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Comparative oncologists are looking to dogs for clues about human cancers.
Review the reviewers

By Steven McKnight

A large fraction of the National Institutes of Health’s budget is spent in support of extramural research. These funds are the lifeblood of biomedical research in the United States. NIH grant applications are reviewed, in most instances, by members of 176 study sections organized by the Center for Scientific Review. How can we know whether these reviewers are doing a good job? Are the reviewers reviewed?

The review of reviewers happens in spades at the Howard Hughes Medical Institute. The senior leadership of the HHMI, including its president, Robert Tjian, sits in on each and every investigator review. They also listen to the talks of candidates for new appointments to the HHMI. The HHMI leaders continually judge the capabilities of their contracted reviewers too. “We monitor reviewer performance on an ongoing basis. If a reviewer exhibits anything other than substantial competence, that person is relieved of his or her responsibilities,” Tjian told me.

The NIH is composed of 27 institutes, each headed by a director. On average, these 27 institutes disburse around $500 million each in external funding per year. This is about half the amount of funding disbursed annually by the HHMI. If the HHMI can review its reviewers effectively in the disbursement of $1 billion annually, it should be possible for individual
institutes of the NIH to do the same.

Each institute director should care as passionately about the disbursement of his or her institute’s funds as the president of the HHMI cares about the distribution of his institute’s own funds. Like the president of the HHMI, the NIH institute directors should keep a finger on the pulse of the review process controlling disbursement of their precious funds. As such, I offer that it is only reasonable to ask that NIH institute directors pay as much attention to the research review process as does the president of the HHMI. NIH institute directors and their senior staff should be at study section meetings just as the president of the HHMI and its senior leadership are at each investigator review.

How might it be possible for the NIH to review its reviewers? Let’s consider what would be expected of NIH institute directors were they to pay keen attention to how their funds are distributed to extramural researchers. Knowing that there are 176 study sections and 27 institutes, each institute director would — on average — care about the operation of roughly six or seven study sections. The director of the National Cancer Institute should care about the five to 10 study sections that review research proposals in the field of oncology; the director of the National Institute of Mental Health should care about the handful of study sections that review proposals relating to neuroscience; and on and on.

If each study section meets three times a year, and if each institute were paired with the handful of study sections covering the research most relevant to its mission, each institute director and his or her leadership team would need to sit in on roughly 20 study section meetings per year. A bit less than every other week, institute directors would spend two days ensuring the quality of the study section and its decisions about funding. This would consume about a quarter of the time of each institute director.

If institute directors and their leadership staffers were embedded deeply in the review process, they could monitor the performance of reviewers directly. If institute directors and their leadership staff noted anything less than outstanding performance by a study section reviewer, much less the person chairing a study section, they would be expected to relieve that person and replace him or her with a competent one.

For all I know, there might be federal rules in place that directly prevent this. If so, how incredibly foolish it would be to prevent NIH institute directors from directly monitoring and guiding the spending of their substantive budgets.

Recognizing that these ideas likely will be deemed ridiculous and impossible to implement, I close by asking a simple question: Were we just starting to devise a system to disburse federal grant dollars in support of biomedical research, would we choose the hands-on methods of the HHMI or the hands-off methods of the NIH?

Steven McKnight (steven.mcknight@utsouthwestern.edu) is president of the American Society for Biochemistry and Molecular Biology and chairman of the biochemistry department at the University of Texas-Southwestern Medical Center at Dallas.
Is the Precision Medicine Initiative really necessary?

By ASBMB Policy Staff

President Obama introduced the Precision Medicine Initiative during his 2015 State of the Union address. The goals of the initiative are to harness not only the power of advanced genomic sequencing but also of a million-patient cohort and to develop new methods for managing and analyzing large data sets that could accelerate biomedical discovery.

National Institutes of Health Director Francis Collins wrote in the New England Journal of Medicine in February, “What is needed now is a broad research program to encourage creative approaches to precision medicine, test them rigorously and ultimately use them to build the evidence base needed to guide clinical practice” (1).

But launching such an ambitious initiative will not be straightforward. Critics of the initiative point to several barriers. First are strict privacy rules guarding health information. To conduct the large-scale genomic studies to achieve the initiative’s goals, information about patients and their genomic data must be encrypted and anonymized. A second obstacle is lack of communication between scientists and hospitals. Robust mechanisms for scientists to share big data with doctors do not exist, and there remain major barriers to sharing electronic patient health records among doctors. Finally, finding a million volunteers willing to relinquish their genetic information could be challenging.

Obama’s fiscal 2016 budget sought $215 million for the initiative. In response, the U.S. House of Representatives and the U.S. Senate proposed $200 million in their appropriations bills. Under the austerity of the Budget Control Act, these funds will need to be taken from other programs. This could jeopardize critical research in other important fields.

Is it really necessary to have the PMI to advance methods for managing and analyzing large data?

Independent investigators can propose and pursue big-data research questions through existing funding mechanisms. For example, Wladek Minor at the University of Virginia received an NIH Big Data to Knowledge grant to develop a management strategy for archiving X-ray diffraction raw data and an online portal to gain access to it. Minor was concerned about the massive amount of raw data in his field that goes unpublished. “What we propose is to build the system to keep all diffraction data (and) structural data. People are saying to do that would cost millions of dollars in equipment. And our request for equipment was $20,000. Why? Because we use the newest technology, and we are building computers by ourselves quite often. Not because it’s cheaper, but because we can create something (that) is better than what you can buy” (2).

Creating a resource for preserving this raw data will allow other scientists to gain insight from experiments that otherwise might have gone unpublished, and developing a management strategy for wrangling massive data sets advances the field of big data.

While the NIH grapples with barriers, Alphabet’s Life Sciences (formerly a part of Google X) has waltzed casually into the conversation and announced its intention to explore the promise of precision medicine. In addition to developing a glucose-sensing contact lens for diabetic patients, the Life Sciences team has been working with scientists from Duke University and Stanford University to design the Baseline Study, which will collect anonymous genetic information from 10,000 people to create a baseline picture of what a healthy human looks like on a molecular level. The study is unlikely to face many of the challenges of the PMI. If participants buy in, Life Sciences could provide both the medical and technological advances of processing and utilizing genomic data from a large patient cohort, and the Baseline Study could deliver the type of technological advances sought by the Precision Medicine Initiative without additional federal investment.

The NIH’s Big Data to Knowledge program already is delivering advances in data management. Life Science’s Baseline Study appears poised to leverage advanced genome sequencing to enhance our understanding of health. Bogged down in privacy laws and funding battles, the PMI may not even be necessary.

Send questions or comments to publicaffairs@asbmb.org.

REFERENCES
Hudson receives Earl Sutherland Prize

Billy G. Hudson, the Elliott V. Newman professor of medicine and professor of biochemistry, pathology, microbiology and immunology, and cell and developmental biology at Vanderbilt University, won the Earl Sutherland Prize for Achievement in Research in August. Vanderbilt established the prize in 1976 and presents it annually to a faculty member who has garnered critical reception and recognition nationally and internationally for achievements in research, scholarship or creative expression. The prize comes with an engraved pewter cup and a purse of $5,000. Hudson's research focuses on the structure and function of type IV collagen. He has discovered and characterized collagen-IV proteins in which structural alterations cause the pathophysiology of four kidney diseases. He also discovered the novel sulphur-nitrogen bond that stabilizes collagen-IV networks. Additionally, Hudson co-founded the Aspirnaut program, which helps develop and promote science, technology engineering and math education for rural and underrepresented K – 20 students through internships and the beaming of STEM labs into classrooms.

Marletta wins Alfred Bader Award

The American Chemical Society honored Michael A. Marletta with the 2015 Alfred Bader Award in Bioinorganic or Bioorganic Chemistry. The award, which comes with a $5,000 prize, is sponsored by the Alfred R. Bader Fund and recognizes a scientist's outstanding achievements at the intersection of biology and organic or inorganic chemistry. Marletta holds the CH and Annie Li chair in the molecular biology of diseases at the University of California, Berkeley, where he is a professor in the departments of chemistry and molecular and cell biology. He long has explored nitric oxide signaling and uncovered many aspects of nitric oxide function. More recently, his lab also has undertaken investigations of polysaccharide monoxygenases.

IN MEMORIAM: Robert Labbé

Robert Ferdinand Labbé, professor emeritus at the University of Washington, passed away in March due to complications from Parkinson’s disease. He was 92. Born on Nov. 12, 1922, in Portland, Ore., Labbé’s interest in chemistry started in high school. After a short stint in the navy, he finished his undergraduate degree at the University of Portland and later obtained a Ph.D. in biochemistry from Oregon State University. In 1958, Labbé joined the medical faculty at the University of Washington, where he worked his entire career. Beginning in the department of pediatrics, Labbé joined the department of laboratory medicine in 1974 and became the head of clinical chemistry in 1980. Labbé’s research interests included the study of porphyrins, metalloporphyrins and other porphyrine compounds, and he developed a section for the school on nutrition. A conservationist who enjoyed international travel, photography and music, Labbé married Norma Lee Wiley in 1955. Norma Lee was a registered nurse who shared Labbé’s interest in the role research played in the medical field. In her honor, Labbé founded the Robert F. and Norma Lee Labbé Endowed Faculty Fellowship in Laboratory Medicine at the University of Washington. The fellowship supports the laboratory research programs of faculty members who are early in their careers.

Written by Erik Chaulk

MEMBER UPDATE

Scholarship update

After our September article on the American Society for Biochemistry and Molecular Biology’s Distinguished Undergraduate Scholarship was published, a change in recipients was announced. Shelby Newsad declined her scholarship, and the Minority Affairs Committee is pleased to announce it has awarded Nicolas Oropeza of Arizona State University one of the five scholarships.

Oropeza is studying biological sciences at the Arizona State University School of Life Sciences, where he also volunteers as a mentor to incoming freshmen. He is a trained emergency medical technician, and in the summer he volunteers as an EMT for underprivileged communities in Sonora, Mexico. Oropeza is passionate about sharing his background and experiences with those from diverse groups and says he wants to demonstrate that “their barriers are not limitations on what they can accomplish.” He intends to graduate from ASU and then enter a joint Ph.D./M.D. program.
Down syndrome strides

By Indumathi Sridharan

Amned after John Langdon Down, an English physician who first described the disorder in 1866, Down syndrome is the most common cause of birth defects in the U.S. Every year, 6,000 babies are born with the congenital disorder, and the Centers for Disease Control and Prevention reports that cases of Down syndrome have increased by 24 percent in recent years. Although there is no standard treatment, children with Down syndrome can develop basic physical, cognitive, language, and social skills with specialized education and care. During October’s National Down Syndrome month, the National Down Syndrome Society advocates the importance of early intervention and celebrates the unique strengths and talents of those with the syndrome.

What causes Down syndrome?

Down syndrome occurs when chromosome 21 fails to separate equally between two daughter cells during the formation of an egg or sperm. The error is called nondisjunction. If the abnormal cell contributes to a fertilized egg, the resulting embryo will have three copies of chromosome 21 in every cell. For this reason, the syndrome is also known as trisomy 21. The extra chromosome disrupts transcriptional regulation in cells via widespread changes in chromatin structure and methylation patterns (1).

What are the traits of the syndrome?

Common physical traits include low muscle tone, short stature and an upward slant to the eyes. Down syndrome also causes heart defects, cognitive impairment, language delays and poor memory.

What are the latest research developments?

Jeanne Lawrence and colleagues at the University of Massachusetts Medical School are exploring chromosomal therapy for treating Down syndrome. The team inserted a gene called X-inactive specific transcript, or XIST, into stem cells derived from trisomy 21 patients (2). XIST condenses and inactivates one of the two X chromosomes during mammalian female development. When inserted into the cells, XIST silenced most of the genes in the extra chromosome 21. The silencing also improved the stem cells’ ability to differentiate into neurons. Chromosomal silencing could improve cognitive function by restoring neuronal cells.

Other researchers are investigating the biochemical mechanisms behind cognitive defects observed in people with Down syndrome. Huaxi Xu and colleagues at the Sanford–Burnham Medical Research Institute found that a protein called sorting nexin 27, or SNX27, is abnormally low in people with Down syndrome. SNX27 helps neurons retain glutamate receptors, which is essential for synaptic signaling and brain function. Xu’s team showed that those with Down syndrome have low levels of SNX27 because the extra chromosome overproduces microRNA-155, a key inhibitor of SNX27 (3).

In 2013, the National Institutes of Health launched a national registry for Down syndrome called DS-Connect. This centralized website enables easy exchange of information between patients, doctors and scientists. In 2015, the NIH introduced a Web portal within DS-Connect that allows approved scientists to access anonymized data about patients’ health. The portal will help scientists to coordinate clinical studies with eligible participants, perform customized searches and generate new research ideas based on the collective information available in the portal.

REFERENCES
ChIP-ing away at DNA–protein interactions

By Aditi S. Iyengar

What is it?

The chromatin immunoprecipitation assay, popularly known as ChIP, is a technique used to capture and examine interactions between DNA and proteins. The basic principle behind ChIP is the achievement of a selective enrichment of genomic material when antibodies bind to and pull out protein–DNA complexes in vivo.

How does it work?

The assay begins with capturing a snapshot of protein–DNA interactions by fixing live cells with a crosslinking agent, such as formaldehyde. Once the interactions are preserved or frozen within the cell, chromatin is extracted and broken down either by physical agitation or by enzymatic fragmentation. These chromatin fragments are subjected to immunoprecipitation where specific antibodies recognize and selectively precipitate target proteins. Any DNA sequences attached to the proteins of interest are co-immunoprecipitated as part of the chromatin–DNA cross-linked complex. Finally, the crosslinking process is reversed to allow for further analysis. The separated DNA can be identified and quantified further using standard PCR amplification, cloning and sequencing.

