

# Biochemistry

UNIVERSITY OF WISCONSIN-MADISON

# 2012 NEWSLETTER

*For friends of the Department of Biochemistry at the University of Wisconsin–Madison*





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"Elmer" nestled amongst the Biochemistry buildings

Photo courtesy of Hedrich Blessing

## From the Chair

By Professor Betty Craig



It's been a while since last we wrote, but I think you'll find us worth the wait. Marv Wickens and colleagues have pieced together a mosaic here that I hope gives you a glimpse of the excitement and energy of the department's goings on.

Among my favorites are the increasing opportunities we've been able to offer our undergrads to experience the wider world. Our faculty has worked tirelessly to develop unique study abroad experiences that enhance our students' international perspective and understanding of science. Aseem Ansari's Khorana Program (page 20), James Ntambi's Uganda Program (page 22), and Marv Wickens' SCORE (England) Program (page 21) take students into labs and lives across the globe.

We've also established a summer research program for undergrads in our labs here at home. The program provides students both the opportunity to experience full-time research and the financial assistance necessary to do so, making the important research experience accessible to all. Our two newest scholarships are supported by

the "Henry A. Lardy Undergraduate Research Fund" and the "Karen M. Telander Undergraduate Research Fund." Henry Lardy, as you all know, was a giant of our department. He passed away in 2010 – you may recall a tribute to his enduring example in that year's newsletter. Karen Telander was an undergrad at UW-Madison who went on to pursue a career in research, research ethics, and undergraduate education. She passed away in 2009 – her husband initiated a scholarship in her honor to support women and minority undergrads in chemistry and biochemistry.

I'm pleased to report that as we go to press in spring 2013, the building and renovation so omnipresent in recent newsletters is done. Almost. The new research tower (also known as the "Biochemical Sciences Building") was occupied in January of 2012. The final step, complete renovation of floors 4 – 6 of the "85 wing," will be completed in July of this year. See page 9 for a more complete description of the tripartite complex as documented by Mike Cox, the "architect in charge" of this massive project.

Sadly, we share a long "in memoriam" section to offer tribute to colleagues we have lost since you received our last newsletter – Paul Kaesberg, Chris Raetz, Har Gobind Khorana, and Masayasu Nomura. Mo Cleland, too, died tragically on March 6th this year following a fall on ice.

As his passing occurred so close to our print deadline, you will find only a short mention in the pages that follow. Our next newsletter will provide a full memorial. A symposium in honor and celebration of his lasting contributions to mechanistic enzymology is planned for May 22-24, 2014 here in Madison. We hope to see many of you there. Check our website for updates and an opportunity to contribute to his legacy (<http://www.biochem.wisc.edu/news/default.aspx?id=252>)

In the past few years, we've had three retirements from and two additions to our faculty. I'm pleased to say that while George Reed, Dave Nelson, and Hector DeLuca have all retired, we are lucky to continue to see them frequently around the department, and Hector's lab is still going strong (page 16). We're also pleased to have welcomed Aaron Hoskins and Jill Willdonger to the department in 2011. Both came to us with prestigious NIH Pathway to Independence Awards that have helped them hit the ground running. They introduce themselves and their roads to Madison on pages 10 – 12.

I hope you enjoy what you read and see in this issue – the new, more colorful look of our newsletter. May it bring back pleasant memories of your time in Madison in general, and the department in particular.

Remember, we are always happy to hear from you, and visit us when you can.

E-mail: [alumninews@biochem.wisc.edu](mailto:alumninews@biochem.wisc.edu)  
Regular mail in care of the department  
– see page 66 for address information

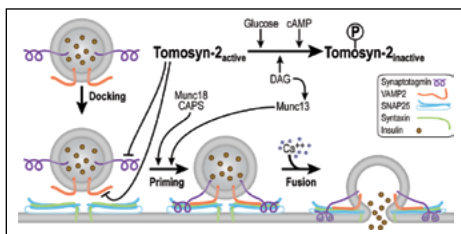
NEW: Like the Department on Facebook  
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## New Discoveries

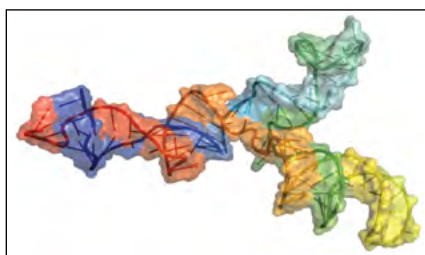
*A sampling of the Department's pioneering research in areas ranging from metabolism to gene regulation to enzymology.....*

**A new regulator of insulin.** The **Attie** lab positionally cloned a gene for Type 2 diabetes, Stxbp5L, which encodes an inhibitor of insulin secretion called tomosyn-2. The work shows that beta-cells produce an inhibitor of insulin secretion and so have to inactivate this inhibitor to secrete insulin.



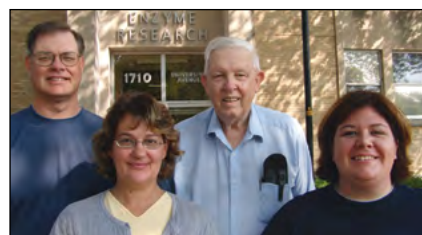
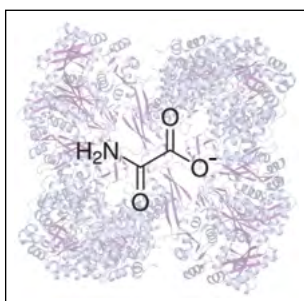
Sushant Bhatnagar & Alan Attie

**Structures of splicing complexes.** **Butcher's** group determined the structures of U6 spliceosomal RNA in complex with its protein and RNA binding partners using NMR, x-ray crystallography and small angle x-ray scattering. These structures reveal how the essential Prp24 protein interacts with U6 RNA to mediate the structural rearrangements required for spliceosome assembly. Additionally, we determined the structure of the U2/U6 RNA complex, providing the first view of this important component of the spliceosomal catalytic core.



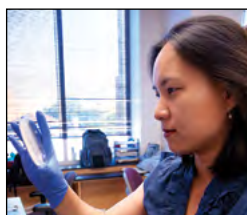
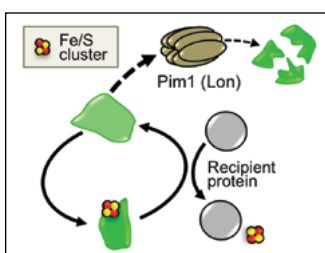
Jordan Burke & Sam Butcher

**New Activity of Pyruvate Carboxylase.** The **Cleland** lab discovered that oxamate, an analog of pyruvate, is a substrate for pyruvate carboxylase, being converted to a carbamate analog of oxaloacetate. The carbamate is very acid-labile, which is why it was not discovered earlier. The study made use of C-13 NMR to detect the carbamate.



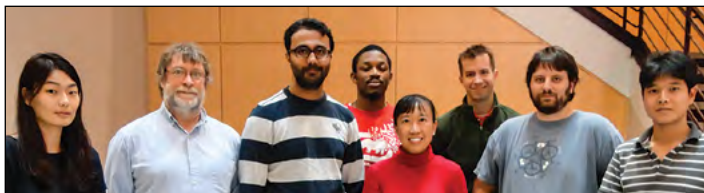
Mark Anderson, Laurie Reinhardt,  
Mo Cleland & Tonya Zeczycki

**Controlling Fe-S cluster biogenesis.** A post-translational mechanism regulating the cellular level of the scaffold protein on which Fe-S clusters are built was uncovered in the **Craig** lab. Degradation by the mitochondrial Lon protease modulates the scaffold's stability over a 10-fold range, allowing cells to rapidly adapt their Fe-S cluster assembly and repair capacity to changing environmental conditions.



Ji-Yoon Song & Betty Craig

**Natural symbiosis in carbon cycling.** The **Fox** and Currie labs showed that pine-boring woodwasps inoculate the trees with a bacterium that enhances the destructive nature of the insect attack, thus providing a new example of symbiotic contributions to carbon cycling in terrestrial ecosystems. The potent mixture of enzymes secreted by the bacterium also gives insight into new approaches for enzymatic deconstruction of cellulosic biomass for industrial purposes such as biofuels production.



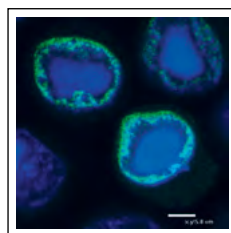
Amy Lim, Brian Fox, Shishir Chundawat, Johnnie Walker, Lai Bergeman, Kirk Vander Meulen, Chris Bianchetti & Taichi Takasuka



**A new viral strategy.** Baculoviruses use a novel mechanism to modulate the host DNA damage response during infection, as shown in the **Friesen** group. While baculoviruses need the host's DNA damage response machinery for their own viral DNA replication, they also encode a novel protein to modify the response to transform it from an antiviral pathway to one that expedites DNA virus multiplication.



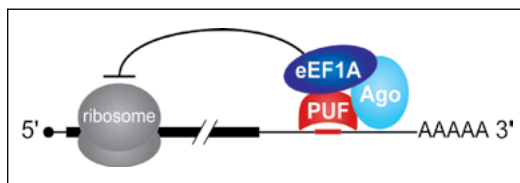
Paul Friesen, Jonathan Mitchell & Nathaniel Byers



**New mechanism of translational control.** A new mechanism for translational control, conserved from nematodes to humans, has been uncovered in the **Kimble** lab. This mechanism brings together a core component of the translational elongation machinery with an Argonaute protein and a PUF RNA-binding protein to arrest ribosomes on selected mRNAs near the site where the nascent polypeptide chain emerges from the ribosomal exit tunnel.



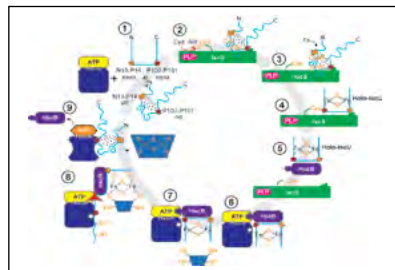
Kyle Friend & Judith Kimble



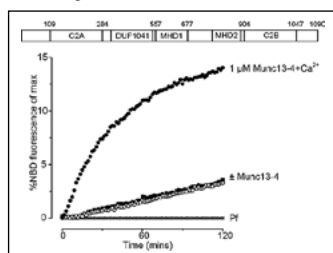
**Protein dynamics and Fe-S clusters.** Iron-sulfur clusters are ubiquitous and their mis-assembly can cause disease. The **Markley** group discovered that the scaffold protein for iron-sulfur cluster assembly and delivery (IscU) is metamorphic. This ancient and highly-conserved protein populates two conformations: one is more structured, and the other, more dynamic (D). The two states differ by the configurations of two peptidyl-prolyl peptide bonds. Both forms of the protein are physiologically important, performing different roles in the cycle of iron-sulfur cluster assembly and delivery.



Jin Hae Kim, John Markley & Ziqi Dai

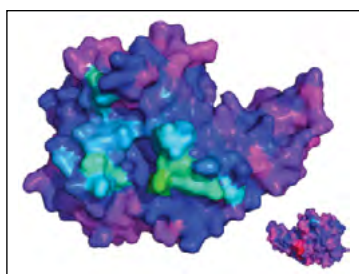


**Proteins that drive membrane fusion.** Vesicle-plasma membrane fusion is responsible for the secretion of inflammatory mediators from mast cells. The **Martin** group found that Munc13-4, which plays a key role in mast cell degranulation, is able to stimulate liposome fusion in a  $\text{Ca}^{2+}$ - and SNARE-dependent manner. This work reveals general principles by which priming/tethering factors operate to drive membrane fusion, and will contribute to understanding genetic diseases involving Munc13-4 mutations.



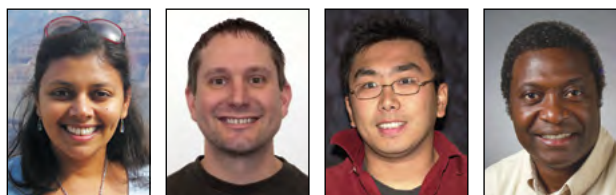
Declan James, Joe Esquibel & Tom Martin  
Not pictured Kristin Boswell & Steve Bruinsma

**Perfecting computational predictions.** Computational prediction of binding mutagenesis effects is a major challenge. The **Mitchell** lab developed models that accurately identify mutations that disrupt protein-protein binding and allosteric communication. In three CAPRI international blind prediction experiments, the lab returned top results in predicting the effects of 19 substitutions/residue on protein-protein binding; in identifying *de novo* designed interfaces that form stable complexes; and in docking heparin to a hypothetical protein of uncharacterized function.



Steve Darnell, Spencer Ericksen & Omar Demerdash  
Not pictured Xiaolei Zhu & Julie Mitchell

**Surprises in your skin.** The **Ntambi** group has discovered an entirely unexpected role for skin monounsaturated fatty acids in the regulation of energy expenditure and the development of obesity. They have found that Stearoyl-CoA desaturase-1 is a key enzyme in the skin, and its expression controls energy expenditure, hyperphagia and protection against high fat induced obesity and insulin resistance.



Harini Sampath, Matt Flowers, Makoto Miyazaki & James Ntambi

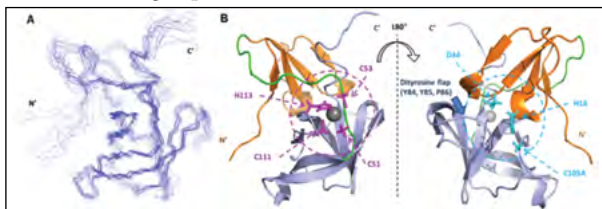
**Controlling mitochondria.** Mitochondria are centers of metabolism and signaling whose content and function must adapt to changing cellular environments. By combining genomics and proteomics technologies with classic biochemistry and cell biology approaches, the **Pagliarini** group has shown that cells use a variety of post-transcriptional and post-translational regulatory mechanisms to adapt to acute and chronic physiological stresses, including fasting, obesity and iron deprivation.



Jarred Rensvold, Joshua Carson, Paul Grimsrud, & Dave Pagliarini



**Relatives of the common cold virus.** More than 150 “types” of human rhinoviruses have been isolated. The fundamental question of why not all of them cause the same disease, i.e. the common cold, has now been answered in the **Palmenberg** lab. A protease called “2A” encoded within each genome shows extensive sequence diversity and consequent mechanistic selectivity for cellular substrates to account for differential pathogenic responses when these viruses infect. Three species of rhinoviruses actually recombine among each other to swap this genome segment providing almost unlimited variation in disease-causing capacity.

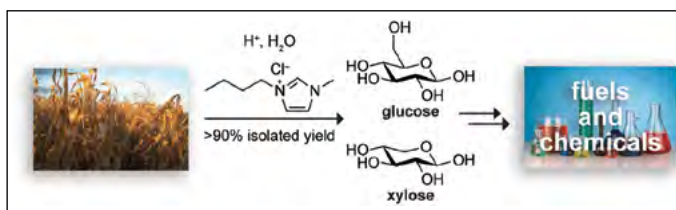


Woonghee Lee & Ann Palmenberg

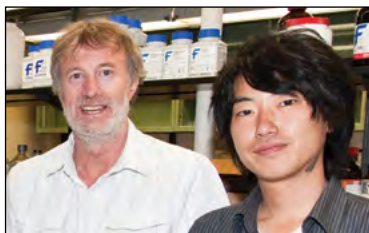
**From crude biomass to sugars.** The **Raines** group has shown that an ionic liquid containing water and catalytic acid can be used to capture nearly all of the latent sugar within any crude biomass. The recovered sugar supports the vigorous growth of bacteria and yeast. This simple process is the basis for an award-winning start-up company: Hyrax Energy, Inc.



