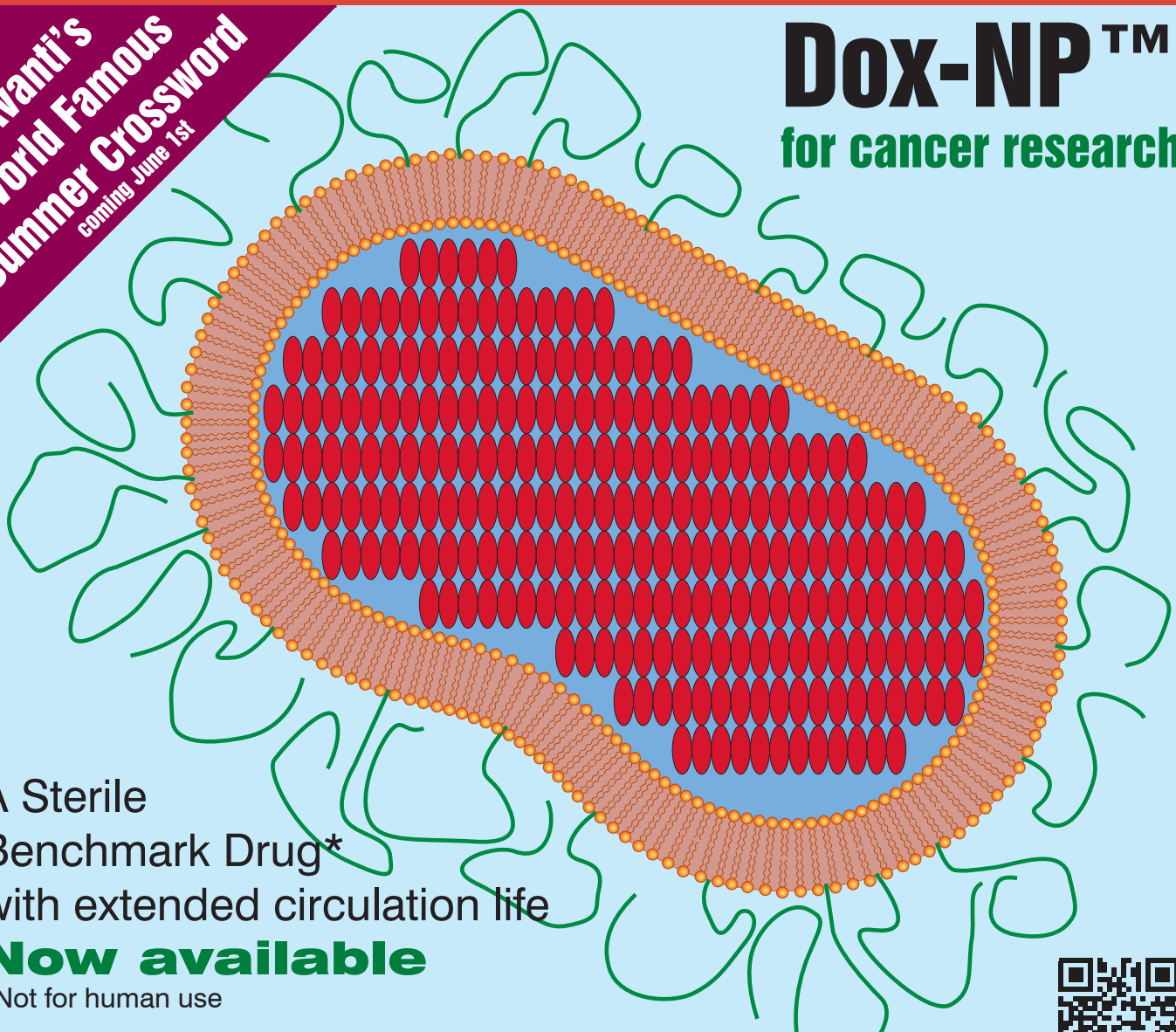

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