Some protocols call for the preservation of the native state of the chromatin, especially when mapping for DNA targets of proteins, such as histone modifiers. In such cases, researchers avoid crosslinking and instead use enzymes to cut up the native chromatin into intact DNA–histone complexes for further purification and analysis.

How did it come about?

In the early 1980s, when researchers avidly were pursuing DNA recombination and gene-mapping projects, a student working with John Lis of Cornell University set out to explore an overlooked aspect of genetics: protein–DNA interactions in vivo. The student, David Gilmour, along with members of the Lis laboratory, became the first to use ultraviolet light to crosslink covalently proteins and DNA in bacterial cells. However, one of the limitations of using ultraviolet light is that it covalently links DNA with only proteins that are in direct contact with nucleic acid segments. In 1988, while mapping the genomic locations of histones, Alexander Varshavsky and colleagues at the Massachusetts Institute of Technology successfully replaced ultraviolet light with formaldehyde. Formaldehyde is a global crosslinker that conjugates DNA to all associated peptides, including elements of protein complexes that that do not interact directly with genes. The reagent increased the versatility of ChIP assays and is still used as a crosslinker in many experiments.

What are its applications?

Data from ChIP analyses augment our understanding of the mechanisms behind transcriptional and epigenetic gene regulation and spatiotemporal expression of regulatory elements in cells, tissues and sometimes organisms. Researchers often combine ChIP assays with DNA microarray assays, called ChIP-on-chip, to investigate the DNA targets of specific proteins, such as transcription factors or regulatory elements, on a genomewide scale. A dynamic and cost-effective version of ChIP-on-chip is the ChIP-seq. It involves high-throughput sequencing of multiple DNA fragments to map precisely global genomic binding sites of proteins of interest. ChIP-seq, which boasts high signal-to-noise ratios and robust outputs, has widened the field of comparative genome analyses and is a valuable approach for studying disease processes and cellular function.
Discovering novel drugs to target G-protein–coupled receptors

By Sapeck Agrawal

Whenever we experience a happy feeling, a sweet smell or a bright light, we have our G-protein–coupled receptors, or GPCRs, to thank. A plethora of signals — odors, hormones, neurotransmitters and photons — exert their biological effect by activating GPCRs. Once activated by a signal, a GPCR engages a G protein that processes GTP to activate downstream players in the biological cascade.

Because of their functional importance, a host of drugs target GPCRs by mimicking a signal or blocking their signal-binding site. Most of these drugs, however, are available for only a small subset of GPCRs, while the majority of GPCRs remain untapped.

As part of a recent minireview series published in the Journal of Biological Chemistry and coordinated by editor Henrik Dohlman at the University of North Carolina at Chapel Hill, pioneering scientific experts in the field of GPCRs offer valuable insights into the challenges of novel drug discovery for targeting a wider variety of GPCRs as well as some very creative solutions to those challenges.

One of the challenges is the need for faster and more efficient ways to screen novel drugs. There are 800 members in the human GPCR superfamily, and the traditional screening method involves testing one receptor at a time, usually requiring a tailor-made, radio-labeled probe or assay. In the first minireview, researchers Bryan Roth and Wesley Kroeze at the University of North Carolina at Chapel Hill describe the various high-throughput screens they and others have developed to circumvent this challenge and test not one but hundreds of receptors at the same time. Facilitating this enormous task are novel tools, such as broad-spectrum readout, sophisticated bioinformatics analysis and high-quality chemical libraries, many available free of charge to the scientific community to accelerate the discovery of new drug candidates.

The other big hurdle in GPCR-targeted drug discovery is enhancing the selectivity of the drug — that is, making sure that the drug regulates only the desired receptor and not any other receptor. One solution to this problem is identifying allosteric sites on these receptor — sites different from the signal-binding sites — which can influence the activity of the protein. Drugs that bind to these allosteric sites may help regulate the activity of one type of receptor but not of another. The second minireview, by Patrick R. Gentry, Patrick Sexton and Arthur Christophoulos at the Monash University in Melbourne, Australia, describes the latest techniques, including recent advances in structural biology, that are being employed to identify molecules, both exogenous and endogenous, that can modulate these allosteric sites.

Crystal structures of GPCRs are instrumental in identifying novel allosteric sites. The third minireview, by Ali Jazayeri, Joao Dias and Fiona Marshall from Heptares Therapeutics Limited, reveals how recent technical advances are accelerating GPCR crystallography and how profound their implications are in the discovery of novel drugs. These include steps in protein purification and engineering as well as the use of computational programs that simulate docking a drug onto the crystal structure of the receptor and play matchmaker between drugs and candidate binding sites.

These insightful minireviews provide a quick glance into the enormous potential of GPCRs in drug discovery and for treating a variety of diseases and conditions including mood disorders and cardiovascular disease.
More good news about aspirin’s effects on cardiovascular disease

AMPK activation in macrophages may reduce development of atherosclerosis

By Nicole Parker

We see commercials every day that remind us that we have no idea when a heart attack or stroke will occur. Then, shortly after that reminder, there is a plug for aspirin. Cardiovascular disease has been a leading cause of death in developed countries for years, and we know aspirin can improve cardiovascular health, specifically through its ability to disrupt prostaglandin synthesis and reduce coagulation.

Recently, the labs led by Gregory Steinberg at McMaster University and Morgan Fullerton at the University of Ottawa, both in Canada, reported a new effect of aspirin. In the Journal of Lipid Research, the researchers reported that salicylate, an acetylated form of aspirin, improves cholesterol levels by targeting AMP-activated protein kinase, or AMPK, in macrophages.

Macrophages are immune cells that play an important role in the plaque formation of atherosclerosis, which is the primary cause for heart attacks and strokes. Atherosclerosis is the buildup of cholesterol and fats in macrophages in the vasculature, which causes plaque formation on the artery walls. This disease often is known as a silent killer, because it shows no symptoms until the plaque buildup is severe enough to block blood flow and cause critical damage that even can lead to death.

Researchers already knew that Ampk has a role in lipid metabolism and that the activation of Ampk improves cholesterol levels. However, the mechanism and importance of Ampk in the macrophage was unknown, so the Steinberg and Fullerton labs decided to study the role of Ampk activation in macrophages loaded with cholesterol, which are known as foam cells.

To activate Ampk, they used direct activators that bind to Ampk, including salicylate, a byproduct of aspirin. Activation of Ampk with salicylate increased efflux of cholesterol from the macrophages to extracellular acceptors such as high-density lipoprotein. They also demonstrated that macrophages that are deficient of Ampk cannot load off cholesterol to extracellular acceptors, which in turn increases foam cell formation.

These findings indicate that Ampk activation is important for controlling the removal of cholesterol from macrophages and that it thereby decreases foam cell formation and progression of atherosclerosis. Most importantly, the study shows that salicylate-based medications like salsalate, a dimer of salicylate, would be great drug candidates.

According to Steinberg, the team already is testing salicylate-based drugs in preclinical animal models and humans. It will be critical to understand more about the role Ampk plays in the progression of atherosclerosis.

Fullerton emphasized: “Ampk is a kinase with more than three dozen targets. It will be important to identify the precise molecular pathway or pathways that are responsible for the effect that is caused by Ampk (activation).” New information about and a better understanding of the mechanism could lead to the development of new therapies or modifications to existing aspirin regimens.

Nicole Parker (nparke11@jhu.edu) is currently completing her Ph.D. in biochemistry and molecular biology at the Johns Hopkins School of Public Health.
Chasing cancer with dogs

Treating canine cancers is helping researchers learn more about human forms of the disease

By Soma Chowdhury
Thunder is a middle-aged mutt with a cheery disposition. He is slim, with a black coat and white patches on his belly and toes. His owner, Jeanneen Terry from Chicago, is unsure of Thunder’s pedigree. “He could be a lab-border collie or lab-pit mix. I don’t know,” she says. “He is a rescue dog.”

Three years ago, Thunder broke his front left leg. A year later, when the leg was still not getting better, his broken leg was amputated, and an X-ray revealed Thunder had osteosarcoma.

Osteosarcoma means “bone tumor” and is the most common and aggressive bone cancer in dogs. It usually spreads rapidly to other organs through the bloodstream, especially to the lungs, and eventually becomes fatal.

Unfortunately, as Terry found out, there aren’t any good treatment options for metastatic canine osteosarcoma. Furthermore, traditional canine cancer treatment is expensive, and she couldn’t afford it. But a friend of hers mentioned a clinical trial program at the College of Veterinary Medicine at the University of Illinois–Urbana Champaign and suggested she look into it. Terry took her friend’s advice and met with the veterinarians who were overseeing the trial program. The doctors assessed Thunder’s eligibility and then invited Terry to enroll him in the program.

The cancer connection in dogs and humans

Cancer is rampant among dogs. According to Michael Kastan, executive director of the Duke Cancer Institute, “Cancer kills more than 50 percent of dogs under the age of ten.” Kastan chaired a meeting at the Institute of Medicine in Washington, D.C., this past June on “The role of clinical studies for pets with naturally occurring tumors in translational cancer research.” He says cancer is similarly widespread in humans, occurring at a rate of one in every three women and in half of all men.

“It (was) always the interplay between the environment and genetic susceptibility that led to the development of cancer in humans and in dogs,” Kastan said during the meeting’s opening remarks.

Dogs and humans have been living together for thousands of years. They evolved together, eating similar food, breathing the same air, and living in the same homes. Elaine Ostrander, who works on both human and canine genetics at the National Human Genome Research Institute, notes that dogs and humans also have a similar genetic makeup. Although dogs have 38 pairs of chromosomes and humans have 23 pairs, “it’s all the same genes and they are basically in the same order,” Ostrander says.

Not surprisingly, the diagnosis and treatment of cancer in dogs and humans is currently very similar. Dogs frequently get skin, breast, head and neck, brain, testicular, and abdominal cancers, and veterinarians and veterinary oncologists often employ X-rays, blood tests, biopsies and physical exams to detect cancers and surgery, chemotherapy, radiation and immunotherapy to treat them. Traditionally, these protocols have been the result of research done on humans.

Looking to dogs for clues

This is where the field of comparative oncology emerges. The National Cancer Institute started the first formal comparative oncology program

CONTINUED ON PAGE 12
in the field in 2003 (see “Sharing is caring”) and began undertaking comparative studies of naturally occurring cancers in pet animals and in humans. A few years later, the Comparative Oncology Research Laboratory at UIUC was born.

Timothy Fan, a comparative oncology researcher and associate professor at the UIUC’s College of Veterinary Medicine, says, “This discipline is about understanding cancers that are shared between people and dogs and then developing new therapies that will hold promise in people and dogs.”

Proponents say studying the canine version of the disease may help answer questions that have persisted despite studies on mice and humans. One of the main limitations of using mice as a model for cancers is that the disease is not naturally occurring in mice but is induced for the purpose of research. Mice also have a shorter life span, with smaller body size and a different immunological makeup than humans. The tiny size of the mice and their associated tumors make them difficult to analyze repeatedly. In contrast, dogs and humans share similarities in tumor genetics, recurrence, metastasis and therapeutic response. The syngeneic relationships with tumor and microenvironment are also consistent in humans and dogs.

But working with dogs has its disadvantages. Dogs that are enrolled in studies today are only there because their families brought them in. According to Fan, “You can’t order dogs that have cancer.”

When starting experiments, cancer can be induced in many mice at the same time, but with dogs, because the cancer occurs spontaneously, the timing of experiments can’t be controlled. “If you are doing an experiment with dogs with cancer with a new drug, you have to have enrollment of the dogs over a longer course of time,” says Fan. “I can’t control how many dogs are going to come through the front doors of our veterinary teaching hospital.”

Researchers do their best to work around this limitation by enrolling dogs at multiple recruiting sites that are able to participate in the clinical trials.

**Comparing the contrast**

Although dogs and humans develop cancers in many of the same ways, there remain interesting differences that could help to answer some oncology questions. For example, there are lots of similarities between dog and human invasive urinary bladder cancers and how they react to common chemotherapy treatments. But an interesting difference between the canine and human versions of the cancer is the presence of a mutation in the BRAF gene. BRAF is an oncogene, and mutation of the gene potentially can cause a normal cell to become cancerous. BRAF is common in the diagnosed dogs, but in humans the mutation is usually not present in urinary bladder cancers but rather in melanomas, colon cancer and thyroid cancer.

The effect of the mutation also seems to be different in dogs and humans. BRAF “seems to be a driver mutation present in dogs but not in humans,” says Heidi Parker, staff scientist at Ostrander’s lab at NHGRI.
“But even if you look at mutations in humans, you see the mutations in the same pathway, just not in the same gene.”

Comparative oncology has the potential to stitch together many gaps in our understanding of how the cancer develops and how it can be treated. “The fact that the dog has the identical mutation that’s found in many other kinds of human cancers means that when we are looking at drugs that target this mutation, we could see how they react in dogs with bladder cancer versus how they react in humans, say, with colon cancer,” says Parker.

"PAC"ing a punch

A key characteristic of a cancerous cell is that it can evade apoptosis, or cell death. Avoiding apoptosis makes the cell immortal. Fan and Paul Hergenrother, a chemistry professor at UIUC, figured out a way to deal with the malignant cell’s death-avoiding trick. They discovered a compound called procaspase activating compound, or PAC-1, that induces the activation of procaspase-3 to caspase-3. Caspase-3 is a protease that cleaves critical proteins in the cell and eventually triggers apoptosis. As procaspase-3 is abundant in cancer cells, “we thought activation of it could be very effective and selective for cancer cells,” says Hergenrother.