Ron Raines & Joe Binder



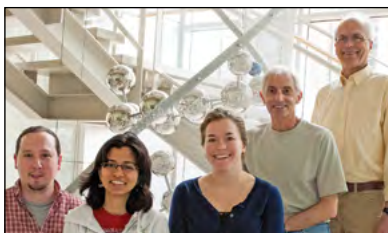
**A new natural plant homopolymer.** Yuki Tobimatsu in the **Ralph** lab, working with collaborators at the Noble Foundation (Ardmore, OK), discovered a ‘new’ natural polymer derived from chemical radical coupling of caffeoyl alcohol, the ‘missing monolignol.’ Vanilla bean seed coats are composed of 80% of this new lignin polymer and 20% polysaccharides. (PNAS cover article, and Science highlight)



John Ralph & Yuki Tobimatsu

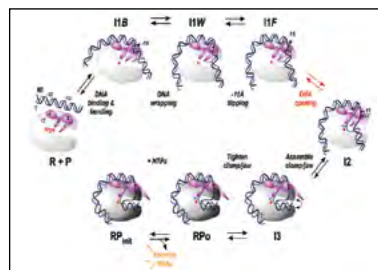


**Dissecting Transcription Initiation.** The steps and intermediates in transcription initiation by *E. coli* RNAP have been analyzed in the **Record** lab. After initial sequence-specific binding, a series of large-scale conformational changes bends the start site region of the promoter into the enzyme’s active site cleft. Then, base flipping nucleates opening 13 bp in the cleft. This initial unstable open complex is stabilized by rearrangement of the non-template strand and step-wise assembly of mobile elements of RNAP on the “downstream” duplex, increasing its lifetime by a factor of  $10^5$ . We now can determine how initiation is controlled by promoter sequence, protein factors, and solution variables.

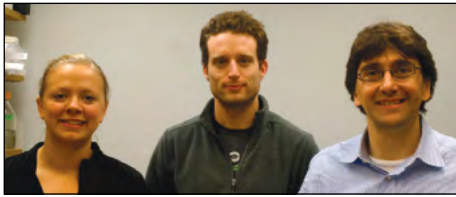


Jan Murray, Raashi Sreenivasan, Emily Ruff, Mike Capp & Tom Record.

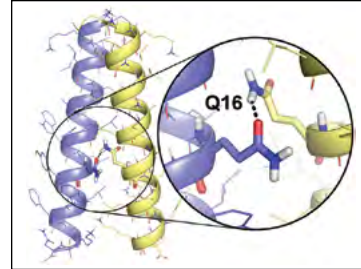
Recent alum researchers in my lab responsible for many of our recent discoveries include Amanda Drennan, Sara Heitkamp, Ruth Saecker, Ted Gries, Wayne Kontur & Carrie Davis.



***The first structural analysis of a membrane protein in the bacterial division complex.*** A sophisticated protein machine -- the divisome -- ensures that bacterial cells divide at the right time and place. The **Senes** group determined the structural organization of FtsB, an essential protein in that complex, using biophysical and computational methods and X-ray crystallography collaboration with Keenan Taylor and Ivan Rayment). Their work defines the structure of its membrane and periplasmic domains, and reveals that FtsB self-associates. Association with another protein (FtsL) appears to stabilize the periplasmic domain of FtsB, which in turn is critical for recruitment of other proteins to the division complex.



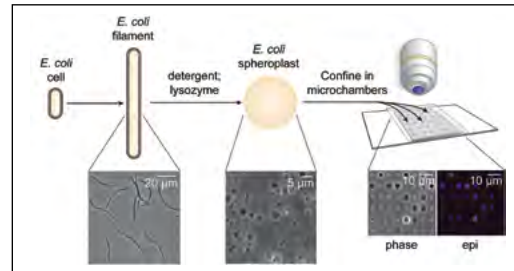
Loren LaPointe, Keenan Taylor (Rayment lab) and Alessandro Senes



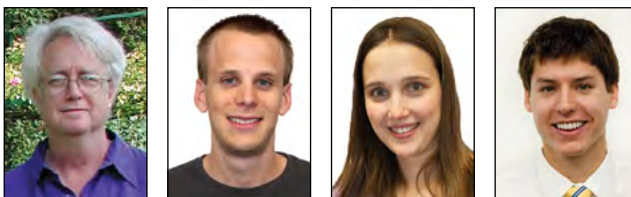
***Discovering the basis of membrane asymmetries.*** The **Weibel** group has shown that strain on membranes alters the local composition of intrinsically curved, anionic phospholipids. It thereby influences the positioning and function of amphipathic proteins in bacteria.



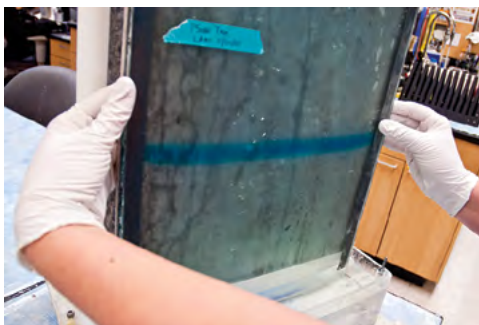
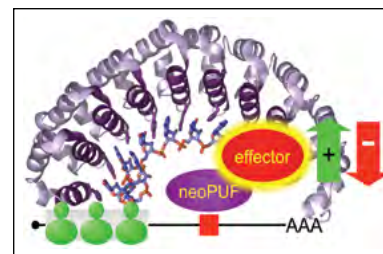
Lars Renner & Doug Weibel



***mRNA regulation by design.*** The **Wickens** lab has used the scaffold of the PUF protein family to create proteins with new specificities. The lab's new selection and deep sequencing methods, termed SEQRS, enable the global specificities of these proteins to be determined. Designed "neo-PUF" can turn up or down the expression of specific mRNAs in early development.



Marv Wickens, Zak Campbell, Amy Cooke & Andrew Prigge





# The New Tripartite Biochemistry Complex

*A major new building and imaginative renovation provide striking and flexible space.*

By Professor Mike Cox



Those of you who have not visited the department in a few years are in for a surprise – a major expansion and redesign of our buildings. The new “Biochemistry Complex” consists of three buildings linked by walkways (see the drawing lower right), and is nearly complete and occupied. The 1912 and 1937 wings remain but have been highly renovated for teaching, while an entirely new building has been constructed that is dedicated to research. The third building is the “Biochemistry Addition,” which has been around since 1998, and houses most of our faculty.

Let me walk you through what we have done:

## *The new old “Biochemistry Building”*

From the outside, the façades of the 1912 and 1937 buildings on Henry Mall and University Avenue are the same. The new, large building – called the “Biochemistry Building” – has our old 420 Henry Mall address. Inside, the building has been completely renovated and redesigned for teaching functions. But there’s much more here than a few new classrooms and teaching labs – though those are present, and radically and beautifully improved. We have added many new functions: a highly computerized classroom to instruct students in the use of modern databases and bioinformatics; a new undergraduate lounge, providing a space for students to wait for classes and study; numerous new meeting rooms; entirely new spaces dedicated to computation.

The infamous congestion outside the hallway of our old Room 125, before and after class, is a thing of the past! The Curry Murals, which I am sure many of you remember, were carefully protected during construction, and professionally cleaned and restored afterwards.

*Right:*

Aerial view of the Biochemistry complex.

Photo by Joe Oliva.



View from Henry Mall  
clockwise from left 1912 and 1937 buildings, 1998 addition (center), 2012 BSB,  
1906 former Ag Journalism building.  
Photo courtesy FLAD Architects.

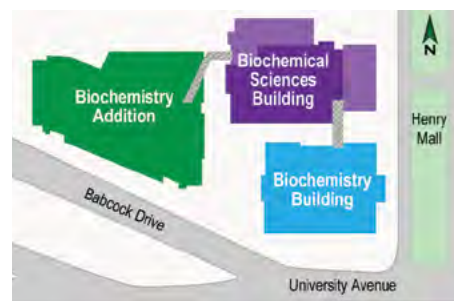
## *The new research tower and “Biochemical Sciences Building”*

An entirely new building dedicated to research has replaced the 1956 wing. This new structure (plus the 1906 Ag Journalism building and the 1985 Biochemistry tower) are all interconnected and constitute the Biochemical Sciences Building. The new labs house the Biomolecular Chemistry department on floors 4-5-6, and Biochemistry faculty on floors 2 and 3. The 1906 part of the building houses some new computational spaces, a faculty meeting room, office suites, and a coffeehouse! The Biochemical Sciences building is connected to the other two by enclosed skybridges.

## *The 1998 Biochemistry Addition*

The third building in the complex is the 1998 Biochemistry Addition, and is now surprisingly the oldest part of the complex! It currently houses and supports the work of 21 Biochemistry faculty and 3 Emeritus Biochemistry faculty.

It is an impressive complex, integrating research with teaching, and providing a flexible and diverse collection of wonderful spaces. And it awaits your visit!





## New Faculty Profiles

*Our two newest faculty, Jill Wildonger and Aaron Hoskins, recount their scientific histories and how they came to join us.*

### Professor Jill Wildonger



Cells are not circles. We may often see them drawn that way, but their shapes and structures are incredibly diverse. Nowhere is the pairing and

complexity of form and function more on display than in the nervous system. Neurons are frequently described as tree-like, having a single axonal “trunk” and an “arbor” of dendritic branches. Extending this analogy, we can think of our brains as small “forests” of neurons, which pass messages to each other via these trunks and branches. I want to know how cells generate these very different shapes, and tailor them for specialized functions – a molecular understanding of how cell shape and activity arise, and are linked to one another.

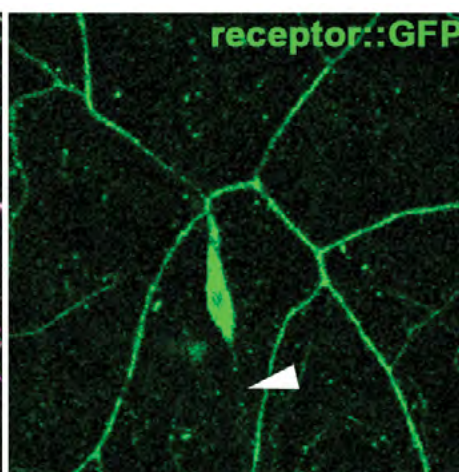
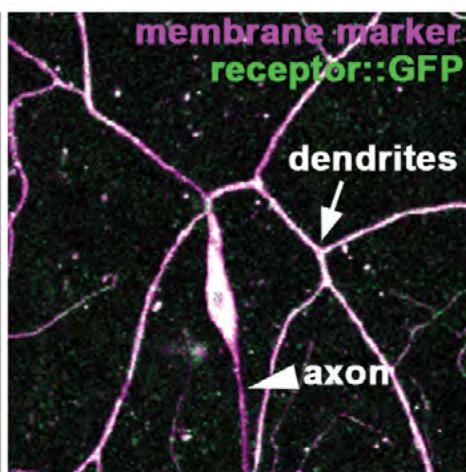
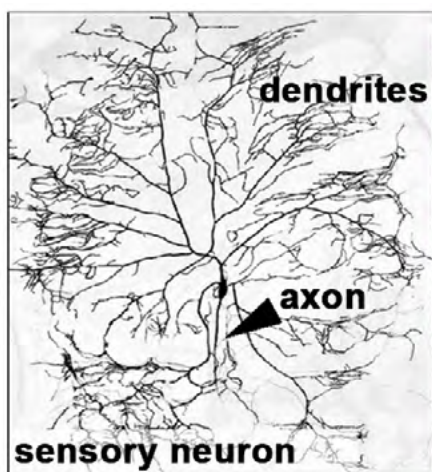
Everyone remembers the first time they fell in love. I was a college sophomore, and the lightning bolt struck while I looked down the eyepiece of a microscope. I had seen drawings and photos of cells, but seeing the neurons of a developing chick retina cultured in a dish was something else. I was mesmerized. The delicate axonal processes grew out

from the retinal explant in all directions, making it look like a many-rayed star. How did these neurons “know” when to sprout an axon, how did the axons grow, and what molecules made it all happen? My undergraduate research experiences were varied, and took me from zucchini to chickens and bullfrogs, using methods from biochemistry, cell biology and electrophysiology. But as I edged toward graduation, I found myself reading more and more papers on neuronal development and nervous system assembly – the beginning of a girl-meets-brain love story.

When I started the graduate program in Neurobiology and Behavior at Columbia University, I felt certain that I would study neuro-development. Yet I was drawn to join a lab in the Department of Biochemistry and Molecular Biophysics headed by Dr. Richard Mann, whose main research interests include Hox protein function and patterning, using fruit flies as a model system. “Do fruit flies even have a brain?” one of my classmates teased. Yet in the next few years, I studied how development of the nervous system is shaped by neuronal specification and programmed cell death, blending genetics, molecular biology, microscopy and biochemistry. We frequently collaborated with other labs,

and those interactions opened my eyes to how research blossoms when people with different expertise join forces. This early experience of reaching out to other groups to learn new techniques continues to inspire me to connect with other groups and work collaboratively.

Even the simplest nervous system is comprised of hundreds of neurons: a nematode worm no larger than a comma on this page has approximately 300 neurons, fruit flies have 100,000, and human beings have a staggering 85 billion nerve cells that form over a trillion synaptic connections. Yet virtually all nerve cells, from worms to flies to humans, share basic structural features: neurons have dendrites that receive signals and axons that transmit them. Defects in axon and/or dendrite morphogenesis underlie many human diseases; nonetheless, I was surprised to find that still very little is known about the molecular mechanisms responsible. So I headed off to San Francisco to join the lab of Dr. Yuh Nung Jan, whose group had recently developed genetic tools to illuminate individual neurons in live intact animals, opening up new approaches to investigate neuronal morphogenesis. A forward genetic screen utilizing these tools uncovered a critical role for the molecular



The cellular complexity of sensory neurons illuminated in a live, developing fruit fly (photo far left). We can track how ion channels are transported within neurons by adding fluorescent tags (see photos on the right). This particular ion channel belongs to a superfamily whose members are activated in response to salt as well as mechanical stimulation and pain.



motor dynein in polarized dendritic transport and maintaining axonal identity. While dynein has a well-known role in “walking” along the microtubule cytoskeleton in cells, our research revealed an unexpected role for dynein in organizing microtubules within axons. These studies sparked my continuing interest in how molecular motor proteins work in concert with microtubules to build neuronal structure and function.

Since one of my favorite aspects of being a researcher is interacting with other people who are passionate about science, I’m thrilled to be a part of the scientific community at Madison. I’m also inspired (and frequently awed) to be the colleague of researchers who have made and continue to make important

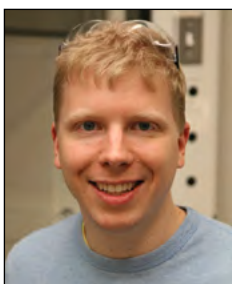
contributions to a range of scientific fields. From the very first, members of biochemistry, neuroscience, fruit fly, and developmental biology groups on campus have given my lab a warm welcome, including us in group meetings and suggesting collaborative projects. Looking back over the past year since the lab started, it’s exciting to see how we’ve grown as a lab, and how projects that were simply ideas on paper last January have come to life (in some cases, quite literally, since we’ve been generating transgenic fruit fly strains). Our very talented and enthusiastic lab manager was joined this fall by several undergraduate students, and we are currently tackling projects ranging from the live imaging of motor protein dynamics and ion channel

localization in neurons *in vivo* to isolating motor proteins for *in vitro* biochemical assays to developing new genome engineering techniques; the latter project I am happy to say is in collaboration with the Cox, O’Connor-Giles and Harrison labs. We are actively recruiting graduate students, and look forward to welcoming a post-doctoral fellow in the spring.