PAC-1 induced death in cancer cells when used in a clinical trial in dogs with metastatic osteosarcoma, a trial in which Thunder is involved. Thunder was treated with oral PAC-1 along with a chemotherapy agent. After a few weeks, his X-rays “showed that two of the smaller tumors were shrinking and the big ones remained the same, which is a lot better than getting bigger,” says Terry.

Currently, a phase-1 dose-escalation study of PAC-1 is being conducted in people with solid tumors or lymphoma at the University of Illinois Cancer Center in Chicago. The goal of the study is to evaluate the maximum tolerable dose of oral PAC-1 in human cancer patients. It’s too early to say what the study results might show.

At the same time, Fan is conducting a clinical trial evaluating the effect of PAC-1 in dogs with brain cancer. “The reason why we are pursuing the evaluation in brain cancer is that PAC-1 gets into the brain, which is something that is relatively unique,” says Fan. Therapies that are currently available for brain cancer are not very effective, so “PAC-1 has the ability to meet an unmet clinical need,” adds Fan.

Main hurdles to overcome

Experts in comparative oncology are enthusiastic about the field’s potential. “It’s an exciting time for us,” says Amy LeBlanc, director of the comparative oncology program at the National Cancer Institute. But she notes there still needs to be more advocacy to enroll pets into clinical trials and to provide better access to the genomic data from canine tumors. LeBlanc says getting more funding is a pressing challenge, as is creating a canine version of The Cancer Genome Atlas that NCI could host. The dog counterpart of the atlas would catalog canine cancer-causing genetic mutations in a comprehensive way for researchers who are using genomics and bioinformatics to understand various forms of the disease in the animals.

For pet owners like Terry, comparative oncology has proven helpful and affordable. Although the osteosarcoma persists and has spread to his lungs, Thunder has enough lung capacity to breathe and doesn’t show too many signs of respiratory distress. He is thin but still enjoying his favorite food and drink – sardines and raw goat’s milk.

Terry says she has no regrets about placing Thunder in a clinical drug trial. “I know that cancer will lead to his ultimate demise, but he will not have gone without a fight and without contributing a little bit to science.”
Meet Bernhard Küster
By Alexandra Pantos

Bernhard Küster at Technische Universität München in Munich, Germany, is a new associate editor of Molecular and Cellular Proteomics. Küster’s research involves studying interactions between drug molecules and protein populations in cells and he is co-founder of the biotechnology firm OmicScouts. ASBMB Today’s science-writing intern Alexandra Pantos interviewed Küster to learn about his research and career trajectory, his position as associate editor, and his work/life philosophies. The interview has been edited for length and clarity.

What is your research group studying?

We analyze proteomes, with a special emphasis on how drug molecules interact with proteins, signaling pathways and entire proteomes. People have realized the idea that one drug only affects one protein is fairly naive. There are ample examples of secondary uses of drugs that work by a different mechanism. We would like to understand this more systematically, so that, ideally, we measure the interaction of small molecular drugs with entire proteomes. We use mass-spectrometry technologies for that because mass spectrometers are the de facto standard for detection and quantification in proteomics. The reason we are so interested in these drug-protein interactions is that we would like to find new uses for existing drugs and be able to explain potential undesired side effects – and also provide a mechanistic understanding of how these molecules work.

Could you describe your academic background and research training?

I’m a chemist by training. I studied chemistry in Cologne, Germany. Then I did a Ph.D. in biochemistry at the University of Oxford in the UK and postdoc’d at the European Molecular Biology Laboratory in Heidelberg and at the University of Southern Denmark. That is when I got into proteomics.

Was there one thing that made you choose science?
After finishing school, it was clear that I was going to study life sciences, but at the time in Germany there weren’t so many biochemistry university courses. I ended up studying chemistry and then specializing in biochemistry later. My Ph.D. was in glycobiology, and to be quite frank, I ran away from it because it was so difficult.

But at that time, when I had to make up my mind what would happen to me, I read about early work by Matthias Mann and John Yates and the like on proteomic measurements. I asked Matthias Mann if he was interested in taking me on as a postdoc. After my postdoc, I spent seven years in the biotech industry. That was from 2000 – 2007, and that was the early days of big hype in Europe about biotech companies. I got caught by that too and joined a proteomics company called CellZome in Heidelberg, which turned out to be very successful. (Author’s note: CellZome is now part of GlaxoSmithKline.) Those seven years provided me with quite invaluable experience not only in doing science but also in managing science. I became responsible both for the mass spectrometry and also for the bioinformatics department in that company. After seven years, I had to choose to stay and keep doing what I was doing, take an offer from big pharma, or go back to university and become an academic with some industry background. And I chose the latter, because it was the best fit for what I wanted to do.

What does the MCP position mean to you?

It’s a very honorable thing to do. I felt flattered these guys thought I was worthy of that position. And of course the second reaction was, “Oh God, this is more work!” No, it’s certainly a great honor to be asked to serve on the board of MCP. Any academic community works by the principle that we all do something for each other, and the better we do that, the better the whole system functions, so it is my turn to give something back.

How would you say your new role is going so far?

So far, I think it’s going quite well. I read more papers than I did before, but I also get to see more comments from colleagues who have an opinion about someone’s work. As a reviewer, you can just write down your frank opinion. As an associate editor, you have to weigh the arguments.

Do you have any hobbies outside of the lab?

I am a keen road biker. Otherwise my family with three kids tends to keep me busy.

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

That’s a difficult one, because I like working, so I tend to spend a lot of time at work. The truth of the matter is that everyone needs to find their own balance. Some people seem to be able to carry on and on, and it doesn’t bother them much. Others need to watch themselves a little more, because they may not have that natural ability to keep going. But clearly, it’s important to have something outside of work just kind of to restart your brain every now and then.

Do you have any words of wisdom for scientists in training?

I think it quite useful as a scientist to try to get rid of one pet hypothesis a day. That keeps your brain alert, or at least you don’t get stuck in a certain way of thinking.
Scientists can be heroic – making lasting advances that better people’s lives. Comic book creators have historically recognized this and given scientists their due by turning them into superheroes in print. The list of comic superhero scientists and science lovers is long, featuring big names like Spider-Man, the Invisible Woman, the Black Panther, Iron Man, and the Incredible Hulk. But any actual resemblance of these costumed crusaders to living scientists can be iffy. In the name of entertainment, comic books play fast and loose with the realities of research, discovery and scientists’ actual abilities to control threats to human survival.

It’s a bird! It’s a plane! No, it’s a … virologist!

Enter “The World of Viruses,” a strikingly illustrated comic book that is the brainchild of Judy Diamond, professor and curator of informal science education at the University of Nebraska State Museum. An American Association for the Advancement of Science fellow, Diamond created a super legion of virologists, science educators, writers and artists to produce the graphic novel, which pits scientists against viruses in a battle for human survival.

Conceived as a new way to increase public understanding about viruses and infectious diseases, “World of Viruses” succeeds in being a comic work of art, taking readers on a visual journey across tundra and space and into the ocean and human bloodstream while personifying the viruses, often as devious and dangerous characters.

Neither alive nor dead, viruses are so small they can only be seen by powerful microscopes. With the potential to wreak havoc on food supplies and sicken scores of people through simple programs of replication, viruses impact nearly every facet of human life.
When Diamond’s team brings them to life, the viruses HPV, foot and mouth disease, HIV, influenza, and Emiliania huxleyi prove to be formidable foes. To make the viruses relatable to an audience, the team has given them humanlike features. This is intended to make it easier, Diamond says, to get readers “to appreciate how things seemed from a virus’s perspective … to get out from a human-centered framework.”

In one story, human papillomavirus, or HPV, is personified as a crafty, blue-skinned girl wearing a leather jacket and boots. To the reader, she playfully explains that all she desires is a “nice and safe place to live and reproduce” as she slips into a host through a small skin cut. Zipping through arteries and veins, she hides from an army of armor-clad, space-soldier immune cells seeking to destroy her. She reveals how viruses replicate through the host and have turned an Indonesian man into a wart-ridden circus attraction with rootlike growths extending from his hands and feet. (In an actual case study, an Indonesian man working in a carnival sideshow with just such growths was dubbed “the Tree-man.”)

A U.S. physician arrives on the scene certain he can help the man and explains how HPV caused the Tree-man’s symptoms and how treatments to kill the virus will reverse them. Swarmed and captured by the soldiers, the HPV girl loses her battle with the immune system but vows to return.

Not all the viruses in the book are bad. The Emiliania huxleyi virus is a teenage hero in a green hooded sweatshirt who combats out-of-control E. huxleyi algae blooms that produce a gas capable of reflecting sunlight and cooling the planet. In the spirit of comic supervillains, the untamed algae bloom erupts from the sea as a giant monster, destroying everything in its path. The boy and his virus friends take small spacecrafts into battle and fight the menacing algae, restoring balance to the sea.

Weaving science into art

Supported by a grant from the National Institutes of Health, Science Education Partnership Awards, Diamond assembled the team behind “The World of Viruses” with the help of comic book illustrator Tom Floyd. Author of the online comic Captain Spectre, Floyd is a graphic artist and illustrator for Nebraska Education Telecommunications and has worked on “Reading Rainbow” and animated
Creating a comic book was no small task for Diamond and Floyd. It required bringing together writers, illustrators, inkers and colorists and finding a way to convey hard science through a medium that traditionally tells fantastical stories.

Floyd brought in Martin Powell to write the stories. The two had worked together on a comic strip for the publisher of “Tarzan.” Diamond and Floyd developed the characters, Powell and Diamond worked on the scripts, and for “The Curse of the Tree-man,” Floyd brought in Josef Rubinstein, an inker for comic book giants Marvel and DC Comics.

As part of the illustrating team, an inker goes over initial pencil drawing outlines with black ink to add depth and dimension to the art. A friend of Floyd’s, artist Scott Beachler, was the colorist, adding, in the final stages, the color, mood and lighting that gives the pages and characters their finished, three-dimensional look.

This looks like a job for scientists!

“Not compromising the story while keeping the science accurate” was the most challenging aspect of the project, Diamond says. All aspects of the book – characters, stories, and scripts – were run by virologists to make sure the science was sound. It was the first time Floyd and Powell had worked so closely with scientists.

The illustrations that bring the stories to life contain clever nods to scientific details. “Specific traits were something we included with each of the characters,” says Floyd. The HPV girl wears an earring that is a graphic representation of the actual virus. The Emiliania huxleyi monster wears wrist-bands that are patterned after the EhV virion structure. Another story on influenza incorporates the shapeshifting nature of the virus by representing it as a villain with an unknowable shape that escapes even the scientists.

With great power comes great responsibility (to teach science)

Recognizing that new and innovative tools urgently are needed for scientific outreach, Diamond happened upon the comic book idea while looking for alternative avenues to educate a young public.
“We wanted to reach teens with information about the science of viruses,” Diamond explains, and “youth librarians advised us that developing comics would be an effective way to reach this goal.”

The advice was not unfounded. Interest in comic books is surging, and Diamond Comic Distributors (no relation to Judy) reports comic book sales of $540 million in 2014 – a number that is up from previous years and continues to rise. Carol L. Tilley, a professor of library and information science at the University of Illinois at Urbana-Champaign, maintains that comics are as effective as the most sophisticated forms of literature in teaching kids. In fact, Tilley’s research has found them just as effective as books, if not more (1).

Perhaps what is most encouraging to Diamond is reader reaction to their particular comic book. “We have lots of anecdotal evidence that kids develop strong attachments to the comics and carry them around in their backpacks. We also know that science teachers are using them in classrooms, because they have requested classroom sets,” she says.

Diamond currently is running studies investigating how teachers are using the comics in formal educational settings. She has published a number of peer-reviewed articles on the project (2,3,4), including one looking at the impact of comics on kids’ interest in science (2). Riding the success of “The World of Viruses,” Diamond is working on a 30-page comic about measles and vaccines called “Contagion,” which she estimates will be released in a year. Onboard for this project is artist, writer, West Coast Avengers creator, and Marvel veteran Bob Hall.

Perhaps researchers and doctors will again appear as daring heroes on a quest for cures, playing into the common theme of good versus evil that makes comics hard to put down. In the case of real scientists, that theme might just contain some semblance of truth.

REFERENCES
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Paul Sirajuddin (psiraju1@jhmi.edu) is a second-year radiation oncology postdoctoral fellow at The Johns Hopkins School of Medicine. A native of Michigan, he ventured to the East Coast for a postbaccalaureate fellowship at the National Cancer Institute in 2008 and then earned his Ph.D. from the Georgetown University Lombardi Comprehensive Cancer Center in 2013.
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Meet the 2016 plenary lecturers
At the 2016 ASBMB annual meeting next spring in San Diego, there will be six plenary lecturers. On the following pages are interviews with those individuals. The interviews were conducted by Rajendrani Mukhopadhyay, our chief science correspondent. The interviews have been edited for length and clarity.

34 Francis Collins: ‘Now look where we are’
36 Anna Marie Pyle: ‘Trust your own imagination’
38 Michael Rosen: Sliding into biology
40 Jared Rutter: Mad about metabolism
42 Peter Walter: An explorer of cells
44 Xiaowei Zhuang: Taking optical microscopy by STORM
We invite you to participate in the 2016 annual meeting of the American Society of Biochemistry and Molecular Biology, to be held April 2 – 6 in sunny San Diego. We have fantastic scientific and education programs planned, as well as workshops in cutting-edge areas of biochemistry and molecular biology and myriad networking opportunities.