A friend from graduate school recently asked me whether I was happy in my new position, and jokingly asked, “Do you skip, dance and sing to lab every day?” I said I usually bike, although there was a pretty big grin on my face. It’s been an amazing year, and I am very excited about what the next ones will bring.

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## Professor Aaron Hoskins



Since starting my laboratory at UW in August 2011, one of the highlights has been how much I enjoy talking about biochemistry with the UW

undergraduates. They nearly always ask me some variation of “Why did you decide to become a biochemist?” It is slightly bewildering to be on the other side of that question. It seems like I was an undergraduate at another Big Ten school pondering my future just a few years ago! Looking back, I became a biochemist because I like to “make stuff” and “measure stuff”. For me, the exhilaration of scientific discovery stems from tackling biological problems with chemical or physical tools that I have created. This synthesis of the physical sciences (chemistry and physics) with biology constitutes the heart of my current research program.

Throwing everything but the kitchen sink (and sometimes that too) at complex cellular processes is an approach that was honed during my graduate work with JoAnne Stubbe at MIT. Often the experiments in JoAnne’s lab required

synthesizing novel molecules, designing complex kinetic experiments, or developing new spectroscopic techniques if current methods or molecules were insufficient. Learning how to step outside my comfort zone and focus on the experiments that will answer questions, not just experiments that my labmates or I knew how to do, has had a lasting impact on my career. Key to this was a thorough and broad training in biochemistry that has since proven invaluable.

After my PhD work, I decided to visit the RNA World. Melissa Moore and Jeff Gelles (UMass Medical School and Brandeis U., respectively) proposed that I use single molecule fluorescence methods to study the spliceosome: a eukaryotic enzyme composed of 5 RNAs and about 100 proteins. The spliceosome removes introns from precursor mRNAs, and this process is a fundamental mechanism for encoding genetic complexity in higher organisms. After a few months in the Moore Lab, I drank the “RNA Kool-Aid” and I’ve been hooked ever since!

When I began my postdoc, single molecule experiments were just becoming mainstream. However, the vast majority of those experiments were carried out on a single strand of RNA or with

highly processive, purified enzymes. The spliceosome, on the other hand, could not be purified, is composed of dozens of components, and is a single turnover enzyme. The key to single spliceosome experiments turned out to be the combination of yeast genetics, chemical tools, and a fluorescence technique called CoSMoS (Colocalization Single Molecule Spectroscopy). Together, this combination allowed me to probe reaction reversibility, kinetics, ordering, and even conformational changes that were occurring during the splicing reaction. Single molecule biochemistry greatly appeals to the “making stuff” and “measuring stuff” aspects of my personality. The microscopes my laboratory uses are built in the lab and are controlled using custom software. This means the microscope looks more like something put together with parts from Radio Shack than anything you might purchase from Olympus. While this equipment can be used for a wide-range of biochemical experiments, often the limiting factor is developing a system suitable for single molecule imaging. This is where a deep-appreciation of chemistry and biochemical “know how” is enabling my laboratory to conduct

unique experiments. Combining traditional biochemical assays, cutting edge chemical biology tools, and single molecule measurement is an extremely powerful approach for studying molecular machines. I often describe my research as making radioactive molecules and then hitting them with lasers.

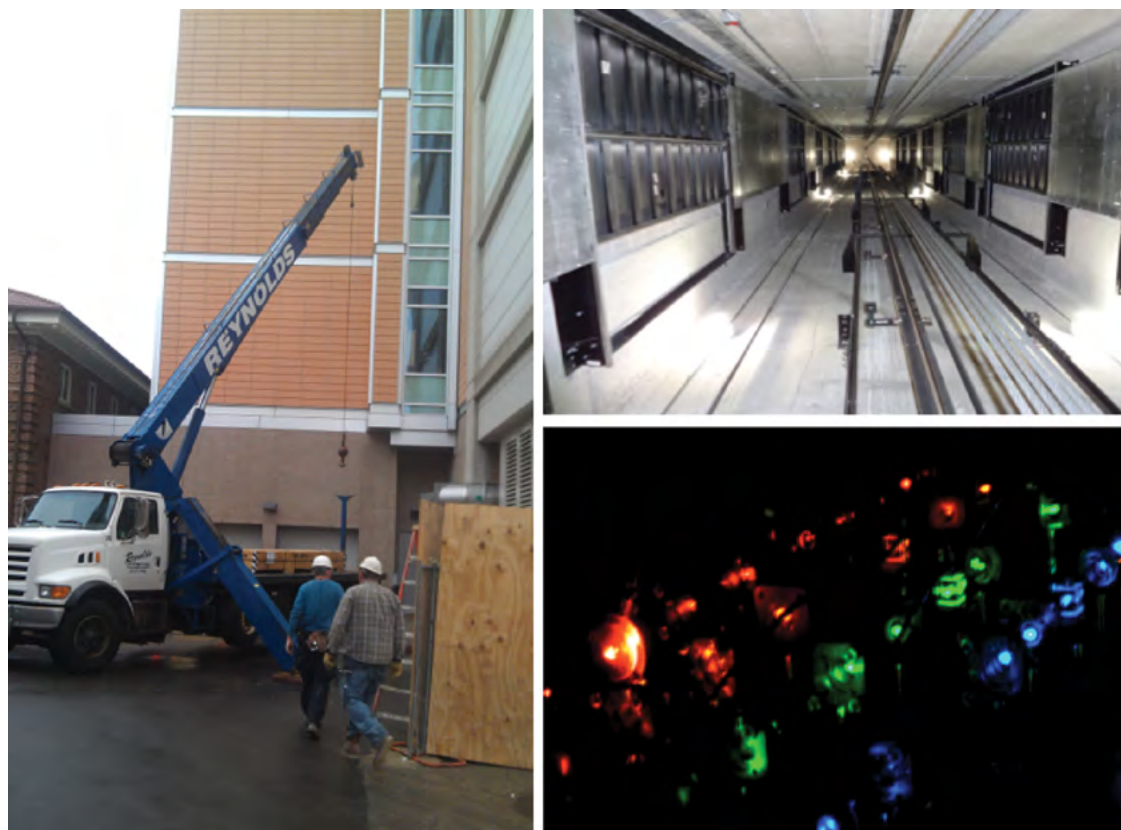
At UW, I'm continuing to use single molecule methods to study various aspects of RNA processing. My laboratory is focused on the initial stages of spliceosome assembly and activation when the splice sites (locations of bond cleavage and formation in the pre-mRNA) are recognized by various spliceosome components. How these sites are correctly identified is a fundamental question in gene expression since aberrant splicing by even a single nucleotide can alter the reading frame of the mRNA. In collaboration with Sam Butcher and David Brow, we have also begun to look at spliceosome recycling and biogenesis. While many mutations in the core splicing

machinery are lethal, defects that disrupt the recycling or biogenesis pathways can lead to serious, incapacitating diseases including retinitis pigmentosa or muscular atrophies. Finally, if there is one thing that I have learned during my career, it is that making fluorescent molecules is hard! We are devoting significant effort towards developing new, enabling methodologies for attaching fluorophores to RNAs or RNPs *in vitro* and *in vivo*.

Over the past year, I have recruited a wonderful trio of graduate students as well as four undergraduates, and the laboratory has started to take off! In January 2012, we moved into our new laboratories in the Biochemical Sciences Building (I think we were the first lab to move in) and in March, we began constructing our microscopes in remodeled space in the basement of the 1985 building. One particularly memorable event was figuring out how to maneuver a 12-inch thick, 4' x 12' optical table weighing 2000 lbs down the elevator shaft into

my laboratory. This involved an exciting ride on the *top* of the freight elevator in the new Biochemical Sciences Building, and this was by far the closest I've ever felt to being John McClane in "Die Hard"!

Working at UW in the Department of Biochemistry has been an absolutely wonderful experience. The scientific culture and heritage of the department and campus is astounding and for someone who works on RNA, I am humbled every time I step into the Khorana Auditorium. I am particularly enjoying interactions with new colleagues across campus in genetics, physics, chemistry, virology, or other departments. The breadth of science at UW is staggering and has already opened my eyes to new directions for my research. Looking down the road into my future, I suspect that I will always be "making and measuring stuff" but given the pace of scientific discovery at UW, I am even more excited to learn what that "stuff" may be.



Clockwise from left:

(1) Delivery of our optical tables by Reynolds Moving to the new BSB building in February 2012.

(2) A view looking up the BSB elevator shaft from a ride on top of the freight elevator.

(3) The Hoskins Lab CoSMoS microscope showing the red (633 nm), orange (594 nm), green (532 nm) and blue (488 nm) lasers and optics.



## Alumnus Profile: Scott Lowe

*Scott Lowe, an Alumnus of the Department, recalls his time in Alan Attie's lab and his progression to cancer research in the Howard Hughes Institute.*



Dr. Scott W. Lowe is Geoffrey Beene Chair for Cancer Biology and Associate Director for Basic Cancer Research in the Memorial Sloan-Kettering Cancer Center. He is also an Investigator in the Howard Hughes Medical Institute.

Scott's scientific career began at the University of Wisconsin, where he initiated his undergraduate studies in chemical engineering program. By the end of his sophomore year, it was clear to him that engineering was not in his future, and he began to take a broad range of courses in an effort to find a major. At that time his future trajectory was set by a series of events in the biochemistry department. First, he was inspired by a Biochemistry course by Dave Nelson, whose enthusiasm for the topic was contagious. This, together with a wonderful course in Genetics given by James Crow made Scott interested in biochemistry and molecular biology. Perhaps the single most impactful event in setting Scott's trajectory in research was triggered by his participation in an honors lecture series associated with Nelson's biochemistry course, where he heard a lecture from Alan Attie about cholesterol metabolism and lipoprotein biochemistry. At the end of the lecture, Alan mentioned he had opportunities for research in his lab, and Scott immediately took him up on the offer.

Alan took him into the lab, where Scott completed a senior undergraduate project and eventually stayed on as a technician. At that time, the Attie lab was located in the basement of the old biochemistry building on Henry Mall, and then moved to the second floor. Scott's first project focused on the contribution of de novo synthesized and exogenous cholesterol to various bile acids. With this project, Scott learned a range of methods, and importantly much

about experimental design. As time went on, he changed projects in order to assist the lab in characterizing lipoproteins from a mutant strain of pigs with high cholesterol. There he also learned an enormous amount about cell culture and receptor-ligand interactions. Still, perhaps one of his most memorable experiences involved animal husbandry associated with propagation of the mutant strains of pigs, which involved some amusing scenes involving artificial insemination and drinking beer with a new mother pig to enable her to tolerate valuable newborns. He learned the value of animal models of human disease, but also struggled with the challenge of the slow pace of research with these systems. Much of his more recent career has been devoted to developing more rapid strategies to study gene function in (smaller!) animal models.

Scott's time in the Attie lab was a time of key scientific development and gave him the hunger to pursue a career in biomedical research. Alan was a great mentor for him, teaching him a lot about the field, but also gave him the freedom to explore his own ideas. Scott's time in the Attie lab was also one of great fun, and he made many friends in the Attie lab and throughout the Biochemistry Department. He realized that science was a serious business but also had to be fun. He also realized that having a good research environment is as important as having good ideas. These early lessons helped guide his research throughout his career.

Scott applied to several premier graduate programs and was accepted into MIT...this certainly was not due to his grades – which suffered owing to an excess of time spent at the Memorial Union – but rather the experience and productivity he had in the Attie lab. He performed his graduate studies at the Massachusetts Institute of Technology under the supervision of Dr. H. Earl Ruley, and received his Ph.D. for research on the role of the p53 tumor suppressor in oncogenic transformation, apoptosis, and chemosensitivity. After a brief postdoctoral position in the MIT Center for Cancer Research with Drs. David Housman and Tyler Jacks, Dr. Lowe initiated independent research at Cold Spring Harbor Laboratory, where he rapidly rose through the ranks eventually becoming Deputy Director of NCI-designated Cancer Center.

Scott's work resulted in important contributions to our understanding of the p53 tumor suppressor pathway and the process of multi-step carcinogenesis. He was among the first to recognize the role of oncogene-induced senescence as a tumor suppressive mechanism and has continued to pursue both the causes and consequences of replicative death as it relates to tumor suppression. He made fundamental contributions to our understanding of programmed cell death as an innate anti-tumor mechanism and as a response to chemotherapy. Most recently, he has helped to found the comparative oncogenomics movement, combining novel mouse models and RNA interference tools to filter the most important driver mutations from the panoply of variation present in most human tumor genomes, and to identify cancer specific vulnerabilities that may serve as new therapeutic targets. After 16 productive years at Cold Spring Harbor, Scott moved to Memorial Sloan Kettering Cancer Center, where he is active in the Program in Cancer Biology and Genetics. There, he hopes to combine powerful genetic and animal modeling tools to develop better cancer therapies.

Scott's work has been recognized by a number of awards. He was named as a Sydney Kimmel Foundation Scholar and a Rita Allen Foundation Scholar. He received the Outstanding Investigator award by the American Association for Cancer Research and was awarded an American Association for Cancer Research –National Cancer Research Foundation Professor. He received the Paul Marks Prize for Cancer Research and the Alfred G. Kundsén award for Cancer Genetics. He has also recently been named an American Association for the Advancement of Science Scholar.

Scott Lowe in the Alan Attie lab



## Boyer Award Winner 2011

*The Boyer Award is a generous donation of Paul Boyer, and is awarded to an outstanding post-doctoral fellow. Dr Boyer received his PhD from our department in 1943, and a Nobel Prize in Chemistry in 1997. Last year's awardee, Lars Renner, recounts how he came to Madison as a post-doc to study spatial localization of proteins and where it has taken him since.*



My love of cycling brought me to Madison, Wisconsin.

I met Doug Weibel in 2007 at a meeting on the coast of Spain (Sant Feliu de Guixols). Doug gave a talk at the conference and I presented a poster on my graduate research, however I don't think we spent much (or any) time discussing research. Our shared passion for cycling dominated our conversations. I kept in touch with Doug after the meeting and our paths crossed annually, including a one-week cycling excursion through the Italian and French Alps. During the course of our interactions, I became interested in using my background in materials science and polymer science to study microbiology.

I studied Bioprocess and Chemical Engineering at the Technical University Dresden, Germany. After receiving my diploma I worked as a Research Associate at the Leibniz Institute for Polymer Research Dresden and the Max-Bergmann-Centre for Biomaterials studying protein adsorption on

biomaterial surfaces. My Ph.D. research was performed with Carsten Werner and centered upon the study of artificial supported lipid membranes for the study of transmembrane proteins. After several years of contact with Doug, I came to Madison in 2009 as a DFG-funded Postdoctoral Fellow in the Weibel lab. I fell in love with Madison, the seasons in the Midwest, the beautiful landscape, the rolling hills for cycling and skiing, and the very special people in the Midwest.

In Madison, I began studying a central question in cell biology: how is the temporal and spatial organization of the cell machinery established, maintained, and replicated within the cell? Recognizing that numerous, functionally unrelated proteins localize to the poles of rod-shaped bacterial cells, I explored whether the mean curvature of this region of the cell wall plays a role in biomolecule localization. I used techniques from material engineering to test whether membrane strain at the polar regions of bacterial cells influences phospholipid heterogeneity and the localization of amphipathic proteins. Our results were consistent with a model in which membrane curvature created strain and positions microdomains of the intrinsically curved, anionic phospholipid

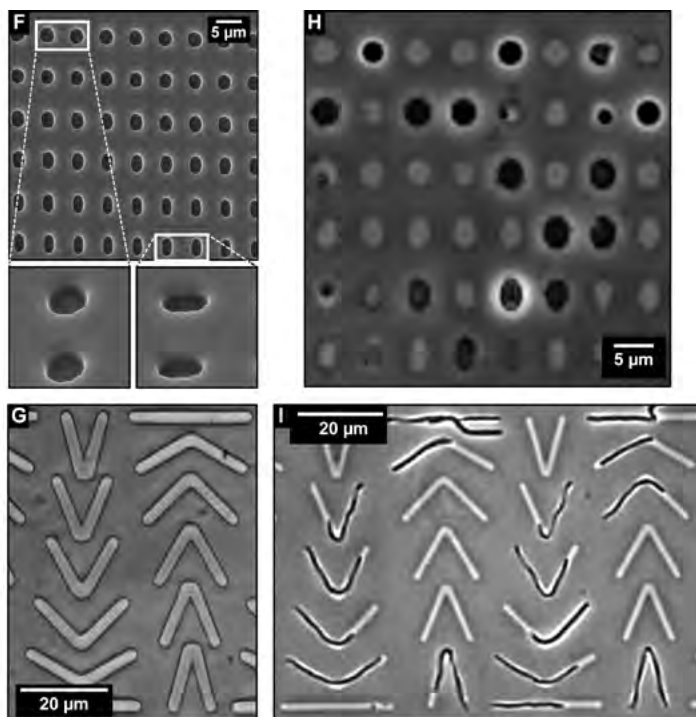
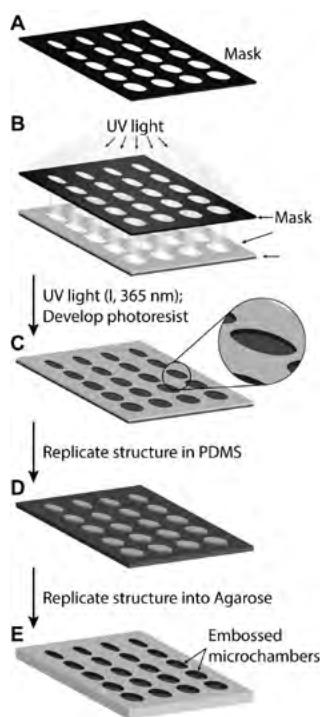
cardiolipin. Using the division protein MinD as a model system, we demonstrated that the behavior and function of this protein in vivo is controlled by its interactions with cardiolipin (and anionic phospholipid) microdomains. The results from these studies provide a framework for understanding the behavior of membranes in response to cell curvature and the role of phospholipid anisotropy in cellular biochemistry.

I was tremendously honored to receive the Boyer Postdoctoral Excellence Award in 2011 in recognition of this research. Paul Boyer's foundational work in the biochemistry of ATP synthase inspired my interest in biochemistry and there is a loose connection between the proteins that I have worked on and the proteins for which Paul Boyer received the 1997 Nobel Prize in Chemistry.

In 2012, I took a position as a Group Leader in Molecular Nanosensors at the Technical University Dresden. I returned to Dresden with an extended family (including my American-born daughter Charlotte), a cache of fond memories of Madison, and several new bikes. I remain an avid cyclist and am certain that cycling will play an instrumental role in my future visits to Madison.

Methodology: **A-E** application of soft lithography to fabricate microstructures that we used to analyze the temporal and spatial behavior of lipids and proteins in bacterial cells.

**F-I** Bacterial cells are adapting to the imposed geometry.





## Dave Nelson: Researcher, Teacher and Collector

*A perspective on an exceptional historian of UW and our Department.*

Adapted from the original article By Nia Sathiamoorthi of the *Daily Cardinal*

A room in the Biochemistry Building overflows with scientific equipment – the dull glint of old microscopes and beakers on every available flat surface. Hidden behind this hodgepodge sits Professor Emeritus David Nelson.

Nelson is a collector of old laboratory instruments. Those in his office are simply a small fraction of his stockpile, overflowing many rooms and closets on this campus. It is because of Nelson's love for science and the University of Wisconsin-Madison's rich academic history that this collection continues to grow.

Nelson was born and raised in Fairmont, Minnesota, and it was in this small town he discovered his appreciation for the sciences. He credits his good teachers, especially his high school chemistry teacher, with spurring his excitement for chemistry.

"I took things apart and put them back together. I was a ham-radio operator. But basically, it was chemistry that I loved," Nelson said.

Nelson pursued his undergraduate studies at Minnesota's St. Olaf College. Majoring in both biology and chemistry, he ultimately realized his desire to study medicine or the underlying causes of behavior. He was all set to go to medical school until the summer of his senior year when he worked full-time in a research laboratory. Nelson discovered he loved working in the lab and nothing else came close as a real challenge or pleasure. He changed his plans suddenly and went to graduate school at Stanford University.

Nelson joined Arthur Kornberg's laboratory in 1964. Just a few years prior, in 1959, Kornberg received the Nobel Prize in Physiology or Medicine for his discovery of DNA synthesis mechanisms. Under Kornberg, Nelson studied the use of bacterial sporulation as a model for cell differentiation. When bacteria form spores, a part of the cell pinches off to make that spore. We now know a new set of genes is expressed, but Nelson's group was still asking the simple questions about cellular differentiation.

"At Stanford, I was a greenhorn in a parade of first-rate people. But they took us graduate students on as equal colleagues," Nelson said. "I was there at a wonderful time. This was after the structure of DNA

was known but before the code was really worked out. So, everyday somebody would come in the door shouting, 'They've got phenylalanine,' or something else from the code. It was just intoxicating."

After receiving his Ph.D., Nelson traded the West Coast for the East Coast when he started his post-doctoral work at Harvard Medical School in Eugene Kennedy's laboratory. Nelson found Kennedy's broad approach to research very different from Kornberg's narrow-focused one. While he acknowledged both were important, Nelson favored breadth in his own laboratory when he became part of the UW faculty in 1971.

It was the research on bacterial attractants and repellents by another prominent UW professor of biochemistry, Julius Adler, that first brought Nelson to Wisconsin and inspired him to study the free-swimming unicellular organism called paramecium.

After jump-starting his own laboratory, Nelson began his teaching career with Biochem 501. He appreciated how the class forced him to know the entire field and gain the vocabulary to converse with any colleague, regardless of research topic.

Twenty years later, Nelson had the opportunity to teach for a year at Spelman College, a small African-American women's college in Atlanta. He discovered he loved the depth achieved in teaching a smaller course so much he almost stayed on, but returned to UW to create a longer two-semester biochemistry course, 507 and 508, with his teaching partner, Michael Cox.

It was with Cox that Nelson took on the revision of Lehninger's "Principles of Biochemistry" textbook. "It has been a really fabulous partnership. Dave really cares about the book and teaching," Cox said. The book, in its fifth edition and produced in 12 languages, has become the most widely used biochemistry textbook in the world.

Nelson actually came into his collection of old scientific instruments from a retiring UW professor, and grew to see the beauty

of them. "Before long, everyone in the department knew if they had a piece of junk, they should bring it to me," Nelson said.

The equipment is an important feature in a College of Agricultural and Life Sciences course, Inter-Ag 375 Ground



Breaking Research in Life Sciences at UW: Past and Present, facilitated by Nelson and other professors. In the course, the first discussion of every week revolves around historical discoveries and the second discussion focuses on the current UW research derived from those discoveries. The lab allows students to repeat historical experiments with historical equipment. Teaching this course inspired Nelson to consider authoring a book on the history of science at UW-Madison.

"I love biochemistry and I love to teach. What motivates me, as it does most teachers, is seeing the lights come on in their eyes. Students take both biology and chemistry, and in biochemistry, they see it finally coming together," Nelson said. "I hope what students learn from my teaching, both in class and the laboratory, is a healthy respect, maybe even an awe, for life."

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To see the original article, published March 19, 2013 in its entirety, please visit: [http://host.madison.com/daily-cardinal/science/dave-nelson-researcher-teacher-and-collector/article\\_a9f7d6b8-910e-11e2-90cd-001a4bcf887a.html](http://host.madison.com/daily-cardinal/science/dave-nelson-researcher-teacher-and-collector/article_a9f7d6b8-910e-11e2-90cd-001a4bcf887a.html)

## D and D Break New Ground

*Hector DeLuca's lab continues to develop Vitamin D analogues with exciting therapeutic potential for kidney dialysis, autoimmune disease and diabetes.*



Never mind the title -- that's the editor's fault. It is true though that our laboratory does remain functional in the area of Vitamin D -- with a special focus on the development

of new pharmaceuticals based on the Vitamin D structure. Currently through external support, we maintain a group of synthetic organic chemists who prepare new and interesting analogs of the vitamin D structure, which we hope will have specific biological activities. Several of these analogs are in various stages of development in the pharmaceutical pipeline, and especially our lead compound called 2MD which is 2-methylelene-19-nor-20(S)-1 $\alpha$ ,25-dihydroxyvitamin D<sub>3</sub>. It was designed initially for treatment of osteoporosis but more recently we have found it promising for the treatment of secondary hyperparathyroidism in dialysis patients. 2MD is extremely effective in increasing bone strength in ovariectomized rats and in monkeys. It has gone through phase 2 clinical trials in human patients. Although it did not increase bone mass, it greatly increased bone turnover that we strongly believe results in a much stronger skeleton. Unfortunately to develop a drug for osteoporosis requires a 3-year, phase 3 fracture study costing approximately \$1 billion. So far we have been unable to locate a firm willing to commit to this amount. We have, therefore, focused our attention in a shorter goal, namely the treatment of bone disease of kidney failure patients who lack the ability to produce the vitamin D hormone in any quantity. This compound is currently in a phase 2 clinical trial in dialysis patients to correct their metabolic bone disease

caused by hyperparathyroidism. At the same time, learning the lessons of 2MD we have been developing new analogs that possess the ability to synthesize new bone *in vivo* but with reduced ability to cause bone resorption. We feel these compounds will increase bone mass in osteoporotic patients and could be the next generation of development of vitamin D compounds for this widespread disease.

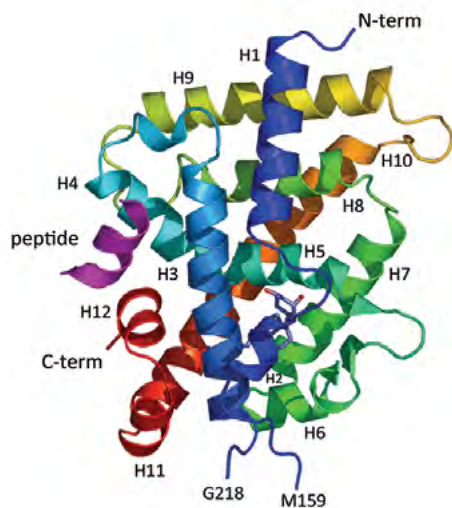
A major focus is in the area of autoimmune diseases. We have focused for the last 20 years on multiple sclerosis (MS) and have first been enamored by the possibility that vitamin D might be involved in protecting against MS. However, our group as well as another group in France have clearly demonstrated that vitamin D deficiency does not increase the incidence of experimental autoimmune encephalomyelitis (EAE, a model of MS in mice) but rather suppresses it. Furthermore, elimination of the vitamin D receptor in such animals also eliminates the incidence of disease. Thus unexpectedly, vitamin D deficiency in this autoimmune disease results in reduced incidence, contrary to experiments or surveys that show a correlation between high blood levels of 25-hydroxyvitamin D and reduced incidence of MS. Further examination of this has resulted in our discovery that a wave band of light that does not produce vitamin D is responsible for protection against EAE and presumably

MS. This, therefore, has moved our focus away from vitamin D onto ultraviolet light and its possible use in suppressing MS.

Another topic of great interest has been type 1 diabetes. Previous work in our group clearly showed that vitamin D deficiency markedly increases incidence and severity of type 1 diabetes in the NOD mouse (the animal model of this disease). Of great interest is that the islet cells of the pancreas contain large amounts of the vitamin D receptor and in addition to its role in the immune system, the vitamin D hormone plays an important role in the cells that produce insulin. We found an analog of the vitamin D hormone that will suppress type 1 diabetes in the NOD mouse. We have preliminary evidence that this analog will stabilize transplanted islet cells into animals that have lost their natural islet cells through autoimmune disease.

Another area of interest has been the relationship between diet and the incidence of type 1 diabetes in the NOD mouse. We can clearly show that a chow or crude diet causes almost a 100% incidence of type 1 diabetes in the NOD mouse. If the same mice are placed on a highly purified diet with a particularly highly purified casein as a protein source, the incidence is near zero. We have prepared extracts of the natural diet that when added to the purified diet will restore the high incidence of type 1 diabetes. An interesting and important project is to try to find out what it is in the crude diet that supports the development of type 1 diabetes in these susceptible mice.

To summarize, we are still having a lot of fun with vitamin D and we are very interested in the autoimmune diseases and what could be done to help in their therapeutics. In the meantime, a major effort is the timely development of pharmaceuticals for the treatment of a variety of diseases, especially bone disease resulting from kidney failure.



VDR ligand-binding domain.



## Henry Lardy, Bob Burris, Van Potter

### *South Dakota's Gifts to the UW.*

By Professor Dave Nelson



One research laboratory at South Dakota State College (SDSC, now SDS University) was responsible for starting the careers of three distinguished

UW professors in the life sciences: Van Rensselaer Potter (who joined the faculty of the McArdle Laboratory in 1940); Robert H. Burris (who joined the Biochemistry faculty in 1944) and Henry A. Lardy (Biochemistry/Enzyme Institute, who joined the faculty in 1945).

Van Potter, born in 1911 on farm near Coteau des Prairies, South Dakota, earned his B.S. in Chemistry and Biology in 1933, then took a position in the chemistry laboratory at the SDSC Agricultural Experiment Station under Professors Kurt Walter Franke and A. L. Moxon. Franke and Moxon used chemical methods to determine, in feeds and tissues, the levels of selenium, which caused “blind staggers” in farm animals. Potter’s next

move was to become a graduate student in Biochemistry at the UW under professor Conrad Elvehjem, earning his Ph.D. in 1936. After postdoctoral work, he joined the McArdle Laboratory at the UW.

Robert H. Burris grew up a block away from SDSC in Brookings, and earned his B.S. in Chemistry there in 1936. He and Van Potter became acquainted at SDSC, where Burris also worked in the Franke/Moxon lab. While Burris was still an undergraduate, Potter, by then already at the UW, recommended him for a summer position in the laboratory of Perry Wilson (UW Bacteriology). Wilson, pleased with Burris’ work, invited him to come back to the UW as a graduate student, which he did, finishing his Ph.D. in 1940.

Henry Lardy, a native of rural Roslyn South Dakota, also began his graduate

work at UW following his graduation in Agriculture and Dairy Science from SDSU in 1939. As an undergraduate, Lardy, too, had worked in the laboratory of Moxon on problems related to selenium toxicity. Lardy earned his Ph.D. with Paul Phillips at the UW in 1943, and joined the UW faculty after a postdoctoral period. Lardy and Burris worked in the same UW department (Biochemistry) from the 1940’s until their deaths in 2010. So Potter, Burris, and Lardy all got their starts in the Franke/Moxon selenium laboratory at SDSU.