The meeting will feature 11 scientific themes and one theme focused on education and professional development, with lectures from the most prominent scientists in biochemistry and molecular biology. Several of the themes represent traditional areas of interest within the ASBMB membership, such as gene regulation and chromatin modification, enzyme catalysis, protein synthesis and degradation, and lipids and lipid signaling. However, new and emerging fields also are featured, such as systems biology and metabolic networks, glycoscience, and the development of new chemical tools to interrogate biological questions in vivo. Themes that will pervade many of the symposia will be the molecular basis of disease; how the development of new techniques facilitates a more detailed understanding of biomolecules like DNA, RNA, proteins, lipids and carbohydrates and how they interact with each other; and how the enormous bodies of genomic, proteomic and molecular and cellular imaging data are being used to gain new insight into the functions of novel macromolecular complexes and their posttranscriptional or posttranslational modifications.

Excitingly, the 2016 meeting will inaugurate a new session — organized and chaired by graduate students and postdoctoral scientists — that will feature lectures by renowned scientists Corey Wilson of Yale, Donald Hilvert of ETH Zurich, Laurie Read of University of Buffalo, and Feng Schao of the National Institute of Biological Sciences, Beijing, China. The new session will include opportunities for other student and postdoctoral scientists to speak on topics related to protein engineering and post-translational modifications.

Indeed, the 2016 annual meeting will engage scientists at all levels within the ASBMB membership. Moreover, in addition to lectures delivered by our award winners, plenary lectures will be given by Francis Collins of the National Institutes of Health; Anna Pyle of Yale University and the Howard Hughes Medical Institute; Michael Rosen of the University of Texas Southwestern Medical Center and HHMI; Jared Rutter of the University of Utah and HHMI; Peter Walter of the University of California, San Francisco, and HHMI; and Xiaowei Zhuang of Harvard University and HHMI. (Read Q&As with them starting on page 32.)

As always, each symposium within a theme will incorporate short platform presentations selected from the submitted poster abstracts, and will sponsor a poster competition with cash awards for the winners. Undergraduate and graduate students are especially encouraged to submit abstracts and to apply for generous travel awards.

The ASBMB annual meeting will offer you the atmosphere of a small, specialized conference organized by themes and moreover provide you with opportunities to learn from and interact with scientists outside of your research area. Furthermore, in conjunction with the 2016 Experimental Biology conference, you will have an unparalleled opportunity to learn about the latest discoveries in every facet of biology.

Your participation will be rewarded with exposure to great science, opportunities to establish collaborations and to network, and access to mentoring and career advice. We promise not only wonderful science but also awesome weather! Submit your abstracts today and prepare yourselves for a fascinating experience!

Squire J. Booker, Pennsylvania State University and Howard Hughes Medical Institute
Wei Yang, National Institutes of Health
2016 program co-chairs
Discoveries often happen in the gaps between disciplines, and, with the world’s population projected to grow from 7 billion to 9 billion by 2050, the next generation of chemists and biologists will use those discoveries to tackle new challenges. These challenges include controlling microbial infections, improving food production, understanding cellular communications and managing global sustainability. Chemists and biologists approach these fundamental questions armed with vast genomic information, powerful analytical tools and an eye toward solving real-world problems. This 2016 American Society for Biochemistry and Molecular Biology annual meeting symposium will highlight research that crosses the boundaries between chemistry and biology and explores new applications and opportunities for chemical biology.

The postantibiotic era
Last year, the World Health Organization warned of a coming post-antibiotic era resulting from the spread of resistance to antimicrobials. The first session will examine how chemical biologists are using new strategies for antibiotic discovery and for understanding resistance mechanisms.

The greening of chemical biology
Although chemical biology has its roots and many successes in biomedicine, its application to plants is just beginning. The second session will highlight how the interplay of chemistry and biology is advancing knowledge both of how plants grow and of the biosynthesis of pharmacetically important molecules.

Chemical communication, biological regulation
All organisms use small molecules for communication to control biological responses. These inputs and responses occur inside cells and across the environment. New approaches for visualizing and manipulating metabolic and cellular systems will be the focus of the third session.

Chemistry, biology and sustainability
The challenges of global sustainability are wide-ranging and complicated. But there are rich, new opportunities for the application of chemistry and biology to these challenges. This final session will showcase how advances in biocatalysis and systems/pathway engineering are aiming to meet these problems.

Enzymes are the sophisticated molecular machines that catalyze myriad biochemical reactions occurring in nature. For nearly a century, a large body of research has provided a wealth of insight into enzyme-catalyzed reactions and allowed us to learn a tremendous amount about how enzymes function. Despite this, there is still a lot to be unraveled about enzymes. In the four sessions of this symposium, our invited speakers will take the audience on a tour of the forefront of enzyme research, offering a look under the hood of some of the most sophisticated enzymes.

Metalloenzymes and radicals in catalysis
Many enzyme-catalyzed reactions are chemically difficult, yet proceed with ease in ambient conditions. Typically, such reactions involve highly reactive intermediates that activate the substrate at a specific, often inert, position. What is perhaps most remarkable about such enzymes is the fact that the enzyme scaffold controls and directs the reactivity by suppress-
LIPIDS AND LIPID SIGNALING

Lipids continue to surprise us

By James Ntambi & Tobias Walther

It has become increasingly clear that lipids play key roles as structural, signaling and regulatory molecules. Understanding pathways of lipid metabolism regulation is fundamental to deciphering how cells and organisms grow, develop and respond to external stimuli. Four sessions of American Society for Biochemistry and Molecular Biology 2016 annual meeting in San Diego will feature leaders in the research of lipid function in health and disease.

Membrane contact sites and lipid trafficking

Recent breakthroughs in cell biology highlight that many cellular organelles are in tight, molecular contact. A major, emerging function of these organelar contact sites is transport of lipids. The first session will highlight the molecular architecture and physiological functions of membrane contact sites.

Lipid membrane regulation

Maintaining membrane homeostasis is important for cellular organization and integrity. In this session, leaders in the field will present the importance of post-translational regulation of phosphatidic acid and phosphoinositide metabolism enzymes in maintaining lipid homeostasis. Attendees also will hear the latest on the transcriptional regulation of lipid metabolism by sterol regulatory element-binding proteins, or SREBPs.

Lipid signaling

Signaling lipids control many cellular processes, including cell growth, apoptosis and metabolism. This session will feature the diverse signaling mechanisms of lipids, focusing on nuclear and G-protein–coupled receptors as paradigms. The presentations will extend to cover the key roles of some signaling lipids in obesity and diabetes.

Lipids and energy metabolism

Neutral lipids are essential to the storage of metabolic energy. The final session will highlight advances in the understanding of cellular lipid storage mechanisms. It will provide insights into synthesis and regulation of fatty acids, their desaturation, and how these mechanisms affect whole-body energy metabolism as well as insulin signaling.
The ultimate goal of most scientists who work in biological chemistry is to understand and affect human health. As our understanding of biological processes at both the macroscopic and molecular levels increases in complexity, new approaches and concepts rapidly feed into drug-discovery programs, producing new tools that further inform our understanding in an iterative way. Drug discovery is an early adopter of biochemical innovation, and this 2016 American Society for Biochemistry and Molecular Biology annual meeting symposium will highlight some of the approaches being taken to engage the most recent advances in biochemistry and molecular biology.

**Big data: adding -omics**

The front line of contemporary -omics is moving beyond transcripts and proteins to the more analytically demanding tasks of quantifying lipids and metabolites. The first session will highlight these advances and their integration with the blueprints (DNA and RNA) and effectors (protein). It also will consider how activity-based probes applied in cell or tissue lysates have accelerated our understanding of the proteome in normal and disease states.

**Mechanism matters**

The second session will consider how biochemical insights into processes as basic as protein synthesis provide new guide posts for innovative approaches to treating disease. Pathway-driven genetic methods of understanding druggability can take a lot of the guesswork out of target selection. And bringing together a detailed understanding of the enzymology and mechanism of neurodegenerative diseases rapidly is advancing therapeutic approaches using the tools of structure-based design.

**Natural beauty: harnessing evolution**

Natural products are fascinating examples of evolutionary masterpieces, often perfectly fit for their natural niche. The third session will discuss how chemically modifying these works of natural art often is daunting, but new metagenomic approaches to identifying families of naturally occurring analogs have the potential to transform the field. Integrating natural products with structural biology and detailed mechanistic understanding provides new hope for exploiting naturally evolved antibacterials against humankind’s most ancient diseases.

**A thousand words**

The final session will dig into how modern imaging methodologies accelerate understanding of complex systems, diseased or normal. Imaging mass spectrometry now allows unparalleled understanding of small molecule distribution and spatial localization in tissues. Activity-based imaging promises to transform pathogen detection. Whole-body imaging using positron emission tomography, or PET, and computed tomography, or CT, routinely is used clinically, but new generations of probes built on understanding the biochemistry of disease are potentially transformative.
Currently afflicting more than 30 percent of the U.S. population, nonalcoholic fatty liver disease, or NAFLD, rapidly has emerged as a major epidemic. Although the disease is disproportionately prevalent in Hispanic Americans, increasing incidences in India and Brazil highlight its global impact. NAFLD is the most common cause of liver failure and transplantation and the most prevalent liver disorder in industrialized nations, and it is linked to the development of type 2 diabetes, cardiovascular disease, dyslipidemia and metabolic syndrome. Three sessions at the 2016 American Society for Biochemistry and Molecular Biology annual meeting will provide an update on the signaling pathways that contribute to hepatic dysfunction and NAFLD and insight into the genetic determinants that contribute to the etiology of the disease.

**Hepatic lipid signaling**
The JNK and hedgehog signaling pathways have become pivotal players in the development and progression of NAFLD. Understanding the prominent role that nuclear receptors play in the transcriptional program that underlies varied disease states including NAFLD has led not only to new information about the molecular mechanisms behind hepatic dysfunction but also to considerations for an attractive therapeutic strategy.

**Genetic determinants and extrahepatic complications**
Population-based studies and exome-wide association studies have enabled researchers to uncover genetic variants that confer susceptibility to NAFLD. These studies, coupled with investigation into the role of fetal hepatic inheritance in the development of metabolic diseases in the offspring of obese parents, have increased our understanding of the complex molecular mechanisms that underlie NAFLD. Significantly, NAFLD increases susceptibility to other metabolic disease states, which has spawned the need for a multipronged therapeutic approach including the use of mitochondrial protonophores.

**Metabolic insight into the enzymatic players**
Multiple hepatic enzymes, including fatty acid elongases and thioesterases, coordinately regulate lipid homeostasis. Consequently, aberrant catalytic activity of these lipid metabolic enzymes has been shown to confer alterations in fatty acid concentrations that are causally linked to NAFLD. Finally, mounting evidence has established a prominent role of branched-chain amino acid metabolism in multiple pathophysiologic states including the hepatic dysfunction that contributes to the etiology of NAFLD.
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theme will consider how, as new tools and methods are developed, unanticipated paradigms are being formed in this complex and exciting field.

A new paradigm in translation regulation

RNA makes up the functional centers of the ribosome and is the building block of its enzymatic activity. The first session will explore how different types of RNA regulate protein synthesis.

LEGO them up

Building with LEGOs often involves dealing with misassembled, missing or extra pieces. The cell faces a similar problem when it comes to the expression of giant protein complexes, such as the proteasome and nuclear pore complex. The second session will explore the emerging mechanisms the cell uses to build complex molecular machines.

The good, the bad and the ugly

The cell handles critical regulation of protein functions through diverse quality control programs, licensing only “good” polypeptides to function while sentencing “bad” ones for destruction. The third session will focus on newly discovered quality control pathways as well as unconventional mechanisms.

Why it takes so many proteins to destroy one

The proteasome and autophagy systems are surprisingly complex as exemplified by the large number of regulators required to destroy a single protein molecule. The last session’s discussion will center on how these regulators cooperate and why a cell and a multicellular organism need so many of them to maintain fitness.

ORGANIZERS: Christine Dunham, Emory University, and Yihong Ye, National Institutes of Health.

CELL SIGNALING, KINASE, AND CHEMOTHERAPY

New concepts from bench to bedside

By Dan Leahy & Susan Taylor

Kinase-mediated signaling plays essential roles in cell growth, differentiation and homeostasis. Kinases signal by switching between “on” and “off” states, and many inputs regulate the activity of each specific kinase. Abnormal kinase activity, often the result of mutation, is associated with many cancers, and kinase inhibitors have become a highly successful and growing class of anti-cancer agents. This 2016 American Society for Biochemistry and Molecular Biology annual meeting symposium will focus on emerging insights into the molecular mechanisms by which kinase activity is regulated and how these insights are influencing strategies to target kinase activity in cancer.

Molecular mechanism

Intra- and intermolecular interactions, phosphorylation and combinations of such events influence kinase activity. The first session will highlight new insights into the molecular mechanisms governing the activity of key kinases, how the activity of these kinases becomes deregulated in disease and how an understanding of mechanism has influenced strategies to target kinases therapeutically.

Spatiotemporal control

Movement of kinases both within membranes and to and from different membrane compartments is known to affect the nature and timing of kinase signaling. The second session will highlight state-of-the-art studies of the movement of specific kinases during signaling and how location modulates signaling activity.

Therapeutic strategies

New strategies for designing kinase inhibitors are discussed in terms of pseudokinases, active kinases and allosteric sites. In the third session, new approaches for discovering target genes will be described as will new targets that lie downstream of kinases.

New roles for old kinases

Kinases are dynamic molecular switches that easily can be hijacked to create oncogenes that drive cancers. The final session will discuss how both kinases and pseudokinases can drive tumors and introduce new roles for PKC and PKA as tissue-specific tumor drivers and tumor suppressors.