Van Rensselaer Potter (1911 - 2001)

Van Potter spent his entire career studying enzyme levels in transplantable animal tumors, and the effects of various inhibitors on enzymes of tumors. Today’s practice of combining several inhibitors in cancer therapy is derived in part from Potter’s work. He was elected to the National Academy of Sciences and was president of the American Society for Cell Biology in 1964. His second serious interest was in the field he named “bioethics”, and his book *Global Bioethics*, published in his retirement years (1988) showed the way for much of the modern effort to bridge science and humanities.

Bob Burris learned, in the laboratory of Harold Urey, to measure the conversion of  $15\text{-N}$ -labeled  $\text{N}_2$  to  $\text{NH}_3$  by nitrogen-fixing bacteria, and then spent his whole

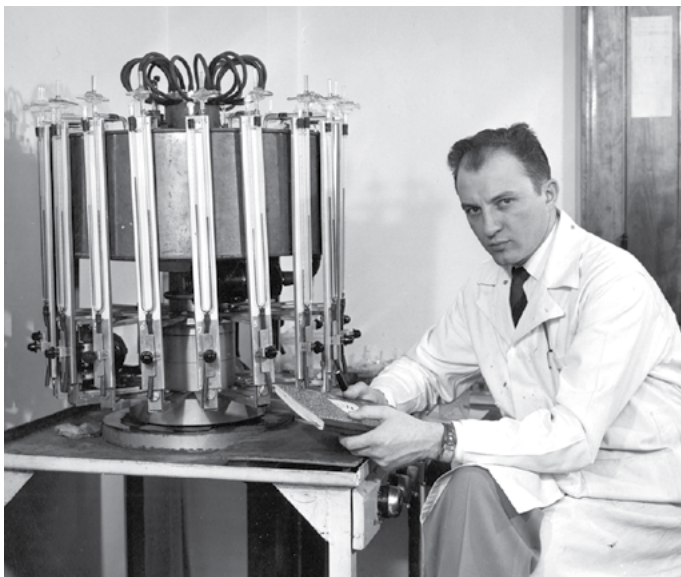
research career studying this process and the bacterial enzyme (nitrogenase) that catalyzes it. Over his long career he trained 71 graduate students and a similar number of post-docs. Burris served as Chairman of Biochemistry from 1958 to 1970, was elected to the National Academy of Sciences (1961), was awarded the National Medal of Science in 1979, and won the Wolf Award in Agriculture (often considered the Nobel Prize in Agriculture) in 1985.



Robert H. Burris (1914 - 2010)

Henry Lardy was a member of the UW Biochemistry Faculty and one of the original Co-Directors at the Institute for Enzyme Research when it opened in 1949. Lardy made research contributions in many aspects of metabolism. In his doctoral work with Paul Phillips, Lardy developed a medium that maintained the viability of bull sperm for long enough to be used to artificially inseminate cows far away from the bull, enabling the wide dissemination of the genes of a prize animal. For this early work, he won the Wolf Award in Agriculture (1981).

Over the rest of his career he continued his studies of respiration in spermatozoa; shared in the discovery of biotin function; studied thyroid toxicity



Henry A. Lardy (1917 - 2010)

and the thyroid hormone; made major contributions to the understanding of the coupling of oxidation to phosphorylation in mitochondria, and of uncoupling by agents such as dinitrophenol; defined and studied respiratory control in mitochondria; purified, crystallized, and characterized a number of phosphate-

transferring enzymes; and studied the regulation of gluconeogenesis in detail. He worked in his laboratory every day until shortly before his death at 92 in 2010. During the last decade of his research career he entered a new area, the metabolism of the human steroid DHEA and the effects of its metabolites on cellular processes. Ironically, one of the potential uses for

such metabolites was the treatment of prostate cancer, the cause of Lardy's death.

During his long career, Lardy trained 64 graduate students and 110 postdoctoral fellows, and published more than 500 papers! He was elected to the National Academy of Sciences in 1958, just thirteen years into his

career, and won a number of prestigious awards in addition to the Wolf Award.

Outside the laboratory he was a committed social activist; during the McCarthy Era in Wisconsin, Lardy was president of Citizens Against McCarthy, and his last public lecture included his strong plea to end the discrimination against gays and lesbians.

Lardy's attitude toward research is captured in this typed sign, which was pinned to the wall in his office:

*"Beginning February 1st 1958 and effective thereafter, working time which is lost while preparing for examinations should be deducted from your vacation allotment. Anyone qualifying for advanced degrees should be able to acquire his scientific knowledge during class periods and leisurely evening reading. Knowledge gained while re-reading class notes is either false or short-lived. What you learn at the laboratory bench is yours forever and may even benefit the rest of mankind."*



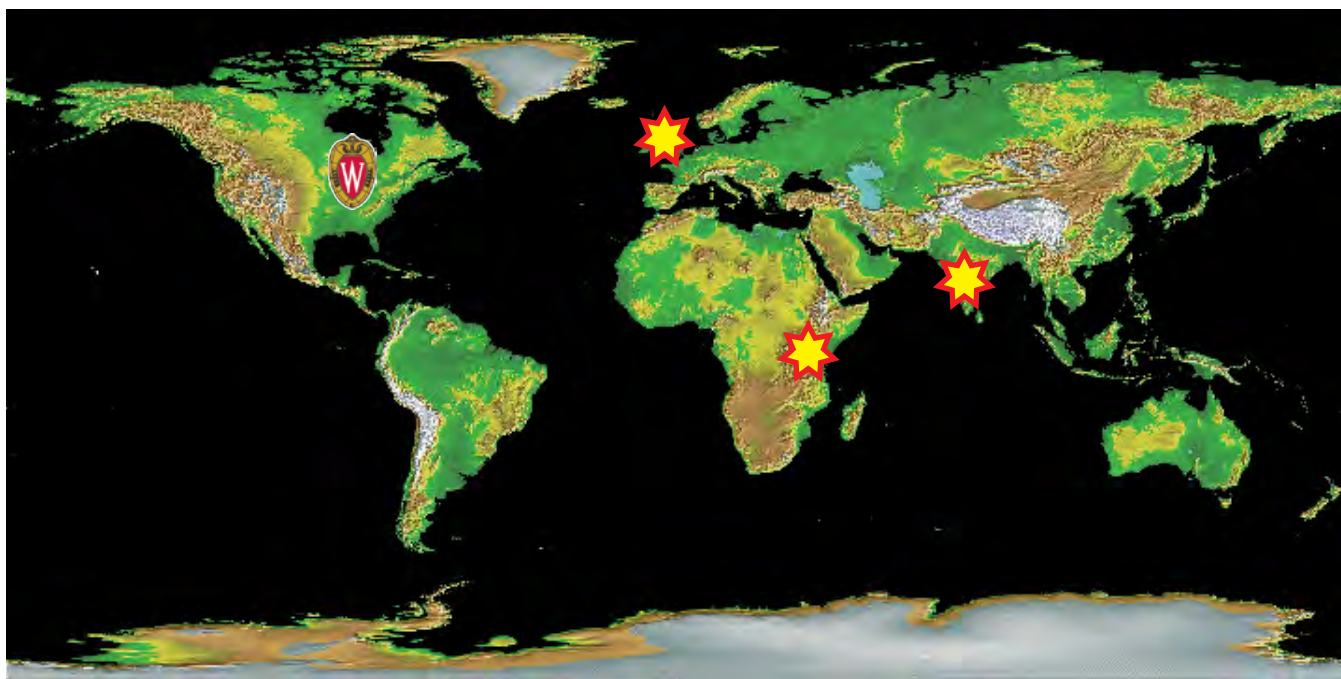
The Beckman DU Quartz Photoelectric Spectrophotometer was an instrument that revolutionized biochemistry and was used by all three of the South Dakotans. The Beckman Model DU was the first ultraviolet and visible spectrophotometer. Introduced in 1941, this instrument retained essentially the same design until it was discontinued in 1976, a commercial lifetime of 35 years.



## International Programs: Giving Our Undergraduates a Global Perspective

*Three innovative programs enhance the Biochemistry Department's undergraduate education by creating hands-on experience on three continents.*

By Professor Marv Wickens



Every practicing scientist knows that science is international. It is not just that the conclusions we reach are universal. It is also that great results are obtained across the world, that collaborations extend to many continents, and that each culture builds on its own strengths, perspectives and history.

Scientists, companies and policy-makers greatly benefit by having first-hand knowledge of these other cultures. Three innovative programs in the Biochemistry Department now provide that for our undergraduates.

Each program has a unique emphasis, and can have dramatic impact on the students who participate. The Khorana Program (Dr. Ansari) brings students from India to UW (and now other institutions). Through new initiatives, it now also enhances agriculture and Tech Transfer in India, drawing on the expertise of the Department, the UW, and WARE. The SCORE Program (Dr. Wickens) sends talented UW undergraduates with a serious commitment to science to study in Cambridge and Oxford, committing themselves to an intense summer of research. The Uganda Program (Dr. Ntambi) sends students to that African nation, to learn first-hand how biochemistry and nutrition impact Uganda's health care. Each of these experiences come at a formative time in an undergraduate's life – and so has ripple effects into the future.

The three programs engage the UW in the international community of science in a different way than our extensive scientific collaborations. They send some of our most exceptional students out into the world and let the rest of the world know that UW has something special to offer.

This year, the creators of the programs describe recent developments and the impacts the programs have on students. We also have asked the students to speak for themselves, and explain in their own words how their participation changed their lives.

Each program faces important challenges as it builds on its strengths and moves into new areas. We seek your support to enhance these rare strengths in undergraduate training in Biochemistry.

☞ The Khorana Program is expanding into new areas of science, and seeks support for UW students to go to India.

☞ The SCORE program is soon going to include additional outstanding institutions elsewhere in the world, and has begun to develop year-long experiences for our most gifted majors.

☞ The Uganda program looks for stable funding for its students to have an eye-opening experience in human health.

If you have suggestions or wish to contribute, please contact Betty Craig (Department Chair) or any one of the three heads of the programs: Aseem Ansari (Khorana) Marv Wickens (SCORE), James Ntambi (Uganda).

Please see page 66 for contact information.

## The Khorana Program - India

*New initiatives and growth in this program further extend the Wisconsin Idea to India, and intimately link our department and the UW with that burgeoning culture.*

By Professor Aseem Ansari



The University of Wisconsin – Madison (UW), in close partnership with the Government of India and the bilateral Indo-US Science and Technology Forum (IUSSTF), initiated a scholar exchange program in 2008. This prestigious research internship program was named after Har Gobind Khorana, an Indian-American scientist who pioneered the use of chemical approaches to solve fundamental biological questions. Gobind epitomized the importance of transcending scientific, cultural and geographic boundaries (see Khorana biography on page 38).

To celebrate Gobind's contributions, we developed a program guided by the following principles:

- Identify and nurture future “Khoranas” building long-term bridges between scientific communities,
- Extend the Wisconsin idea to India, focusing on sustainable rural development,
- Partner with industry to develop innovative products to meet needs across the globe.

### Future “Khoranas”

A key goal of the program is to ignite the imagination of talented students from US and India. Selected students are invited for summer internships in leading laboratories. US students work in some of the best labs in India, and Indian students who are selected from a nation-wide search work in top labs at UW and its 10 US partner universities. The participating labs in both countries are world leaders with reputations for nurturing talent.

Scholars work with senior lab members on specific projects. Our central goal is for students to learn to frame scientific questions and experimental paths to answering those questions. Along the way, many make remarkable research breakthroughs.

Khorana scholars learn about each other's research projects in meetings every week, which typically last 4-6 hours. Beyond science, we arrange talks and meetings with exceptional individuals across a wide range of disciplines. These have included:

- Sam Pitroda, the father of India's telecom revolution and advisor to India's Prime Minister, inspires scholars to think big;
- Carl Gulbrandsen, managing Director of WARF, discusses how scientific ideas can change the world;
- Krishna and Suchitra Ella encourage students to take the path less travelled, describing creation of an Indian vaccine company that has made vaccines affordable to the world's poor;
- Richard Davidson, a neuroscientist inspired by the Dalai Lama, has revealed the remarkable ability of meditation to alter the brain;
- Gerald Chan, a billionaire biotech investor with a PhD in Biophysics from Harvard, has emphasized the importance of passion in the creative process.

In addition, several scientific visionaries, including Nobelists Phil Sharp, Ham Smith, and Gobind, have shared their own scientific journeys as have diplomats and entrepreneurs. All is aimed to nurture bold thinking among the students.

Several Khorana scholars won awards for their research. The quality of their work is also reflected in the surprising number of publications and patents that have resulted from a short summer internship.

### Expansion and doubling down

In early 2010, due to the overwhelming increase in high quality applicants, UW invited the group of Big 10 Midwestern schools that form the “Committee on Institutional Cooperation” (CIC) to join the Khorana Program. We took a delegation of Deans from several CIC schools to meet Minister Sibal in March of 2010. It took nearly 18 months to meticulously assemble the framework of the shared program. Professor Tom

RajBhandary, Gobind's close colleague and friend, brought MIT onboard. Georgetown joined soon thereafter and several other universities have expressed interest in partnerships in the near future.

To commemorate Gobind's passing on November 9th 2011, the Government of India doubled the scope the program and extended the funding for another three-year cycle. Private funds bring the total number of scholars to about 40 per year. Each of the ten partner schools received 3-5 students. Cohesiveness is maintained through an orientation event at UW, weekend video conferences, and an annual symposium in Delhi at the internship's end in early August. The community is close-knit, helping foster future international collaborations and seamless bridges between scientific communities across the globe.

### Khorana Technology Transfer Program

Scientists in the Department of Biochemistry have excelled at finding commercial applications for their scientific discoveries. From the outset, Minister Sibal saw parallels to the tech-transfer challenges India faced. These similarities led to the Khorana Technology Transfer Program, in which India sends a mix of excellent scientists and policy makers "to learn how a government supported institute such as UW can generate such IP and commercialize it so successfully." India overlooked other highly visible schools to launch the *Khorana Tech-Transfer Program* (<http://indousstf.org/Khorana/khorana.html>). The program leverages WARF's unique strengths in commercializing scientific advances and the UW-Business school's Weinart center for entrepreneurship.

An intensive two-week course in 2012 was tailored to the Indian context. Home institutions were incentivized to make investments so that their trainees would be able to create the necessary entrepreneurship and innovation ecosystem. Ambitious, yes! However, the opportunities for India to build on its intellectual strengths and demographic dividend are enormous as are the potential benefits to the US and India.



## Rural Development

Another major goal of the Khorana Program was inspired by the Wisconsin Idea – that research at the university should benefit the public. We took the Idea half way across the globe and applied lessons learned in Wisconsin to improve Rural conditions in one of the poorest parts of the world – the eastern edge of UP, India's largest state with nearly 300 million people. The USAID and three Indian institutions sponsored this project. John Peters, the Director of Soils Testing lab at UW, boldly chose to relocate to India. John and his wife lived and worked in India for two years and established 100 soil testing labs where less than 5 labs existed across the nation. Best agricultural practices were developed and shared with thousands of farmers. Women were taught to maximize milk production and use funds to support their family. For details see:

<http://news.cals.wisc.edu/communities/2012/10/22/helping-women-help-themselves/>

### Expanded scope and impact

We now plan to expand the scientific scope of the program, funding similar

numbers of "non-Biotech" and "Agriculture, Dairy and Food Security" scholars. Taken together the numbers would approach the volume of Fulbright scholars who travel to India to learn about her culture as well as her spiritual and social structure. A thriving partnership requires that US students travel to India to learn how innovative technological advances are transforming India. For that we continue to seek your advice and support.