ORGANIZERS: Dan Leahy, Johns Hopkins University School of Medicine, and Susan Taylor, University of California, San Diego.

Abstract submission deadline: Nov. 5
Carbohydrates are the only one of the four major biomolecules of life that modifies the other three. This is perhaps unsurprising, since glycosylation is well suited for increasing the functional diversity of resulting glycoconjugates. The various monosaccharides found in glycans, coupled with the variability in how they are attached to each other, confers onto glycans incredibly high information content that is reflected in their diverse structures and topologies. This 2016 American Society for Biochemistry and Molecular Biology annual meeting symposium will focus on how glycosylation impacts biology and how technological advances are providing novel insights into the roles of glycans in basic cellular processes and pathophysiologies.

The emerging role of O-GlcNAc

The first session will highlight the structurally simple yet influential O-GlcNAc modification that modifies hundreds if not thousands of nuclear, mitochondrial and cytosolic proteins. While O-GlcNAc has been associated with myriad biological functions, this session will focus on the emerging role of O-GlcNAc in regulating gene expression. Talks will cover how O-GlcNAc contributes to regulation of RNA Pol II and ChREBP as well as how mutations in OGT associated with X-linked intellectual disability, or XLID, impact the transcriptome.

Structural and enzymological advances

The second session will crystallize recent advances gained primarily by structural biology and enzymology approaches with carbohydrate processing enzymes. New molecular insights into how glycosidases and glycosyltransferases recognize and processes varied glycoconjugates will be discussed.

The power of chemical biology

The third session will highlight the power of chemical biology approaches in glycosciene. Topics to be covered include recent findings regarding comparative and competitive activity-based glycosidase profiling, cotranslational addition of O-GlcNAc to proteins and the use of photoprobe to investigate protein glycosylation within the secretory pathway.

Glycan complexity

The final session will cover the structurally complex glycans found in bacterial glycosylation and the microbiome. Recent data regarding glycan-dependent interactions between host gut and bacteria including pathogenic processes will be described.

SYSTEMS BIOLOGY AND PROTEOMICS

The molecular linguistics of biological systems

Understanding a complex biological system, be it a single cell, multicellular organism or multispecies consortia, requires understanding its language: its means of functional communication between numerous individual components. In a post-genomic era, the next bottleneck of this learning process is mapping meaningful combinations of individual “words”—that is, active components. This challenging endeavor requires integration of high-throughput experimental platforms (most importantly, proteomics) with computational modeling. In this 2016 American Society for Biochemistry and Molecular Biology annual meeting symposium, experts from these intersecting fields will enlighten

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us as to how to decode the language of molecular complexes and interactions in various biological systems.

Where proteomics meets medicine
Proteins are undoubtedly the most informative class of biomolecules in biomedical research not only due to their direct biological relevance to human pathologies but also as major drug targets for many diseases. The next generation of mass spectrometry enables systematic analyses of human proteomes for improved disease diagnostics and treatments.

Networking in the cell
The explosion of Web-based social networks coincided with our growing appreciation of an intricate web of molecular interactions driving each living cell. Cellular networks of various types (metabolic, signaling and regulatory) contain broadly conserved as well as unique aspects, which together comprise a subject of adaptive evolution. Recent progress in network modeling yields new insights into the linguistics of biological systems.

The sociology of protein machines
Protein complexes are macromolecular machines that coordinate the functions of the cell. These functional modules are dynamic entities whose relationships are orchestrated carefully to maintain cell homeostasis. Innovations in mass spectrometry-based approaches have made it possible to dissect structural and functional dynamics of protein machines and to understand their action mechanisms.

Molecular crosstalk between species
The final session will take us to the next layer of molecular interactions: between cells of different types and even different species (as in environmental or host-associated microbial consortia). Recent progress in this rapidly expanding field heavily relies on next-generation meta-omics technologies as well as on new approaches to systems-level data analysis and predictive modeling.

Organizers:
Lan Huang, University of California, Irvine, and Andrei Osterman, Sanford Burnham Prebys Medical Discovery Institute.

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Nobelist Sir William Lawrence Bragg once said, “The important thing in science is not so much to obtain new facts as to discover new ways of thinking about them.” This quote raises the question of how today’s educators should structure training programs so that students maintain their sense of wonder about the world both in and out of academia. The 2016 American Society for Biochemistry and Molecular Biology annual meeting education and professional development symposium explores how programs can offer a deep and quantitative understanding of biochemistry and molecular biology, engage students on both a theoretical and an experiential level, and prepare them for a range of science, technology, engineering and math careers.

Leading the way in the undergraduate classroom: Depth, breath or a totally different approach?
Biochemistry can be daunting, and, while a thorough understanding of foundational principles is essential, concepts often are obscured by a thick layer of details and jargon. The first session will present some proven pedagogical strategies to stimulate student interest and meet the competencies of today’s biochemistry and molecular biology education. These include using threshold concepts to scaffold student learning, improving quantitative thinking about molecular dynamics and integrating research into BMB courses.

Graduate and postdoc training: Ensuring the attainment of rewarding STEM careers

Biochemistry Education
Training the next generation of biochemists and molecular biologists

By Celeste Peterson & Margaret Carroll
As part of President Obama’s Precision Medicine Initiative, researchers will gather genomic, transcriptomic and other data from a cohort of a million volunteers. Will we have the ability to interpret the enormous amount of information that will emerge from this effort? In particular, will we be able to define the significance of differences that occur between individuals and that could predispose a person to one of many diseases that contain a genetic component? The answers will depend in large part on our understanding of the mechanisms of gene regulation.

In the time since Jacob and Monod first proposed the concept of transcriptional regulators and cis-regulatory sequences 55 years ago, the field of gene regulation has undergone a series of important developments. Among these are an ever greater understanding of the enzymes and proteins that shape chromatin architecture and the realization that three-dimensional chromatin architecture is involved intimately in gene regulation. The development of high-throughput technologies for defining chromatin structure and organization, the identification of potential cis-regulatory sequences at a genomic level, and the discovery of roles for noncoding RNAs in chromatin remodeling and gene regulation have facilitated this paradigm shift. Our symposium for the American Society for Biochemistry and Molecular Biology 2016 annual meeting will make sense of these developments and consider the intimate links between transcription regulation, genomic stability and human disease.

CHROMATIN ORGANIZATION AND GENE REGULATION
Making sense of genetic switches

By Joan Conaway & Bing Ren

Prepping for the MCAT
The content and goals of the MCAT changed dramatically in 2015, with a renewed focus on biochemistry and the social sciences. The third session will examine the first year’s performance of the MCAT 2015, provide curriculum ideas on preparing for medical school and discuss the role of physicians in today’s biomedical health care system.

You’ve got to see it to believe it

The molecular world is too small for the naked eye to see. The last session will focus on how new tools in three-dimensional printing, animation software and social media are helping students to better see what’s going on in cellular biochemistry and molecular biology.

Transcriptional regulatory mechanisms
Many transcription regulators have been identified over the past two decades. But much remains to be learned about the molecular mechanisms by which they work together to control transcriptional output during normal development and cellular function and during disease states. Presentations in this session will highlight how mutations in components of the basic transcription machinery give rise to developmental disorders and cancer. Also addressed will be our increasing appreciation of the cross-talk between transcriptional regulation and DNA repair processes.

Chromatin remodeling and epigenetics
The third session will focus on mechanisms of epigenetic regulation. DNA methylation is a well-established epigenetic mark with important roles...
CONTINUED FROM PAGE 29

in gene regulation. Emerging evidence that methylation of mRNAs and other transcripts also can have an impact on regulatory processes will be discussed. Understanding mechanisms responsible for epigenetic regulation via chromatin requires a detailed knowledge of histone chaperones and chromatin remodeling enzymes, and these also will be a focus of this session.

Noncoding RNA and gene regulation

With most of the human genome transcribed into RNA during at least some stage of development, a major challenge is to understand the biological functions, where they exist, of the plethora of newly identified noncoding RNA transcripts. A variety of such RNA transcripts have been characterized and linked to gene regulation, and these will be featured in the fourth session.

DNA REPLICATION, REPAIR AND RECOMBINATION

Make no mistake about it

By James Berger & Agata Smogorzewska

Every human cell contains roughly two meters’ worth of DNA. As a consequence of this great length, over the course of an average human lifetime, the body will have synthesized enough DNA to reach about halfway to the nearest star, two light-years away! How cells manage to make this extraordinary amount of DNA while avoiding errors that can lead to mutation and disease remains one of the foremost questions in molecular biology. This 2016 American Society for Biochemistry and Molecular Biology annual meeting theme will focus on how DNA replication, repair, and recombination is done right.

First things first

In the first session, speakers will discuss how the process of replication is initiated and terminated properly. Although replication initiation is extremely complex, we now know enough about the players and their regulation to be able to recapitulate many aspects of this critical event using purified components in a test tube. The growing lines of evidence also point to sophisticated mechanisms that tightly control replication termination.

How do you use your sister to repair yourself?

During and immediately after DNA replication, cells have an option of repairing mistakes using the just-duplicated sister chromatid to avoid permanent changes to the genetic material. In the second session, we will discuss how recombination-based repair is regulated in the presence and absence of a sister. DNA gymnastics, anyone?

Fix it up

A veritable hive of proteins swarms around DNA, looking for mistakes and patching them up. The third session will highlight recent structural and mechanistic insights into the fundamental processes that cells use to recognize and repair mistakes. Mechanisms for cutting and pasting entire DNA segments, such as occurs during transposition, also will be discussed.

What happens when replication proceeds through a difficult terrain?

In the final session, we will discuss what happens when replication forks become stressed or stall at roadblocks, such as damaged bases, nicks or covalent crosslinks. Along the way, we will sneak in some discussion of chromatin and examine what happens to histones during replication and repair.
Attention grad students and postdocs

Reasons to attend
• Present your research: oral and poster presentations available
• More than 200 travel awards of $1,000 each are available to grad students and postdocs
• New professional-development events for grad students and postdocs

Important dates
• Abstract submission deadline: Nov. 5
• Travel award application deadline: Nov. 12
• Early registration deadline: March 1
• Learn more and submit your abstract: www.asbmb.org/meeting2016/

Events
• Professional-development event to learn about different career paths, present your research and network with colleagues
• ASBMB Game Night, a new networking and social event
• Scientific sessions organized by grad students and postdocs
• Workshop and scientific sessions on teaching undergraduates.
• Workshop to develop competitive broader impacts statements for those applying for NSF awards
• Workshop to improve science communication skills through storytelling
• Dedicated networking event for women scientists
Doctor, doctor
Engineered proteins show great promise in medical applications. These categories focus on how engineered proteins and protein scaffolds can be used as therapeutics.

You've gotta find a method
Developing novel proteins requires knowledge of current engineering techniques. These categories focus on methods and predictive modeling for protein engineering.

It's electrifying!
Much debate surrounds the future of energy, be it generation, transfer, or storage. These topics center on how engineered proteins can be used in various energy applications.

It's not easy being green
Many environmental issues that arise today can be mitigated by “green” technologies. Protein engineering has a large potential for employment in the green revolution, as discussed here.

Living in a material world
Many of the products that surround us everyday are made possible by advances in materials science. These categories pertain to the application of protein engineering in material products.

You're motoring
The grunt work of a cell is performed by molecular machines, these systems can also be used ex cellulo to create or power products. These topics touch on the utility of engineered assemblies.

Recent Advances in Protein Engineering
San Diego Marriott Marquis Hotel
Tuesday Evening, April 5, 2016

Organizers:
Michael White
University of Maryland, Baltimore County
Danielle Schmitt

Session Keynote Speakers
Dr. Donald Hilvert,
ETH Zurich
Dr. Corey Wilson,
Yale University

Grad/Postdoc first authors submitting abstracts to topics for this session will be considered for short talks and must also present posters. All others will be programmed for poster presentation. Topic categories are #2100-2110. Abstract submission deadline: Nov. 5th.
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Abstract submission deadline: Nov. 5th

Dr. Corey Wilson, Yale University
Dr. Donald Hilvert, ETH Zurich

Organizers:
Michael White                          Danielle Schmitt
University of Maryland, Baltimore County

STRAIGHT FROM THE BENCH: 2016 ANNUAL MEETING
SESSIONS LED BY GRAD STUDENTS AND POSTDOCS

Post-translational Modifications and the Microorganism Response
Tuesday, April 5, 2016 | San Diego Marriott Marquis Hotel

Interested in...
... non-traditional protein modifications?
... protein quality control?
... bacterial pathogenesis?

Learn more at www.asbmb.org/meeting2016

Submit your abstract!
Topic categories: 2001-2009 Submission deadline: Nov. 5
The NIH is due to send a five-year strategic plan to Congress at the end of this year. What are you hoping to put in that plan?

The goal is to lay out in broad strokes what an exciting time this is for biomedical research. There will be a particularly strong case made for the importance of fundamental science, which undergirds everything we’ve ever achieved and will achieve.

(The plan) will also explain how we set priorities, because Congress and the public are often puzzled about that. The process is a complex mix of scientific opportunity and public-health need. (The plan) will also talk about stewardship and the importance that NIH attaches to making sure that every dollar that we receive from Congress is thoughtfully applied in a way that will ultimately produce the most useful results. We will include comments on such things as rigor and reproducibility. The plan will refer prominently to the strategic plans of the 27 institutes and centers. We’re not trying to replicate all of the things that they have already outlined. This will be more of an overarching perspective of how the whole NIH works together with the scientific community to achieve remarkable advances at this exceptionally promising time in scientific history.