### An unexpected challenge:

#### *Funding Passages to India*

Funds for the Indian Khorana scholars are generously provided by Government of India's DBT and IUSSTF. To our utter surprise we found virtually no support to send US Khorana scholars to India. NSF and NIH were enthusiastic but offered little financial support. IUSSTF has temporarily stepped in to fill the void. We set out to find 20 talented UW students but were only able to identify 4-5 highly qualified students who were interested in going to India for research.



Late Prof. Har Gobind Khorana interacts with some of the 2009 of Khorana Scholars.

The absence of a reasonable stipend that most UW undergrads rely on to cover the extracurricular costs through the academic year turned out to be a serious problem. Consequently, we are seeking potential sources of funding to be able to provide a stipend and airfare to future American Khorana scholars. We want to reach equal reciprocity of scholars between US and India and welcome creative ideas.

For more information on the Khorana Program, please contact Aseem Ansari ([ansari@biochem.wisc.edu](mailto:ansari@biochem.wisc.edu)) and Nishritha Bopana ([nbopana@indousstf.org](mailto:nbopana@indousstf.org)).

## The SCORE Program - Britain

*Undergrads enhance their passion for science and gain international perspective through an intense summer experience in Oxford and Cambridge.*

By Marv Wickens, with a past participant, Amanda Buyan



For two intense months, the students work in laboratories, conducting research in a specific lab, attending seminars and participating in scientific discussions.

They study a broad range of problems in biochemistry, molecular biology and genetics. The mentors are outstanding, and have included Fellows of the Royal Society and EMBO, and a Nobel Prize recipient.

The program enables students to see science and themselves through an international lens. Most of the students have not traveled outside the US before. On their return, students often comment that they have gained a deeper appreciation for how much they love science itself. Their

passion for research is heightened by the intensity of the summer's focus on science. Most are even more committed to science than they were when they left.

Amanda Buyan, a past participant in SCORE, is now doing her PhD work in Oxford, and writes about her experience in the program.

I was elated when I got that email saying that I'd been accepted. It was a chance to fulfill my dream of going to England, and to do research at Oxford – a great university and as I soon discovered, a beautiful place as well. It was the first real chance I had seen at UW to study abroad as a science major, without extending my time to graduation. The program gave me the chance to do a short, 8-week research project for which I would work full-time – a rare glimpse of what kinds of things I could (and eventually would) be doing as a PhD candidate.

The experience was even richer than I had anticipated. The lab work was intense and satisfying. Oxford was full of European scientists and I traveled a bit, seeing other cultures at a personal level. I became convinced I would continue to do research in the next phase of my life.

That phase was catalyzed by SCORE. While at Oxford, I inquired about PhD opportunities there, my SCORE professor (Mark Sansom) recommended I apply for a Wellcome Trust Structural Biology Programme at Oxford. I ended up being one of the five fortunate people that they select, allowing me to exceed my wildest dreams and pursue a PhD at Oxford for four years in England. I may still be having a few difficulties with the British sense of humour, but love and appreciate what SCORE did for me.

Anticipation from two participants before they leave for SCORE 2013...

*Having never been out of the country, I'm excited...to gain new perspective on the world. And even more excited that will be able to build on the science skills I have gained at UW-Madison.*

**Ryan Birschbach**

*Studying a new disease model, experiencing the rich history England has to offer, working with brilliant researchers - I could not be more eager to get started on this journey.*

**Sarah Larson**



The Cambridge Backs

New initiatives now seeking funding include expansion to other leading institutions in Europe and around the world. It goes without saying that this requires stable funding, and we seek your support to enhance the programs and provide financial stability.

## The Uganda Program

*UW students gain a deep understanding of the importance of nutrition and biochemistry in a poor but inspiring country.*

By James Ntambi, with past participants Beth Stadtmueller, Alex Burford, Matthew Hunt and Eric Monroe



The Uganda Program enables students to examine health and nutrition in a developing country. Prior to leaving the country, students enroll in a three

credit course focused on the Ugandan healthcare system and culture. Topics cover everything from economics to child malnutrition, prenatal care, women's health, education, agriculture, or any other field found interesting to the student.

The end of the fall semester culminates with a three week adventure in Uganda. The journey begins in the capital city, Kampala. While here, the group tours the city, visits the largest hospital Uganda has to offer, and speaks with different healthcare workers. Time is allotted in the evening for students to explore the city's fantastic markets, restaurants, and culture. After spending time in Kampala, the group departs

on a trip west to visit the Queen Elizabeth National Park, Kabale, and Lyantonde.

In Uganda, students come face to face with the reality of HIV/AIDS, women's health, and nutrition. Over the years, largely due to Dr. Ntambi's connections, strong bonds have formed between the University of Wisconsin-Madison and Uganda's Makerere University and the Institute of Public Health. Through these relationships, students gain a truly unique exposure to the intersection of politics, economics, culture, and education as it relates to public health. A past participant, Beth Stadtmueller, describes how the program impacted her life.



UW students at Mwanamugimu Nutrition Clinic.

As a Junior and a Biochem major, at UW, I found myself challenged by a major life decision - What next? I weighed post-graduation options -- find a job, travel, go to grad school, or maybe join the Peace Corps. Two main interests shaped my decision - a fascination with the molecular world, and a deep desire to help the world around me. At the time, it was difficult to identify a path that satisfied both interests. Then my advisor, Dave Nelson, introduced me to James Ntambi, who was developing a new program in Ugandan public health and nutrition. I jumped at the opportunity, and changed forever as a result.

Visiting Uganda in late 2002/early 2003 was an intense experience. I had traveled extensively and had witnessed poverty prior to the trip, but my experiences had never brought me face to face with a public health crisis, nor provided an integral course of study, as the UW Uganda program did. Upon setting foot in Uganda, it became clear that political unrest, limited resources, malnutrition and disease were incredibly intertwined - much more so than is obvious in publications. The situation might have seemed hopeless were it not for the impeccably high spirits of the Ugandan people, their enthusiasm to learn and their remarkable ability to create





UW students in rural classroom.

*If you are looking for amazing people, once in a lifetime experiences, or a better understanding of this big world we all share, I highly recommend the Uganda Program.*

**Alex Burford**  
(2004/2005 program alum)

with limited resources. I was humbled. And I would never see life the same again.

I recall severely ill people asleep on the hallway floors in Mulago hospital, which lacked not only enough beds for its patients, but also many basic medical instruments and in some areas, even running water. I tracked a patient's progress in the Mwanamugimu nutrition unit – her name was Jabeth – she was just over a year old, yet was already battling severe malnourishment, HIV, Tuberculosis and malaria. Jabeth was one of many children in the unit whose prospects for the future seemed dim, yet the unit staff was unfailingly upbeat and their approach of combining nutrition education for mothers with treatment of children was highly effective, promising a brighter future for many.

As the eye-opening experiences piled up, I could see that education was the strongest weapon in use to battle the complex set of circumstances at play in Uganda, yet education itself was also suffering. Even at our host institution, Makerere University, resources were limited. As I walked through campus, I sensed much of the same positive, youthful energy and motivation as at UW, but in contrast the laboratories for science education and research contained instruments in need of repair and were void of many basic necessities. Overall it was clear that Ugandans failed to benefit from much of the education and research that was being conducted throughout the world and this observation concerned me and left a truly lasting impression.

The Uganda Program provided me with a new and global perspective on life and the career decisions before me at the time. Having observed the complexity of a public health crisis, the discrepancy between biomedical research and its global application, and the power of education to promote change I concluded that pursuing a career in academic science would be the best way for me to help combat the challenges facing Uganda and many other parts of the world. Upon returning from Uganda I began graduate training in biochemistry and today I am a postdoctoral researcher studying the human immune system, research that I hope to expand upon in my own laboratory one day. It has been ten years since I set foot in Uganda, yet much of what I learned remains at the front of my mind today – motivating me to pursue research that will help to combat disease and inspiring me to ask how science education can be expanded to train students worldwide and ensure that discoveries become accessible to everyone.

**Beth Stadtmueller**  
(2002/2003 program alum)

The formal program is a collaboration between the Biochemistry and Nutrition Departments, and the CALS Office of International Programs. As Beth's comments illustrate, it enables students to connect classroom studies with real-world learning. The students gain a palpable understanding of the realities faced by so many in the world. Students collaborate intimately with villagers, who in fact identify the projects that are needed.

The program needs financial support to continue. With that in mind, the student alumni themselves created The Village Health Project. This program directly raises funds, applying for grants and fellowships, and seeks donations.

To donate, please send a check to: Village Health Project, 333 East Campus Mall, Room 3207, Madison, WI 53715-1380. For more details concerning the international health and nutrition program in Uganda please contact John Ferrick ([jferrick@cals.wisc.edu](mailto:jferrick@cals.wisc.edu)) Director of International Programs at UW-Madison/College of Agricultural & Life Sciences.

*The Program was eye-opening. Several of us who had been moved by the experience formed a 501(c)3 nonprofit group, the Village Health Project. Thanks to involved students and the generous support of alumni, the Wisconsin Idea Fellowship, and Rotary International, the organization now supports sustainable projects to improve sanitation, nutrition, and education in rural Uganda.*

**Eric Monroe**  
(2010/2011 program alum)

*The experience motivated me to join the Peace Corps as a health educator on projects relating to HIV and maternal and child survival. I now am preparing for a career in medicine working here and abroad. Looking back, it is clear that the Uganda Program expanded my worldview, and instilled passions for global public health and social justice.*

**Matthew Hunt**  
(2004/2005 program alum)

## Pre-college Outreach

The Wisconsin Idea asserts that developments at the University should be brought to the benefit of the people of Wisconsin. Two innovative programs created by Drs. Hazel Holden and Doug Weibel of the Biochemistry Department do just that, with a focus on the education of middle school and high school students.

Here, Dr. Holden describes a program in which middle school students participate in research in her own lab, yielding astounding results all the way from crystals to structures to papers. Dr. Weibel describes his program's collaboration with a committed high school teacher, and the ripple effect that has had on her students.

### Project CRYSTAL

*Middle school students gain hands-on understanding of chemistry and biochemistry by doing crystallography - and publishing papers - in Hazel Holden's lab.*



Project CRYSTAL is a scientific outreach program first established in 2009 through funding by the NSF to the laboratory of Dr. Hazel M. Holden. The name "CRYSTAL" stands for Crystallographers Researching with Young Scientists: Teaching And Learning. The program provides hands-on

laboratory experiences for four selected middle school students each academic year. They spend approximately 1.5 hours in the laboratory per week working on a specific research project. Through both laboratory exposure and interactive lectures, these students learn the fundamentals of chemistry and biochemistry. At the end of the school year they leave the Holden laboratory having experienced such techniques as DNA cloning, *E. coli* cell growth, protein purification, X-ray crystallography, and protein modeling.

The 2011-2012 Project CRYSTAL class was composed of four seventh grade students, Melissa, Malaika, Gwen, and Sarah, from Edgewood Campus Middle School. IPiB graduate students Rachel Kubiak, Becky Phillips, and Matthew Zmudka mentored these middle schoolers. Through their efforts, they were able to clone, purify, crystallize, and solve the structure of a protein referred to as ChmJ. It is a fascinating enzyme involved in the biosynthesis of mycinose, an unusual sugar found attached to the antibiotics chalcomycin and tylosin. A paper describing their results has now been accepted for publication in *Biochemistry*, with all four middle school students serving as co-authors. This is the second time that middle school students in this program have been authors on a paper published in *Biochemistry*! It was a bittersweet moment for all of the Project CRYSTAL team when "graduation day" arrived because these young women brought such enthusiasm and laughter to the laboratory each week.

Project CRYSTAL began its 2012-2013 season on September 11th with four eighth graders, Odoi, Malachi, Rosie, and Lilli, from Spring Harbor Middle School. Their project, which also involves studying

the structure and function of an enzyme involved in unusual sugar biosynthesis, is off to a great start. The cloning has been going well, and purified protein is expected within the next coming months!

During the 2012 summer months, the Project CRYSTAL team began production of a biochemistry textbook specifically geared towards middle school students. Thus far six chapters have been written and illustrated. Members of this year's class are serving as reviewers, and their comments have been terrific. It is already clear that this book is making a profound difference in how fast these students are learning the concepts being taught during the lectures.

Project CRYSTAL has now been featured as one of the NSF exemplary projects and has been highlighted by the National Science Teacher Association. It has also been written up in Science Daily, C&E News, Inside UW-Madison, and the RCSB PDB Newsletter. Recently, Project CRYSTAL was cited by Prag Chitnis, director of the Division of Molecular and Cellular Biosciences at the National Science Foundation, for its broader impact component. We are happy to announce that Project CRYSTAL was refunded for an additional three years.

More details concerning Project CRYSTAL can be found at its Facebook page: (<http://www.facebook.com/ProjectXTAL>) or at: <http://www.projectcrystal.org/>.



The 2011-2012 Project CRYSTAL Class.



Graduation Day! The class enjoyed ice cream at Babcock with their mentors.



The 2012-2013 Project CRYSTAL Class.



## MicroExplorers

*The thrill of discovery excites high school students about science through a collaboration between a high school teacher and Doug Weibel's lab.*



MicroExplorers participated in a range of activities in 2012. A highlight was our collaboration with local chemistry and biology high school teacher, Melissa Hemling. Melissa returned for her second summer as an intern in the Weibel lab through the NSF-funded, Research Experience for

Teachers program and she was on a mission to integrate microfluidics into her classroom. Microfluidics is the study and application of fluid flow at the microscale. The physics of fluids at small scales is non-intuitive and enables us to manipulate bacteria in new ways. Working closely with graduate student John Crooks and postdoctoral fellows Katie Brenner and Piercen Oliver, Melissa integrated microfluidics into a segment of her chemistry curriculum. In October 2012, John, Katie, Piercen, and Doug spent the day in Melissa's chemistry classroom at Beaver Dam High School participating in the activity with her classes. Katie summarized her experience:

We caught one another in the act: sizing up the long row of tall green lockers. Would we fit inside, if stuffed in? <A nervous laugh> It was crazy to think that we would be nervous, however none of us had particularly fond memories of high school chemistry. Does anyone? As we were about to relearn, fantastic teachers can have a transformational role in chemistry (and science) education.

Around the corner, past the lockers, a jolting vision awaited: a standard, public high-school lab. It probably looked about the same when we were in high school, however it looked very different from the environments to which we have become accustomed that are sparkly, dazzling, and full of blinking lights and very expensive stuff. The high school lab was old and plain. Melissa was about to transform this space with her energy and creativity. Over the summer, Melissa designed a set of experiments to introduce her students to microfluidic devices and we were here to work with the students on these activities. By the end of the hour we spent with each class, students designed and made Shrinky Dinks and used them to create microfluidic devices in a transparent silicone elastomer that they would use to perform acid-base chemistry experiments. Using an iterative approach, the students learned about the laminar flow of fluids through hands-on activities, and used it to design, create, and test microfluidic devices to solve a chemistry challenge provided by Melissa.

I was assigned to hang out with a group of four girls for the class period. As we began the lab, they seemed more concerned about an upcoming volleyball match than chemistry. However their conversation took a turn as they watched Shrinky Dinks buckle, curl, and shrink in hot oil. The turning point was when one of them began cutting funky shapes from the leftover Shrinky Dink polymer. Their attention suddenly shifted and they hypothesized about what might happen if starfish shapes, shapes with bristles, or winding shapes were submerged in the oil. It was thrilling to watch them engage and get excited about their experiments. As their unique shapes shrank in the oil, we discussed whether we could create a microfluidic system based upon these shapes, and what might happen to fluid flowing through a device. All four of the girls were excited. I shared with them what may very well have been the only useful thing I said all day: that this moment of discovery is what makes science so exciting. The experience was a reminder to me about how truly lucky I am to get to be here, every day, surrounded by sparkly, dazzling, blinking lights, studying fascinating biological questions.



John Crooks, left, with his group of student scientists.



Katie Brenner, left, with her group of student scientists.

## Biochemistry / IPiB Degree Listings December 2010 - December 2012

Degree	Name (Major Professor)	Program	Thesis Title
PhD Dec 2012	<b>Jon Mayers</b> (Audhya)	IPiB	Roles for ESCRT-0 in Sequestering Ubiquitin Modified Cargos into the Endosomal/Lysosomal Pathway
PhD Dec 2010	<b>Jae-Young Yun</b> (Amasino)	Biochemistry	Molecular Mechanisms of Vernalization in <i>Arabidopsis thaliana</i>
PhD Dec 2012	<b>David Zhang</b> (Ansari)	IPiB	RNA Polymerase II Controls Transcription Dynamics
PhD Aug 2011	<b>Stephen Tumas</b> (Butcher)	IPiB	Structural Studies of the Yeast Prp24-U6 RNA Complex
PhD Dec 2012	<b>Jordan Burke</b> (Butcher)	IPiB	The Central Role of the U2/U6 snRNA Interaction in Spliceosome Structure and Recycling
PhD Aug 2011	<b>Allyson Anding</b> (Clagett-Dame)	Biochemistry	Mechanism of 4-hydroxybenzylretinone Action in Chemotherapy
PhD Dec 2011	<b>Justin Brumbaugh</b> (Coon)	IPiB	Application of Mass Spectrometry to Study Pluripotent Cells
PhD Dec 2010	<b>Marielle Gruenig</b> (Cox)	IPiB	RecA and its Regulators: Surprising Activities
PhD May 2012	<b>Khanh Ngo</b> (Cox)	IPiB	Biochemical Regulations of the Bacterial RecA Protein
PhD Dec 2012	<b>Asher Page</b> (Cox)	IPiB	Structural and Biochemical Studies on the <i>Escherichia coli</i> Protein MgsA
PhD Dec 2010	<b>Masaya Hayashi</b> (Craig)	Biochemistry	Molecular Evolution of Mitochondrial J-proteins in Yeast
PhD Aug 2009	<b>Alison E. Meyer</b> (Craig)	Biochemistry	Characterization of the Specialized role of the Ribosome-associated J-protein, Jjj1, in Ribosome Biogenesis
PhD Aug 2011	<b>Brittany Albaugh</b> (Denu)	IPiB	Mechanisms of Acetylation by the Histone Acetyltransferase-chaperone Complex Rtt109-Vps75
PhD Jan 2012	<b>Samuel Oliver</b> (Denu)	IPiB	Context Dependent Protein Interpretation of the Histone Language
PhD May 2011	<b>Michael Goren</b> (Fox)	IPiB	Studies on Stearoyl-CoA Desaturase and Sphingolipid Synthase using a Wheat Germ Translation System
PhD May 2011	<b>David Taggart</b> (Friesen)	Biochemistry	The Baculovirus Transcriptional Regulator IE1 Acts as an Origin-binding Protein to Initiate Viral Genome Replication
PhD May 2011	<b>Rianna Vandergaast</b> (Friesen)	Biochemistry	Domains that Negatively Regulate SfiAP Control Apoptosis During Baculovirus Infection
PhD Aug 2011	<b>Justin Spanier</b> (Hayes)	IPiB	Mechanisms of Vitamin D-Mediated Suppression of Experimental Autoimmune Encephalomyelitis
PhD Aug 2011	<b>Amanda Carney</b> (Holden)	IPiB	The Structural and Functional Investigations of Deoxyaminosugar N,N-dimethyltransferases
PhD May 2012	<b>Nathan Bruender</b> (Holden)	IPiB	A Structural and Functional Investigation of Enzymes Involved in the Biosynthesis of D-Tetronitrose



<b>Degree</b>	<b>Name (Major Professor)</b>	<b>Program</b>	<b>Thesis Title</b>
<b>PhD</b> Dec 2011	<b>Adam Courtney</b> (Kiessling)	Biochemistry	Synthetic Antigens: Mechanistic Probes of B cell Signaling
<b>PhD</b> May 2011	<b>Clinton Morgan</b> (Kimble)	IPiB	<i>In vivo</i> Chemical Reprogramming of Cell Identity: Implications and Applications
<b>PhD</b> May 2012	<b>James Ellinger</b> (Markley)	IPiB	Application and Development of NMR-based Metabolomics Techniques
<b>PhD</b> Aug 2011	<b>Gregory L. Kabachinski</b> (Martin)	Biochemistry	Localization and Function of Priming Factors in Vesicle Exocytosis
<b>PhD</b> Dec 2012	<b>Michelle Kielar Grevstad</b> (Martin)	Biochemistry	Characterization of the Spatial and Temporal Regulations of Ca <sup>2+</sup> -Evoked Vesicle Exocytosis
<b>PhD</b> Aug 2010	<b>Katie Bishop</b> (Pike)	Biochemistry	Mechanisms Mediating Cell- and Species-Specific Regulation of Gene Expression
<b>PhD</b> Dec 2012	<b>Paul Goetsch</b> (Pike)	IPiB	Integrating Components of the Vitamin D Transcriptional Regulatory Network
<b>PhD</b> Dec 2011	<b>Gregory A. Ellis</b> (Raines)	Biochemistry	Small Molecules to Facilitate Chemotherapeutic Delivery
<b>PhD</b> Dec 2011	<b>Michael N. Levine</b> (Raines)	IPiB	Applications of the Trimethyl Lock in Fluorogenic Enzyme Substrates
<b>PhD</b> Dec 2012	<b>Sean Newmister</b> (Rayment)	IPiB	Structural Investigations of Enzymes Responsible for the Modification of Trichothecene Mycotoxins Associated with Fusarium Head Blight
<b>PhD</b> Aug 2012	<b>Amanda Drennan</b> (Record)	IPiB	Key Conformational Changes of <i>E. coli</i> RNA Polymerase and Promoter DNA in Transcription Initiation
<b>PhD</b> Aug 2012	<b>Sara Heitkamp</b> (Record)	IPiB	Characterization of Transcription Initiation Intermediates for <i>E. coli</i> RNA Polymerase Using Fast Footprinting and Equilibrium and Stopped-flow Fluorescence
<b>PhD</b> May 2012	<b>Matthew Copeland</b> (Weibel)	IPiB	The Structure and Dynamics of Flagella on Swarming Cells of <i>Escherichia coli</i> and <i>Proteus mirabilis</i>
<b>PhD</b> Aug 2012	<b>Marie Foss</b> (Weibel)	IPiB	Chemical-biological Investigation of Subcellular Organization and Cell Division in Bacteria
<b>PhD</b> Dec 2012	<b>Ye-Jin (Jenna) Eun</b> (Weibel)	IPiB	Development of New Physical and Chemical Tools for Studying Microbial Physiology
<b>PhD</b> Dec 2012	<b>Hannah Tuson</b> (Weibel)	IPiB	Bacteria-polymer Interactions: Providing Novel Insights into Environmental Effects on Growth and Motility
<b>MS</b> Dec 2012	<b>Ashley Richie Hoggard</b> (Butcher)	IPiB	
<b>MS</b> May 2011	<b>Anli Feng</b> (Craig)	IPiB	
<b>MS</b> May 2012	<b>Mathangi Srinivasan</b> (Craig)	IPiB	



## Biochemistry Advisor Degree Listings December 2010 - December 2012

Degree	Name (Major Professor)	Program	Thesis Title
PhD Aug 2011	<b>Amanda C. Wollenberg</b> (Amasino)	CMB	Genetic Exploration of the Acceleration of Flowering by Shade and Cold Exposure in <i>Arabidopsis thaliana</i>
PhD Aug 2011	<b>Josh Tietjen</b> (Ansari)	MBTG	Dissecting the Complexity of the CTD Code
PhD Aug 2011	<b>Colleen M. McMichael</b> (Bednarek)	CMB	The Arabidopsis SCD Proteins, Putative Mediators of Clathrin Dependent Trafficking in Cytokinesis and Cell Expansion
PhD Dec 2011	<b>Audrey Klingele</b> (Cox)	Microbiology	Directed Evolution of Radiation Resistance in <i>Escherichia coli</i> : Many means to One End
PhD Aug 2012	<b>Jeanette K. Ducett</b> (Craig)	CMB	Activation of the Pleiotropic Drug Resistance Regulon by the Molecular Chaperones Ssz1 and Zuo1
PhD Dec 2010	<b>Lingyin Li</b> (Kiessling)	Chemistry	Synthetic Surfaces to Control Cell Fate
PhD Dec 2011	<b>Rebecca A. Splain</b> (Kiessling)	Chemistry	Synthesis of Galactofuranose-based Acceptor Substrates for the Study of Galactan Biosynthesis
PhD May 2012	<b>Joseph R. Klim</b> (Kiessling)	CMB	Tailored Surfaces for Investigating Human Pluripotent Stem Cells
PhD May 2012	<b>Margaret Lee Wong</b> (Kiessling)	Chemistry	Chemistry for Probing Protein-protein Interactions
PhD Dec 2012	<b>Shane Mangold</b> (Kiessling)	Chemistry	Synthesis and Evaluation of Quinoxalinones as Inhibitors of the Lectin DC-SIGN
PhD Dec 2012	<b>Samira Musah</b> (Kiessling)	Chemistry	Synthetic Substrata to Instruct Human Pluripotent Stem Cell Fate: From Novel Ligands to Functional Biomaterials
PhD Aug 2011	<b>Dyan E. Morgan</b> (Kimble)	CMB	Stem Cells and Differentiation in the <i>C. elegans</i> Male Germline
PhD Aug 2011	<b>Joshua J. Snow</b> (Kimble)	CMB	FOG-3/Tob Can Either Promote or Inhibit Proliferation in the <i>Caenorhabditis elegans</i> Germline
PhD Dec 2011	<b>John J. Jeong</b> (Kimble)	CMB	Interplay Between Cell Cycle Regulators and Developmental Signals in the <i>Caenorhabditis elegans</i> Germline
PhD Dec 2011	<b>Aaron M. Kershner</b> (Kimble)	CMB	Control of Stem Cell self-renewal in the <i>Caenorhabditis elegans</i> Germline
PhD May 2012	<b>Jason M. Peters</b> (Landick)	Genetics	Genome-scale Studies of rho-dependent Transcription Termination in <i>Escherichia coli</i>
PhD Aug 2011	<b>Kuang-Lung Hsueh</b> (Markley)	Biophysics	NMR Investigations of the Rieske Protein from <i>Thermus thermophilus</i> Support a Coupled Electron and Proton Transfer Mechanism and a Diffusion Model
PhD Aug 2011	<b>Jin Hae Kim</b> (Markley)	Biophysics	Investigation of <i>Escherichia coli</i> IscU, Partially-Folded Iron-Sulfur Cluster Scaffolding Protein
PhD Dec 2012	<b>Ziqi Dai</b> (Markley)	Biophysics	Studies of Conformational States of Proteins involved in Biosynthesis of Iron-Sulfur Cluster
PhD May 2012	<b>Natalia S. Morsci</b> (Martin)	CMB	The Role of Kinesin-like Protein 6 in Structure and Function of Ciliated Sensory Neurons



<b>Degree</b>	<b>Name (Major Professor)</b>	<b>Program</b>	<b>Thesis Title</b>
<b>PhD</b> Dec 2010	<b>Omar N.A. Demerdash</b> (Mitchell)	Biophysics	Modeling of Protein Function at the Intra- and Inter-protein Level: Computational Models for Allosteric Hotspot and Protein-binding Prediction
<b>PhD</b> Aug 2011	<b>Christopher M. Bianchetti</b> (Phillips)	Biophysics	Structure and Functional Characterization of Cellulases and Their Interactions with Cellulose
<b>PhD</b> Dec 2011	<b>Aaron N. Bryden</b> (Phillips)	Computer Sciences	Visualization and Analysis of Protein Flexibility
<b>PhD</b> Dec 2011	<b>Aram Chang</b> (Phillips)	Biophysics	Enzyme Structures and Analysis of the Region Specificity in Natural Product Biosynthesis
<b>PhD</b> Aug 2012	<b>He Zhang</b> (Phillips)	Biophysics	Modeling Reaction-diffusion Process in Modular Biomolecular Systems with a Lattice Monte Carlo Algorithm
<b>PhD</b> Aug 2011	<b>Amit Choudhary</b> (Raines)	Biophysics	$n \rightarrow \pi^*$ Interactions in the Molecules of Life
<b>PhD</b> Dec 2011	<b>Nadia K. Sundlass</b> (Raines)	Biophysics	Electrostatic Interactions of Biological Processes: Cellular Internalization of Pancreatic-type Ribonucleases and Salt-bridge Formation in a DNA-wrapping Protein
<b>PhD</b> May 2012	<b>Sayani Chattopadhyay</b> (Raines)	Chemistry	Collagen Mimetic Peptides for Wound Assessment and Healing
<b>PhD</b> May 2012	<b>Michael J. Palte</b> (Raines)	MCP	Characterization and Exploitation of the Glycocalyx for Drug Delivery
<b>PhD</b> Aug 2012	<b>Benjamin R. Caes</b> (Raines)	Chemistry	Catalytic Systems for Carbohydrate Conversions
<b>PhD</b> May 2011	<b>Jacqueline J. Chritton</b> (Wickens)	MBTG	Translational Repression by Yeast PUF Proteins <i>In Vitro</i>
<b>PhD</b> Aug 2011	<b>Amy Cooke</b> (Wickens)	CMB	CAF1 Deadenylation. To Deadenylate or Not: That is the Question
<b>PhD</b> Dec 2011	<b>Yiling Yvonne Koh</b> (Wickens)	Microbiology	RNA Recognition by the PUF Protein Family
<b>PhD</b> May 2012	<b>Jacqueline Baca</b> (Wickens)	CMB	Characterization of a Staufen Homolog in <i>C. elegans</i>
<b>MS</b> Dec 2012	<b>Lauren Michael</b> (Butcher)	Biophysics	
<b>MS</b> Aug 2012	<b>Anthony Fowler</b> (Kiessling)	Chemistry	
<b>MS</b> Aug 2012	<b>Jack Ho</b> (Weibel)	Engineering	
<b>MS</b> Dec 2012	<b>Daniel Pauw</b> (Weibel)	CMB2	

**CMB:** Cellular and Molecular Biology

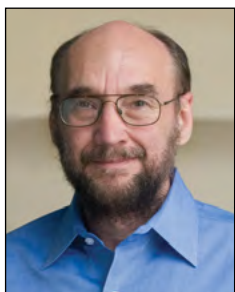
**MBTG:** Microbiology Doctoral Training Program

**MCP:** Molecular and Cellular Pharmacology

## Postdoctoral Training

*Postdoctoral fellows further develop their research and teaching skills, preparing for independent positions.*

By Professor Robert Landick



Postdoctoral training in the Department of Biochemistry has a long and storied history, but has never played a more vital role in our research success than it does today. Currently over 50 postdoctoral trainees conduct research in one of the lab groups led by our 32 faculty. Many are supported on research grants, but at least ten current trainees are supported by individual postdoctoral research fellowships from a variety of sources including the National Institutes of Health, the American Cancer Society, and the Life Sciences Research Foundation.