There is a perception among scientists that the NIH is focusing more on translational than on fundamental research. What are your thoughts on that perception?

I’m concerned about that perception. I certainly feel strongly that much of our success over the decades has been in the basic science arena. When we use our standard coding scheme to catalog NIH’s investments, about 53 percent is basic, and 47 percent applied, and that balance has not changed significantly in decades.

Some would argue, however, that when you look at what we call basic science, some of it is not quite as basic as it used to be. More of NIH-sup-
ported basic science now has a connection to a possible disease application. Some of that evolution reflects the way in which science is moving forward. We are learning more about molecules and pathways in a way that attaches them to insights about disease.

I want to, however, assure basic scientists that we talk about this situation a lot at NIH. We’ve looked to see how basic science grant applications score in review and they actually do better, on the average, than translational grant applications.

You know what I think the main problem is? Everybody is really stressed right now. NIH has lost almost 25 percent of its purchasing power over the last 12 years. That means that there is no field that is having an easy time.

Both the U.S. House and Senate have proposed increases to the NIH budget in the upcoming budget. Isn’t that right?

That’s right, and we’re thrilled to see this kind of strong bipartisan support to help turn around the 12-year slide in our resources. Both the House and Senate appropriations subcommittees have voted for a significant (budget) increase for NIH. That, I think, deserves cheering.

You’ve been at the NIH since 1993. How have things changed there?

The science has changed enormously. In 1993, the genome project was just getting started. There were great concerns about NIH getting into “big science,” where teams would be brought together to work on large projects. Technology was seen as not quite as elegant as other kinds of fundamental bench research. Nowadays, we see technology as such a powerful driver.

Certainly, you can’t look at the biomedical literature without realizing that the number of articles that have multiple authors has grown substantially over 22 years. That is an indication of the way in which science is now much more of a team effort. Some of the most rewarding experiences scientists are having now come from being part of interdisciplinary teams that bring skills from multiple perspectives to the same problem.

Has your own scientific thinking been changed by being NIH director?

Dramatically. We’ve gone from science that, by necessity, had to be focused on a limited snapshot of what was going on in biology to approaches that allow you to ask questions that are much more comprehensive, with the word “all” in them. Just as an example, my own lab at NIH is pursuing explanations of the ways in which genomewide chromatin structure within pancreatic islet cells confers understanding about diabetes risk. That approach would have been unthinkable 10 years ago, and yet now can be done by a relatively small group of dedicated and computationally sophisticated researchers.

Technology has opened up those doors to us. We can push much faster and further than I thought possible in my lifetime to understand how a genome, a cell, a tissue and an organism works. Trainees just getting into research can’t imagine how we ever learned anything without the ability to ask such comprehensive questions. They look at what we were able to do 20 years ago and say, “Surely you didn’t stop there!” Well, we had to. But now look where we are.

Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the chief science correspondent for the American Society for Biochemistry and Molecular Biology. Follow her on Twitter at twitter.com/rajmukhop.

PHOTO COURTESY OF NATIONAL INSTITUTES OF HEALTH
How did you become interested in working with RNA?

When I was a graduate student, I was working on designing small molecules that would recognize sequences and features of double-stranded DNA. Around that time, the discovery of ribozymes was made. I got really excited about the potential for elaborate structure in RNA. So I decided that if I was interested in molecular recognition by nucleic acids, I should probably work on RNA. That’s when I contacted Tom Cech about working in his lab. I’ve been working on RNA ever since.

What does your lab focus on?

About half of the lab works on large, highly structured RNA molecules. Some are catalytic, and some are epigenetic control elements. The other half of the lab works on a very specialized class of motor proteins that are RNA-stimulated ATPases. They are important for remodeling RNA and some of them function as RNA-activated signaling enzymes. They all belong to the same phylogenetically conserved family.

Although most of the lab does experimental work, we do have a big computational contingent. We do a lot of development of new programs for modeling, analyzing and predicting RNA structures. We’ve had to develop tools to enable us to better solve structures.

What triggered your interest in science in the first place?

I grew up surrounded by people who were interested in science in Albuquerque, N.M. We did a lot of playing around with rocks and minerals. We would go hiking. We also had elaborate chemistry sets, and we’d play with prisms. I was surrounded by a scientific mindset. To me, one of the things that is exciting about life is that physics and chemistry pervade everything.

But I didn’t commit to a scientific career early on. I went to a liberal arts institution – to Princeton (University). I studied a lot of different things, including public policy and Slavic languages. It wasn’t until very late in the game that I decided that I was going to get a Ph.D. in chemistry.

Were your parents scientists?

My dad was a cardiologist and a medical researcher. He also was involved in the space program and the military. But he was also a chemistry undergraduate, and he envied me going to graduate school instead of medical school! He got to enjoy it vicariously through me.

You mention your training in public policy and languages. Do you think that’s been important to you as a scientist?

It has. All of the education that
I was fortunate enough to receive help with my writing and communication skills. The fact that I was required to take a lot of history, language and literature has been a tremendous asset. I sometimes think that the time my favorite history professor, Dr. Arno Mayer, spent teaching me how to write a good paper was one of the most educationally important times in my life!

I suspected that one of the best ways to get involved in science policy was to become a strong scientist. That has turned out to be true. I decided that if I cared about science policy, I should get out there and understand how to do good science and make an impact scientifically.

**What do you think are some of the big challenges in your area of research?**

It's become clear that we transcribe many large, functional RNA molecules that do not encode proteins. But we know very little about what they are doing. We have few phenotypes and functional readouts of their biological roles. Beginning to get a good intellectual handle on what all of these different noncoding RNAs actually are doing mechanistically is a huge challenge. A parallel challenge is to organize and draw mechanistic conclusions from the wealth of bioinformatic data that is emerging on noncoding RNAs. Another challenge is how to organize the mechanistic and structural information that is accumulating about RNA and RNA-binding proteins and leverage (the information) for small-molecule inhibitor and activator design. It's a big frontier out there. A lot of these molecules are really interesting targets. It also would be great to bring together people who are trained classically in rigorous enzymology with projects that involve fascinating new enzyme families, such as those involved in epigenetic phenomena and signaling.

**What advice would you give young scientists wanting to be successful in research?**

The advice that I most frequently give is that you want to pick problems that you're really passionate about. It should make you happy to know that you're going into lab that day to work on that problem. That's a very personal thing. There's always a lot of pressure to work on what other people think is interesting. I think you have to reach inside yourself and determine what you find interesting. The rest really does follow if you're doing something that makes you happy and is really exciting to you.

But I can't underscore enough how personal that is. Students are constantly buffeted by trends. You really should decide what you personally find is interesting. In the beginning, other people may not see it the same way as you. But as my grad school advisor, Jackie Barton, used to tell me repeatedly, trust your own imagination to know why something is really significant and why you want to explore it.
How did you become interested in cell organization?

In 1996, I started my lab at the (Memorial) Sloan Kettering Cancer Center, just a few years after Alan Hall’s lab published seminal observations reporting that the Rho family GTPases control the actin cytoskeleton. I thought that would be a great thing to start my lab in.

But my interest has shifted over time from the signaling molecules to the actin cytoskeleton itself. We were studying a very important actin regulatory protein called WASP, the Wiskott-Aldrich syndrome protein. We hit on a molecular interaction that was very confusing. This was five years ago. The WASP protein has a large, disordered loop and a string of binding sites for what are called SH3 domains. It turned out that one of the important ligands of WASP is a multivalent protein, and somewhere around nine binding sites for the SH3 domains in the WASP protein. We pretty quickly realized that was going to be a biochemical mess.

A lot of the work that we do in the lab is with (nuclear magnetic resonance spectroscopy) and (X-ray) crystallography. You can’t deal very well with mixtures in NMR and definitely not with crystallography. It was a really confusing problem for us. But it was an important one, and we needed to figure out how to solve it.

I got very lucky. I had two terrific students, Pilong Li and Hui-Chun Cheng, who went away one summer to the quantitative biology course that’s taught at Los Alamos National Laboratory. They heard a seminar there where people were trying to use ideas from polymer chemistry to understand multivalent proteins and their multivalent ligands. It turns out it’s an old problem in the field of polymer chemistry that was solved in the early 1940s.

The polymer world has told us how molecules like these should behave, although the polymer scientists weren’t thinking about big proteins. They were thinking about making polyester for the war effort back in World War II. They figured out that polymers will phase separate. They will become like oil-and-water mixtures.

Sure enough, that is the way our system behaves. The WASP protein and its ligand, NCK, when mixed together in sufficient concentration, phase separate. You get these little droplets that float around in the aqueous solution. The connection that we made was that perhaps this could be a mechanism to organize the cytoplasm and the nucleoplasm of cells.

There are many different cellular compartments that are not bound by membranes. Most of the organelles people think about—the nucleus, mitochondria and lysosomes—are membrane-bound compartments. But there are also a whole bunch of much less well-understood compartments that are not bound by membranes. Maybe the mechanisms that we’re studying in vitro also can account for these cellular structures.

It’s interesting you’re borrowing ideas from chemistry. How does crossing two different areas influence your ideas?

I have a dual (undergraduate) degree from the University of Michigan. One’s in chemistry, and one’s in chemical engineering. It’s been a slide toward biology since then. Chemistry gives me a strong quantitative foot-
I want to understand biological processes in quantitative terms.

Kay and Tony Pawson. Lewis came from Ad Bax’s lab. (Authors’ note: Ad Bax is well-known for his development of NMR methods and their applications to biology.) Tony discovered the SH2 domain and recognized that it bound phosphotyrosine. I was lucky to do a joint postdoctoral appointment between those two labs who were already collaborating (at the University of) Toronto.

**What drew you into science?**

The way you phrase that implies that there was a time when I was not interested in science! I was the kid who, at the earliest age, memorized the names of dinosaurs. I was the kid who loved running around at the beach and looking for stuff in the sand. I remember wanting to be a mathematician and have always enjoyed math. That kind of morphed sometime in high school into science and engineering.

**Do you have any hobbies?**

I really love science. Much of the time, if you ask me, “Hey, Mike, what are you thinking about?” it’s something to do with science. I’m not entirely one-dimensional, though. My wife and I love to cook and eat. We also like to travel a fair bit. I didn’t know early on, but you get to travel as a scientist. There are very good professional reasons to be in different places of the world. While you’re there, you meet people, taste the food, do a little bit of sightseeing. It’s a really nice side benefit.

**How did the slide into biology happen?**

I did my Ph.D. with Stuart Schreiber. I joined Stuart’s lab the year that he moved from Yale (University) to Harvard (University). Stuart was a hardcore synthetic organic chemist at Yale but always had been interested in applying chemistry to biological problems. When he moved to Harvard, he allowed his interests to manifest in his research program. I was teamed up with a postdoctoral fellow from Martin Karplus’ lab to solve the structure of the FK506 binding protein as my thesis project. A lot of the lab was doing synthetic chemistry. I was the oddball doing structural biology using NMR, the same tool as the chemists but in a different way, applying it toward the structure of a protein.

I became interested, along with a lot of people in Stuart’s lab, in signal transduction at that point. It was the rise of the signaling era right as I was finishing my Ph.D. As a postdoc, I realized that I needed to strengthen my skills and knowledge in NMR spectroscopy, and I also needed to learn biology.

I did a joint postdoc with Lewis Kay and Tony Pawson. Lewis came from Ad Bax’s lab. (Authors’ note: Ad Bax is well-known for his development of NMR methods and their applications to biology.) Tony discovered the SH2 domain and recognized that it bound phosphotyrosine. I was lucky to do a joint postdoctoral appointment between those two labs who were already collaborating (at the University of) Toronto.

**What would you say are the big, challenging questions in cellular organization?**

I certainly think membrane-independent compartmentalization is a very interesting and very important idea. How do these structures form, and what do they do? How does the mitotic spindle get together? Or the microtubule-organizing center? Or clusters of membrane receptors? There’s got to be some way of organizing these things. Why should cells go to the trouble of creating any of these other structures? It’s not clear why concentrating molecules together like that should be useful to biology.

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I know your lab works on cellular metabolic homeostasis. Can you tell me in a little more detail about the ongoing projects?

The overarching question that my lab tries to address is how do cells adapt their metabolism to be optimally suited for the behaviors that they are engaged in. A complementary part of that is when cells are forced to change their metabolism through mutations or through a change in the environment, how does that cause them to change their behavior or fate? Those are the two interlinked questions on which my lab is focusing.

We have a couple of other projects that are focused around mitochondrial quality control. What happens when mitochondria become aberrant or damaged? How does a cell respond to that to repair the damage or adapt to it?

Another segment of the lab is working on kinase signaling. A specific kinase we’ve worked on for some time called PASK integrates metabolic information and signals to control the behavior of cells in different ways, including how cells use their available energy.

How did you develop an interest in metabolism?

It came pretty early on in my scientific career. I’ve become convinced that the metabolic situation of the cell is a really important environmental factor that, until recently, was largely overlooked as anything other than just providing ATP and enabling the cell to go about and do its job. I have become convinced that metabolism is much more active in determining what the cell does rather than just doing what it’s told.

Who drew you into science?

I have an uncle who is a prominent scientist. (Author’s note: Rutter’s uncle is William Rutter, formerly at the University of California, San Francisco, and now at Synergenics.) His influence encouraged me to think about science. I fell in love with it when I started taking the classes and doing a little bit of research as an undergraduate.

I went to (the University of Texas-Southwestern at Dallas) as a graduate student. I had a really great experience there. It encouraged me to pursue a research career in academia. I stayed and did a postdoc for about a year and a half. Then I took a job in Utah, and I’ve been here ever since. (Author’s note: After completing his Ph.D. with Steve McKnight at UT-Southwestern, the ASBMB’s current president, Rutter continued his training there through the Sara and Frank McKnight Fellowship.)

What are some of the big questions in your own field?

One of the biggest challenges in our field is the metabolic heterogeneity of cells. When we grind up a liver, for example, and measure some parameters, we make an implicit assumption that we’re measuring 10 million cells that are roughly the
same. In reality, the 10 million cells are different, and our measurements typically average over those 10 million cells. The result is we get a pretty low-resolution view of whatever parameter we're studying.

One of the areas that I think is very interesting is to study metabolism at a single-cell level and get at the metabolic heterogeneity of a population of cells, whether it's in a tissue, a tumor or a dish. These cells aren't acting in isolation but are actually communicating metabolically. For example, there are a number of situations where cell A will take in glucose and make lactate and cell B will take up the lactate and oxidize it to make CO2. There are several similar situations, and it is critical for us to understand them.

Are there any tools that let you piece this together at the single-cell level?

Not in a simple way. That's something that my lab is hoping to do in the future. There are tools for studying individual cells, but they rarely have been applied to the study of metabolism.

What are your hobbies?

I have four children. My wife and I spend most of our time managing them when I'm not in the lab! I like to play golf. Outside of my family and my work, that's probably the hobby that I enjoy the most. I try to do that whenever I can, especially when I travel. I plan to play golf in San Diego when I'm there for the ASBMB annual meeting! Also, I like to ski. I live in Utah, which is a great place for skiing and other outdoor activities like biking and hiking, which I also enjoy.

What words of advice would you give to scientists in training?

A phrase I heard recently was “the deletion test.” When we evaluate our contributions to science, we should think about the deletion test: If we weren't there, would the progress of the scientific community be any different? I think the best way to pass the deletion test is to be working in areas and using technologies that other people aren’t. That way, we're breaking new ground.
What are some of the current projects going on in your lab? What has you excited?

We have been studying the unfolded protein response for many years. I trained initially as a chemist, so we have a very strong mechanistic angle to understanding how the machinery of the cell works to identify the folding status, communicate it into constructive corrective measures and, if that doesn’t work, make a decision to kill the cell. We’re exploring whether we can modulate the basic cellular mechanisms to find some therapeutic window in which we may be able to do some good in disease. In this sense, we’re trying to build bridges between the basic science discoveries and clinical applications.

What are some the big challenges that you see in research?

To convince the public and the funding agencies that there is an incredible value in basic, curiosity-driven research where the applications aren’t apparent at the onset. It has been a major struggle with the (National Institutes of Health) — having to justify translational implications at the onset rather than letting scientists be explorers and recognizing the incredible value of accumulating knowledge for knowledge’s sake.

You are also the co-author of “Molecular Biology of the Cell.” How has the textbook influenced you?

As authors of this book, we read every chapter. We are all intimately involved with every part of it. (The book) has made me a much better scientist by expanding the scope of my knowledge base and staying at the forefront of what is exciting in numerous different fields.

What are the other fields outside of your expertise that you find exciting?

The technology that we have at our fingertips is just tremendous these days. For example, there’s the CRISPR technology. We can now do incredibly sophisticated genetic experiments and get deep insights into even the most complicated regulatory events. It’s a real revolution in having the tools to engineer mutations in mammalian cells. Basically, mammalian cells are now becoming as accessible as yeast used to be 30 years ago.

In the New York Times...
profile, it mentioned your parents owned a chemist’s shop in Berlin, Germany. What are some of your favorite memories of the shop?

It gave me the opportunity to appreciate the wonders of chemistry. I started as a young boy playing around with chemicals, very much in the pyrotechnical angle! It was incredibly inspiring to me—the conversion of matter and the nice sparks and explosions one can so easily create. (My experiments) became a little more sophisticated as I grew older and started studying chemistry. I found chemistry, personally, a little bit too constricting, and the questions in biology much bigger. I evolved into what I am today, an explorer of how cells are built and function.

Who has been important in shaping you as a scientist?

I had a fantastic chemistry teacher in high school. He was really inspiring and gave us a lot of leeway of playing in the back rooms. In fact, I had fantastic mentors all the way through my career. When I first came to this country, I spent a year in Nashville. My host was an organic chemistry professor, Tom Harris, and it was a wonderful time. Again, he gave us freedom to explore things of our own. And at Rockefeller, my Ph.D. adviser, Günter Blobel, was an incredible mentor and shaped my career in so many ways.

You straddle the worlds of chemistry and biology. Is there something to be said for being trained in one field and working in another?

I always felt that thinking chemically has been an advantage in my career. Proteins are not magic beings. They are complicated chemicals, and they obey the laws of thermodynamics. It puts a more reductionist angle on the questions we ask. I never feel that there are limits to our understanding. And I think that comes with our appreciation for chemistry.

What characteristics are in a good scientist?

Boundless curiosity. Not being discouraged by the many failures that come with scientific pursuit and all of the bureaucracy that nowadays comes with our jobs. A lot of tenacity for sticking with it.

For me, science really is an adventure. It’s not a 9-to-5 job. And it never will be. I tell my students that if they come to the lab and don’t have fun, they should reconsider their careers. They might as well go out and make money.

What are your interests outside of the lab?

I do a lot of art: sculpture, wood-working and welding. These days I don’t do experiments with my own hands, and just sitting all day in front of a computer is not as rewarding as it is to do things manually. I’ll get that kind of satisfaction from my basement projects. Currently, I’m building a fountain for the garden, which I’m welding from copper. It’s been going on for a long time.

Are there any words of advice you wish you were given when you were younger?

I’ve always been surrounded by spectacular mentors and worked in great communities and been given many words of advice. And many things you can only learn by first failing. Overall, I’ve no regrets. Many things happened that were unexpected, but I think if I had been more aware of how challenging it can be to carry on in this job, I might have just been discouraged. So, in a way, I got to live in my dreams.
What’s the cutting edge with STORM?

In terms of technology development, there are a number of things that are very important. One still is the spatial resolution. The first-generation work of STORM got resolution that’s 10 times better than the diffraction-limited resolution. That 10-times-better resolution allows you to see a lot more inside biological specimens than we could see before. But if you could get to approximately 1-nanometer resolution, then you (could) open up another new window. That’s not incremental. It would allow you to study a lot of important problems that we still cannot do with super-resolution imaging.

There’s also the dynamics side. There, two aspects are important: the time resolution and the amount of dynamic information. The simplest way to understand the second aspect is if you have (to think about) a movie. A continuous movie of 100 frames can give a very good idea of the real-time process. If you only get five frames, you get a very choppy movie. With super-resolution imaging, whichever method you use, the number of frames one can get often is limited.

I can tell you about some of our applications. One area is in neuroscience. We discovered a membrane skeleton structure in the neuron using STORM. It’s a beautiful structure in the axons. We saw these highly ordered periodic rings of actin that are connected by spectrin tetramers. This structure is important for the mechanical properties and functions of axons. And it anchors many important membrane molecules and enzymes, so there might be functions in addition to (the) mechanical functions. Mutations in some of its molecular components are found in diseases, so we’re also studying its disease relevance.

(Another area is) how DNA is structured in the nucleus. We know a huge amount of one-dimensional information of the DNA, such as the DNA sequence, the modification profile and the protein-binding profile of the chromatin. But there is accumulating evidence that the three-dimensional structure of chromatin and the dynamics (of the structure) are also very important for the regulation of gene expression, replication and other functions. We’re using STORM to learn what the 3-D structure of chromatin and chromosome is like.
What are you doing with transcriptome imaging?

The goal is to get the spatially resolved transcriptome of individual cells. For many different types of cells, RNAs are not uniformly distributed. The local distribution of transcripts is important for the building and maintenance of local structure. Different types of cells have different gene-expression profiles, and that is important for cell fates, behaviors and functions.

There are about 60,000 different coding and noncoding RNAs (in a human cell). For each RNA, I could have oligo probes, each attached to different colored fluorophores. If I were to have 60,000 colors and if I could distinguish 60,000 colors simultaneously, I would be able to do transcriptome imaging. Obviously that’s not possible.

The other extreme is to use one color but image one RNA species at a time by flowing in (complementary) oligos (one set at a time). I can do it 60,000 times, provided that I have enough students and postdocs with enough patience and the cell is not damaged during that process! That’s equally unfeasible.

I came up with an idea that doesn’t require 60,000 fluorophores and doesn’t require 60,000 rounds of imaging: Image a combination of RNAs in each round but different combinations in different rounds. For example, we can encode RNAs with a binary code. Each RNA is associated with a code of 11011 and so on. In the first round, we only image those RNAs whose binary codes read 1 in their first digit. Then we quench those fluorophores and image a second set of RNAs whose binary codes read 1 in their second digit. In order to distinguish 60,000 different binary codes, I only need 16 rounds of imaging, because two to the 16th power is greater than 60,000. It makes something almost impossible, all of a sudden, possible.

However, I must say that this is an overly simplified picture, because identification of each bit has an error; accumulating errors from 16 rounds of imaging is severe. We solved the problem by using encoding schemes that can detect and correct errors.

How did you become interested in microscopy?

My Ph.D. thesis was on nonlinear optics, which is a spectroscopy approach. It had nothing to do with biology, but it gave me a strong training in optics. My supervisor was one of the pioneers in nonlinear optics, Ron Shen (at University of California, Berkeley). I used it as a tool to study liquid crystals, polymers and so on.

My first microscopy experience was when I was a postdoc at Steven Chu’s lab at Stanford. (Author’s note: Chu is a former secretary of energy for the Obama administration.) My work was looking at how RNAs folded. It was purified RNA molecules scattered on coverslips, and I inferred the conformation of RNA using a spectroscopy approach called FRET. I began to image biological specimens and study biomolecules without taking them out of the cell when I started my independent faculty position at Harvard.

What sparked your interest in science?

Probably family influence, because both of my parents are professors at the University of Science and Technology in China. I’ve always wanted to be a professor – even before I knew exactly what a professor was! I never changed my mind.

I knew that I was probably good at physics when I was little, because my dad told me that I had very good physics intuition. I always liked physics. Even into college, I did not quite like biology and did not think it was as elegant (as physics). Now I really love biology. The fact that there are so many unknowns makes it an extremely fascinating area to study.

What advice would you give to graduate students?

Be fearless. Also, it’s important to be very strongly motivated and willing to spend a lot of effort. Try not to get tunnel vision, but be open-minded to broadly learning about all kinds of new scientific frontiers. Good surprises await if you have an open mind, are fearless and are persistent when you encounter difficulties.
The courage to find myself

By Suzanne Barbour

I’ve only recently developed a five-year career plan. It took nearly half a century of my life and two decades in academia, but I finally found my professional calling.

Like a lot of people, my first career goal was medicine, largely because I was interested in the life sciences and did not know what else a biologist could do. Two realizations changed my path. They both came during high school when I had the chance to be a candy striper at a local hospital. I learned two very important things. One was that it takes a very special kind of person to deliver health care to a patient in a compassionate manner. The other was that I am not that kind of person.

I was very fortunate to be recruited into a biochemistry research laboratory during my first undergraduate semester at Cook College (now the Rutgers School of Environmental and Biological Sciences). Through that experience, I got hooked on research, and I never looked back. There was never a question about whether I would go to graduate school, only which institution I would attend.

I only realized that education and research training would play important roles in my career when I was given responsibility for training an undergraduate student one summer during my Ph.D. training at Johns Hopkins University. Although the experience was not 100 percent successful (the student forgot to dilute TAE buffer and boiled an agarose gel), I realized how much satisfaction I derived from seeing the light turn on in a student’s eyes.

I spent the next two decades turning that light on through formal platform lectures; small group discussions and journal clubs; and, most importantly, one-on-one interactions in my research laboratory at the Virginia Commonwealth University. I supervised students on projects related to my major area of interest, phospholipases and phospholipid metabolism. Over the years, my science came to define me: When asked who I was, I typically answered with “research scientist” or “lipid biochemist.” I was also a member of nearly 100 graduate-student advisory committees and, eventually, a director of a graduate program in biochemistry.

Through those experiences, I learned that I had a knack for graduate education and a gift for connecting with students. I got a lot of satisfaction from watching more lights turn on in the eyes of my colleagues’ students.

I also began to realize that my individual research program was dying. I would never cure a metabolic disease and likely would not uncover a fundamental scientific principle that would lead someone else to a cure. These were sobering thoughts for someone who had defined herself as a research scientist for more than half of her adult life.

And then came another eye-opener of my career: I realized that I might not be the one who cured the disease or uncovered the principle but could be involved in training the person who did. After 20 years in academia, I finally realized that I wanted to be dean of a graduate school.

I had directed a graduate program, served on training-grant study sections at the National Institutes of Health and done strategic planning through my role as the director of research training in the VCU Center on Health Disparities. But I realized that I lacked the leadership and budgeting skills necessary to aspire to a deanship. This was the genesis of my five-year plan.

Becoming a program director at
the National Science Foundation offered the opportunity to broaden my knowledge of the biological sciences and, at the same time, develop the leadership, budgeting and other administrative skills that I needed to aspire to be dean of a graduate school. Although I knew this, I hesitated when I was offered the position at the NSF. It meant leaving my comfort zone, admitting that my research program was finished and redefining myself as something other than a research scientist. It meant checking my ego and finding the courage to look at myself in a different way. My 18-month stint at the NSF not only allowed me to develop the skills I needed but also to learn tough lessons about myself: I don’t handle change well and have a somewhat unproductive need to be in control.

My collective experiences will serve me well in my new position as the dean of the graduate school at the University of Georgia. Although I still miss working in the laboratory, I can keep up with my science through collaborations (we published a paper in the Journal of Biological Chemistry and submitted a grant proposal last spring), by attending seminars (I have a faculty appointment in the biochemistry and molecular biology department at UGA), and by serving on graduate advisory committees (my first UGA oral exam was in October).

At my core, I am still a lipid biochemist, a scientist and a researcher. But now I have added responsibilities that will permit me to watch the light come on in the eyes of students in music, history, forestry and other disciplines that are completely unrelated to mine.

Not bad for someone who took nearly five decades to develop a five-year plan.

Suzanne Barbour is at the University of Georgia as the dean of the graduate school. She can be reached at sbarbour@uga.edu.
Six things your mentor wants you to know (but probably won’t think to tell you)

By P. H. Grey

Most mentors do a solid job informing a new undergrad of the basic requirements of a research position. Typically, they cover the expected time commitment, lab safety procedures, lab dress code, and guidelines for writing a pre-proposal or end-of-semester report. When it comes to working at the bench, most mentors remember to share technical tricks with a new researcher and offer guidance on getting organized, programming equipment and finding research supplies.

But sometimes, because we have been in science for a long time or because we are distracted by our own research goals, we forget what it was like to be a new undergrad adjusting to a professional lab environment. We don’t remember the nervousness or anxiety that often accompanies the unknown. We don’t remember what it was like to try to understand and fit into the lab’s culture. We don’t remember how mysterious our research mentor first seemed or the uncertainty we felt when he appeared to change our experimental plans randomly from time to time. Consequently, it might not occur to us to address these things.

To help ease your transition into your new lab, here are six things that your research mentor probably wants you to know, even if she doesn’t think to tell you.

1. If I don’t hang out and chat at the lab, it doesn’t mean that I don’t like you. It probably means that I’m overextended or don’t have much spare time each day. I might be in the lab more hours per day than you are in an entire week, and I still might not have enough time to accomplish my goals. Alternatively, your lab schedule might overlap with my busiest time of the day, or I might need to leave lab at a specific time each day, leaving me no extra time to socialize. Therefore, I might focus on conversations that teach you how to interpret results or gain a new research skill, because I want our limited time together to make the greatest impact on your research experience. That might mean sticking to conversations about research and science.

2. Just as starting a new research position is tiring for you, working with a new undergrad is challenging for me. And sometimes I need a break just like you do. On occasion, I might send you home early, might not have something for you to do, or might not be immediately responsive to your email or text. It doesn’t mean I don’t like you (see No. 1), but I might need to restructure my time temporarily, or I might need a break from research-like things. Although it might be difficult to believe, I do try to have some type of life outside the lab. This means that I might need to put a new undergrad’s project on the back burner for a short time to make time for my other priorities.

3. I hope that you’ll be inspired by your research project, but if you’re uninterested or would rather be anywhere else than the lab, you’re not going to get much out of your research experience. If you don’t show up regularly or don’t work hard, I won’t go out of my way to tell the professor you’re underperforming, but I’ll be honest when she asks for my opinion. So if you’re not excited about the project or what I have to teach you, it would be better for you to make a professional exit and find a research project that inspires you. I’ll understand, because I know that my area of research isn’t right for everyone. However, if you show me that you value the time you spend in the lab, I’ll be happy to teach you everything you need to succeed — and you’ll earn an epic letter of recommendation.

4. If I say “thank you” more often than “good job,” it’s because I appreciate your efforts, but there isn’t much praise given in a professional research lab for meeting basic expectations. You’ll realize quickly that it wouldn’t mean much if I praised you for learning how to pipette or prepare a 5M sodium chloride solution. I’ll probably save the praise for things such as when you master a difficult technique, come up with a good trouble-
5. Sometimes I brag about how awesome you are to my colleagues. When I do, I probably just call you “my undergrad,” but if you’re working hard and investing in your research experience, I’ll be excited to share how much fun it is to mentor a student who is genuinely enthusiastic about science. And I’ll probably make my spouse listen a few times as well (sometimes until I’m asked to move on to another subject). It’s impossible not to be proud after you present your first poster or give a polished talk at a lab meeting. Watching your CV and self-confidence grow is one of the best parts of being a mentor. Bragging about it is pretty good too.

6. P. H. Grey (phgrey@ufl.edu) works as a molecular biologist and is co-creator of Undergrad in the Lab (undergradinthelab.com). She is co-author of the new book “Getting In: The Insider’s Guide to Finding the Perfect Undergraduate Research Experience.”
Molecular biology and biochemistry educators with a wide variety of viewpoints on best practices for undergraduate education, gathered for the American Society for Biochemistry and Molecular Biology-sponsored special symposium “Transforming undergraduate education in the molecular life sciences.”

The fourth in a biennial conference series that began in 2009, the July 30 to August 2 conference took place at Missouri Western State University in St. Joseph, Mo. Attendees included faculty representing a range of institutions, graduate students, postdocs, administrators and industry representatives.

Mary Huff, one of the conference organizers, said, “The participants were fully engaged, and that is what made this meeting a success! They created a pulse of excitement that reflected the passion we all share for undergraduate education.”

Action plans were a key element of the three-day conference. Group sessions provided time for participants to develop individualized teaching plans that incorporated strategies and activities from the meeting. Participants also were encouraged to expand their support networks by identifying others who could provide them with advice and expertise.

The conference opened with talks from Jennifer Fretland of Takeda Pharmaceutical Company Limited and Bruce Horazdvosky of the Mayo Clinic, who spoke about preparing students for careers in industry and the health professions and highlighted academic and soft skill sets students need for successful careers in the sciences. Cheryl Bailey, the dean of natural and health sciences at Mount Mary University and a former program director at the Howard Hughes Medical Institute, delivered a keynote on critical issues for preparing students for biomedical and STEM careers.

Methods to promote deeper learning were the focus of a talk by Ellis Bell of the University of San Diego, who described the latest results of the ASBMB’s National Science Foundation grant, in which workshops across the U.S. were used both to identify core biochemistry and molecular biology concepts and to develop assessment tools for undergraduate educators. Jenny Loertscher of Seattle University presented on how students’ understanding of threshold concepts can help prepare them for upper-level BMB content, and Martina Rosenberg of the University of New Mexico discussed how discipline-based educational research is helping to assess learning in BMB students.

A number of presenters discussed alternative teaching strategies for use in the classroom includ...
ing case studies (Annie Prud’homme-Genereux, Quest University); molecular visualization (Tim Herman and Margaret Franzen, Milwaukee School of Engineering); and quantitative biology methods (Johan Paulsson, Harvard University Medical School).

Several presenters focused on effectively integrating research into the curriculum. Todd Eckdahl of Missouri Western State University discussed the use of synthetic biology, Christopher Shaffer of Washington University in St. Louis talked about bioinformatics, and Joe Provost of the University of San Diego offered a presentation on research-based laboratory courses.

Regina Stevens-Truss of Kalamazoo College led a workshop on the ASBMB’s Hands-On Opportunities to Promote Engagement in Sciences, or HOPES program, which fosters outreach partnerships between BMB researchers and K–12 teachers in their local communities. And Angela Klaus of Seton Hall University focused on National Science Foundation funding opportunities for primarily undergraduate institutions, while Susan Renee of the University of Missouri focused on using broader impacts to transform undergraduate education.

Informal networking is a key element of the symposium series, and additional activities like an ASBMB Student Chapters luncheon helped facilitate more formal networking among faculty from the same regions of the country.

A memorable and unique interactive theater presentation from the Chapel Hill, N.C. group “Theater Delta” was a conference highlight. Performers took on ethical dilemmas facing undergraduate and graduate students and faculty research advisors including cheating, plagiarism and unauthorized collaboration. Following each scene, the audience got a chance to quiz the characters about their situations and motivations.

Post-conference surveys revealed 97.7 percent of attendees achieved their conference learning goals and would recommend this conference in the future. Participants were pleased to learn active strategies for the classroom and happy with the conference’s emphasis on open dialogue and action plans.

Conference organizers included Quinn Vega of Montclair State University, Mary Huff of Bellarmine University and Ben Caldwell of Missouri Western State University, who are all regional directors of the ASBMB Student Chapters program. The contributions of the entire ASBMB Student Chapters Steering Committee were essential to the planning and success of this meeting.
Drinks, chips and STEM
Rockville’s young adult science café is a win-win

By Tin Lok Wong

During the 2014 – 15 academic year, groups of middle school, high school and college students gathered after hours in a classroom at the Universities of Shady Grove in Rockville, Md., to munch on snacks and spend some time with local scientists. Participants in a series called the Young Adult Science Café, or YA, the group heard presentations and engaged in informal discussions meant to create dialogue, promote interest in and awareness about STEM, and provide opportunities for any would-be scientists in attendance to hear insiders’ takes on potential science careers.

A program of the Rockville Science Center that is organized by the American Society for Biochemistry and Molecular Biology student chapter of the Universities at Shady Grove, the YA series was initiated by ASBMB member Edward Eisenstein in 2012. We chapter organizers keep it going, motivated to create opportunities that we wish we would have had when we were in high school. Back then, we might have known we were interested in science but rarely had opportunities to interact with a scientist and never got the chance to explore and understand different career paths within STEM. We also understand that interacting with scientists can be very intimidating. We developed the program to be informal so that students comfortably can take advantage of the opportunity to meet scientists and satisfy their curiosity about STEM careers. Featured scientists make a special effort to be approachable. Some have debunked myths related to their specialties, and they often tell funny anecdotes and offer sneak peeks into potential breakthroughs in their fields.

Mitra Nusraty, an honorarium committee chair for YA, has seen scientist–student interactions go very well. “Sometimes, students hesitate to ask questions because they are shy. However, we the undergraduates know what questions to ask because we once had these questions within ourselves! It makes us extremely happy whenever we see students approach our speakers during the break session or after the talk. This means that we are creating opportunities — dialogues for these students that we wish we once had,” she says.

Now that the café has been running for a few years, it’s clear we are connecting supply and demand. We connect passionate scientists who are eager to educate with students who want to know what it takes to be a scientist. Attendees learn from speakers, organizers gain leadership experience and opportunities to network with scientists, and speakers are able to do public outreach and encourage the next generation of STEM professionals. As Nana Anguah-Dei, YA chapter vice president, says, “We are all learning!”

Through YA, we strive to provide clarification on the role of a scientist. In 2014 – 2015, students learned that scientists not only perform bench work in a laboratory but also work as grant writers or reviewers for organizations that allocate funding for various research projects, experts on the world stage who combine global efforts to prevent pandemics, or even educators who mentor and nurture generations of new scientists. In order for each student to understand these roles and find where she or he belongs in the future, we found the best way is to meet scientists doing those jobs.

Our location helps. We are fortunate to be in Rockville, Md., one of the world’s centers for scientific research and a town that is just down the road from the National Institutes of Health. Our February speaker, David J. Spiro, who is the influenza section chief at the NIH, remarked that Rockville is one of the most resource-filled cities in the United States for STEM careers. He felt that students interested in STEM fields should take more advantage of those resources. Michelle Aroyo–Perez, who is YA’s treasurer, says that’s part of our group’s mission. “We would like to ensure young scholars can have access to these valuable resources within the community so that the community can grow continuously as a whole.”

Six talks were held at the Universities at Shady Grove over the 2014 – 2015 academic year. Our final gathering took place off campus: a talk and tour of the hottest new labs at the Germantown Campus of Montgomery College co-hosted by James Sniezek, Montgomery College’s collegewide dean of chemical and biological sciences. We see a future opportunity to expand YA to all three of Montgomery College’s Maryland campuses.

The YA series starts up again in October.
Upcoming ASBMB events and deadlines

**OCT.**
- **Oct. 14:** Poster abstract deadline for ASBMB Special Symposium Kinases and Pseudokinases: Spines, Scaffolds and Molecular Switches, San Diego
- **Oct. 27:** Registration deadline for ASBMB Special Symposium Kinases and Pseudokinases: Spines, Scaffolds and Molecular Switches, San Diego
- **Oct. 24:** ASBMB workshop Developing and Sharing Best Practices: From Concept to Classroom, St. Mary’s, Minneapolis

**NOV.**
- **Nov. 5:** Abstract submission deadline for ASBMB 2016 Annual Meeting, San Diego
- **Nov. 12:** Travel award application deadline for the ASBMB 2016 Annual Meeting, San Diego
- **Nov. 11 – 14:** Annual Biomedical Research Conference for Minority Students (ABRCMS), Booth #900, Seattle
- **Nov. 21:** ASBMB workshop Developing and Sharing Best Practices: From Concept to Classroom, San Diego

**DEC.**
- **Dec. 1:** Deadline for 2017 Special Symposia proposals
- **Dec. 5 – 8:** ASBMB Special Symposium Kinases and Pseudokinases: Spines, Scaffolds and Molecular Switches, San Diego
Sample ASBMB Abstract Topic Category Titles (#2000-2697)

- Bioinorganic Catalysis
- Cell Signaling, Kinase and Chemotherapy
- Chemical Biology and Drug Discovery
- Chromatin Organization and Gene Regulation
- DNA Replication, Repair and Recombination
- Education and Professional Development
- Glycoscience in Biology
- Lipids and Lipid Signaling
- Metabolism, Disease and Drug Design
- Non-Alcoholic Fatty Liver Disease
- Post-translational Modifications
- Protein Synthesis and Degradation
- Recent Advances in Protein Engineering
- Systems Biology and Proteomics

Abstract submission deadline: Nov. 5

Travel award application deadline: Nov. 12

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