Research is the primary focus of most postdoctoral fellows. Their scientific accomplishments are too numerous to list, but are a cornerstone in the department's success. Each year, faculty nominate outstanding trainees for the department's Boyer Award for Postdoctoral Excellence, named for Nobel Laureate Paul D. Boyer (see "Boyer Award" essay page 14). This year's recipient is Zachary Campbell, recognized for superior research achievement in Professor Wickens' group.

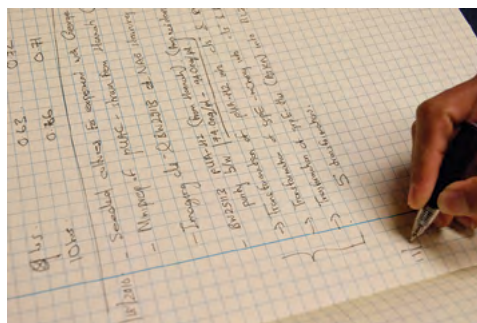
Teaching has become an increasingly attractive career option to many trainees. The Department has responded by creating new opportunities for training in teaching. Trainees have collaborated with faculty to develop lectures in the lab course, Biochemistry 651. Postdoctoral fellows gain teaching experience by developing topics for discussion, and leading seminar sections on a biochemical theme. In Biochemistry 660, trainees work with Professor Wickens to develop lectures on biochemical methods for the incoming graduate students. This approach provides the experience of teaching a course – as many of the postdocs ultimately will do as faculty – but in microcosm, enabling their research to continue unabated. For deeper training, the University of Wisconsin Delta program ([www.delta.wisc.edu](http://www.delta.wisc.edu)) offers a year-long Certification in Research, Teaching, and Learning—an outstanding opportunity for those seeking a teaching career.

Postdoctoral organizations coordinate professional activities and create new opportunities. The UW-Madison Postdoctoral Association for the Life Sciences (PALS) ([www.biochem.wisc.edu/pals/](http://www.biochem.wisc.edu/pals/)), which began in Biochemistry, now is campus-wide. PALS organizes monthly meetings/

social hours with invited speakers that this year have included talks by scientists from local Biotech companies, an intellectual property specialist from the Wisconsin Alumni Research Foundation, and the Director of the Wisconsin Entrepreneurs' Network. PALS also held a poster session and social hour Oct. 25 with prizes donated by BioForward, the Wisconsin chapter of the US Biotechnology Industry Organization, helped organize a Postdoctoral Career Development Conference held at UW-Madison April 6, and has been active in outreach efforts through the UW-Madison Science Expeditions group.

Our postdoctoral fellows are a special group of research scientists at a formative stage in their careers. They often bring new scientific expertise and drive the department's productivity; but they also form critical links with students, faculty and one another. This network brings irreplaceable vitality and unanticipated collaborations.

New developments in postdoctoral training are in the works – tune in to the next newsletter for updates on those initiatives. If you have ideas, suggestions or want to help support our efforts, please contact Bob Landick ([landick@biochem.wisc.edu](mailto:landick@biochem.wisc.edu)).





## IPiB Update

*An update on a critical driving force for excellence and sense of community -- our graduate program, IPiB.*

By Professor Ivan Rayment



IPiB -- the Integrated Program in Biochemistry -- is the major graduate program in the department, and is a collaboration between Biochemistry and Biomolecular Chemistry. As we prepare to welcome our eighth incoming IPiB class this fall, we will try to bring you up to date on the program and its graduates.

The IPiB program consistently ranks among the top ten graduate biochemistry programs in the U.S., and enjoys a stellar international reputation for its ground-breaking research and high-caliber students. Our first PhD degree was conferred in the Fall of 2010 – only four years after IPiB accepted its first graduate class. Since then, 64 PhDs and 10 MS degrees have been earned by graduate students mentored by faculty in Biochemistry and Biomolecular Chemistry. The majority of our graduates have gone on to postdoctoral programs.

To find out what some of our IPiB grads are doing with their degrees, check out the IPiB website at [http://ipib.wisc.edu/ipib-welcome/?page\\_id=27](http://ipib.wisc.edu/ipib-welcome/?page_id=27).

Currently, 111 students are enrolled in the IPiB graduate program. In February and March, the departments of Biochemistry and Biomolecular Chemistry hosted approximately 60 students who have applied to the IPiB program for entry in the Fall of

2013. During one of three recruiting weekends, prospective students have had an opportunity to meet with faculty to learn about their research firsthand, to ask questions and share stories with IPiB student hosts, and to experience everything that Madison has to offer.

Current IPiB students play an active role in the recruitment weekends, escorting guests from their hotel to their meetings on campus, serving as a resource on campus life and the rigors of the lab, and arranging “down time” activities, such as rock climbing and museum haunting. These IPiB ambassadors offer the best perspective to the recruits, because they know first hand what it is like to study and live in Madison!

The program is also gearing up for its biennial Student Retreat in September 2013 at the recently renovated Overture Center on State Street. The Retreat will be a day-long opportunity for students to share their science through oral or poster presentations, possibly uncover new collaborative opportunities, in a setting separate from the focus of work in the lab. To demonstrate that we are

not all-work-and-no-play, some of the entertainment at the Retreat will be presented by members of IPiB in the form of a band. Pearl Snaps is a rock cover band whose members are graduate students: Paul Wrighton and Ginny Kincaid (both IPiB and Kiessling Group members), Andrew Reidenbach (IPiB - Pagliarini Group), and Spencer Scholz (Chemistry - Tehshik Yoon).



**Pearl Snaps:**

Andrew (drums), Spencer (bass) Paul (guitar) & Ginny (vocals & guitar)

Are you a former member of IPiB? If so, please contact us ([alumninews@biochem.wisc.edu](mailto:alumninews@biochem.wisc.edu)) and let us know how being in Madison has benefited your current occupation. Feel free to share a memory from your graduate student days, or tender some advice for current students and you might be featured in our next newsletter or on our web page.

Keep in touch!! Like the Department on Facebook  
[facebook.com/UWMadisonIPiB](https://www.facebook.com/UWMadisonIPiB)

## SFLC IPiB Student Faculty Liaison Committee

*The Student Faculty Liaison Committee, a graduate student organization, reports on its extensive work to support graduate training and serve the Biochemistry community.*

By Loren LaPointe Chair IPiB SFLC 2012-2013



The goals of the SFLC are broad, and draw on students, faculty and outside participants. Let us highlight a few of our recent projects and innovations.

**Foster connections between students and faculty.** Our social chairs work hard to put on annual events to provide an opportunity for department members to socialize, network, and have a little fun together. In 2011 **Kelly Stecker** (Sussman) and **Shruti Waghray** (Wickens) had record turnout for the Halloween and Holiday parties and added a new tradition to our annual costume and ornament competitions: an antique centrifuge from Prof. Dave Nelson to display as a trophy! The trophy will be recycled each year as a new lab gets bragging rights. So far, it resides in the Raines Lab. **Andrew Reidenbach** (Pagliarini) and **Ginny Kincaid** (Kiessling) have taken the reins in 2012 as our social chairs and are in the midst of organizing the biggest social event of the year, the Holiday Party.

**Discussion of career options.** **Chelcie Eller** (Raines), who served as SFLC Chair 2011-12, organized Life Sciences Career Day, a very successful campus-wide event for students and post docs to get information about various career paths for science PhDs through panels of professionals as well as small break out sessions. Hundreds of students participated, not only from IPiB, but including Microbial Sciences, Cellular and Molecular Biology, Cellular and Molecular Pathology, and others!

**The Biochemistry Retreat.** In Fall 2011 the IPiB SFLC brought back the annual Biochemistry Retreat, headed by **Justin Spanier** (graduate of Hayes), with a lot of help from **Khanh Ngo** (graduate of Cox Lab and SFLC Chair 2010-2011). The department hasn't held a formal retreat in several years and we are hoping to

keep it a bi-annual event that is productive and well attended by the department. The retreat features awards and a student speaker elected by graduate students, among other great talks by faculty, students, and post-docs. **Joe Klim** (a CMB graduate of the Kiessling Lab) was voted to speak at the retreat in 2011, and we also had the pleasure of hearing an excellent talk about the history of our department during dinner by **Prof. Dave Nelson**. **Darryl Wesener** (Kiessling) is taking charge of planning the 2013 Biochemistry Retreat (Date TBA in September 2013), which will be held downtown at the Overture Center. It should be very exciting and we hope to see everyone there!

**Invited speaker.** The students of the department nominate a faculty member to speak here at UW-Madison. **Graham Erwin** (Ansari) has been the chair of this committee for the past two years and organized our event in October 2011 where we invited Prof. David Bartell from MIT to give a talk on his work on microRNAs, ~22-nucleotide transcripts that bind to protein-coding genes and repress translation. Graham is also organizing this year's event, which is coming up in December and we have invited Prof. Ed Boyden. Prof. Boyden develops tools for controlling and observing dynamic circuits of the brain, and uses these neuro-technologies to understand how cognition and emotion arise from brain network operation. In 2010, his work on optogenetics was recognized as the

"Method of the Year" by *Nature Methods*, and in 2011 he also gave a TED talk. We are very excited to host him as our student-invited speaker!

**Outreach.** Our 2011 Outreach Chairs were **Basu Bhattacharyya** (Keck) and **Erin Ronayne** (Cox) and the current chairs are **Basu Bhattacharyya**, **Chrissy Petzold** (Keck), and **Andrew Reidenbach** (Pagliarini). They led us to:

- ☞ a set of themed experiments in the Wisconsin Science Festival in both 2011 (The Central Dogma) and 2012 (Sweet Science – the Biochemistry of Sugars).

- ☞ participation in the Second Harvest Food Bank every year and this past October we helped sort 2000 pounds of eggs to donate to local food banks!

- ☞ volunteer at the Science Olympiad at West High School on December 15th.

If you have further ideas for outreach activities please contact Basu, Chrissy, or Andrew!

The website for SFLC has been updated thanks to Sean Johnston (Raines)! The site displays photos from our events, and Sean has also been providing a list of recent publications from IPiB students and post-docs. Check us out at <http://www.biochem.wisc.edu/sflc/>, or link to us via the IPiB website under "Current Students." On the website, you also will find all of our officers' emails and upcoming events.

Please contact us if you have any questions or would like to become more involved!





## UBSO Update (Undergraduate Biochemistry Student Organization)

*An undergraduate organization that facilitates education, research and career planning.*

UBSO functions as a community group for students interested in biochemistry to connect, share ideas, learn from each other, and even have some fun while doing it! UBSO is dedicated to advising its students as well as providing information about job and internship opportunities through meetings and seminars.

Students also have the opportunity to get involved in the community and on campus through UBSO. Meetings are typically 6 pm on Wednesday nights twice a month. There are no membership dues or requirements to become a general member. For more information or to be added to our email list, contact [teamubso@gmail.com](mailto:teamubso@gmail.com) or visit <http://ubso.weebly.com/index.html>.

UBSO provides a special opportunity for undergrads to meet and help one another, learn about the exciting research going on in the department, and to think creatively about science!

### *A few things UBSO has been doing:*

**Orientation:** A few UBSO veterans helped with the Freshmen Biochemistry Orientation program. We gave incoming freshman a tour of the Biochemistry buildings and fielded questions about the organization, classes, and life on campus.

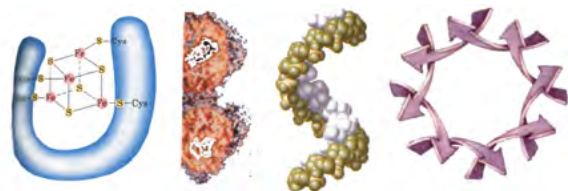
**Mentoring:** UBSO continued its peer mentoring program that launched in 2011. Upperclassmen paired with freshman biochemistry students explain the ins and outs of the department. The mentorship program also provides an opportunity for incoming students to ask questions about time management, how to navigate university resources, and how to make the most of the college experience in order to ease the transition to college.

**Advising:** Each semester UBSO hosts a meeting geared towards exploring the course requirements of the

biochemistry major. Students exchange advice on balancing courses and encourage underclassmen to utilize the excellent professional advising services provided by the biochemistry department.

**Talks by outside speakers:** UBSO helps to illuminate opportunities for graduates by hosting speakers from medical schools, graduate schools, Teach for America, and the biotechnology industry.

**Meetings:** Students in UBSO benefit from learning about professional development opportunities such as "How to get into a Research Lab," "Study Abroad," "How to Write a Research Proposal," and many others.



UW-Madison Memorial Union Terrace

Photo: Jeff Miller

### Science IS Art

Microchannels that create patterns of fluid: The Memorial Union Terrace Chair



Design: Piercen Oliver, Weibel Lab. Photo: Robin Davies



Photo: Jeff Miller

# Remembering Paul Kaesberg

By Professor Paul Ahlquist

Paul Kaesberg, the W.W. Beeman Professor of the Department of Biochemistry and Institute for Molecular Virology, passed away on December 24, 2010 at the age of 87. Paul will be widely remembered for his fundamental contributions to multiple areas of virology, his generous mentoring of students and postdocs, and his roles in initiating some important institutions in the field. His colleagues will also miss his dry wit, administrative insights and other counsels, which all proved valuable in many situations.

Paul was born in Germany but emigrated at age two with his family to the US, settling in West Bend, Wisconsin. Paul conducted graduate studies in Physics at UW-Madison in the laboratory of William Beeman, where he developed X-ray scattering methods for studying biological macromolecules. Paul completed his PhD in 1949, and shortly afterward joined the university faculty in Physics. In 1955 he transferred to the Department of Biochemistry, and remained in that department through the rest of his career.

In 1961, Professors Kaesberg and Beeman founded the University's Biophysics Laboratory, which in 1966 occupied its present site in Bock Laboratories, adjacent to the Biochemistry Department. Paul chaired the laboratory from 1969 through 1988, the longest serving chair to date. In 1987, under his guidance, the laboratory name was changed to the Institute for Molecular Virology to reflect the evolution of its research directions.

Early in his research career, Paul began to turn his attention to viruses as sources of uniform biological complexes that could be purified for physical studies. His subsequent research was characterized by a series of breakthroughs so fundamental to virology that present students can hardly imagine a time when these cornerstones of the field were not known. Prominent examples include some of his early insights from physical studies on the structure of infectious virion particles. Such virions were known to be nucleoprotein complexes, but their organization was uncertain. Paul's early small angle X-ray scattering studies were the first to demonstrate that such particles consisted of an outer protein shell with the nucleic acid on the inside.

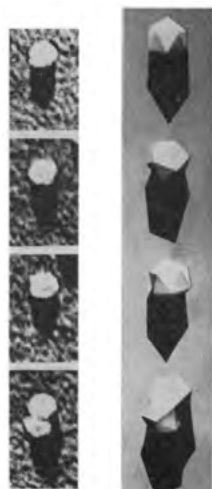
One of Paul's initial faculty

responsibilities was to be in charge of the University's first electron microscope. His X-ray scattering studies and expanding electron microscope investigations contributed substantially to growing evidence that a large fraction of viruses produce virions with an approximately spherical shape. Even more importantly, Paul used ingenious electron microscope



Paul Kaesberg with his electron microscope in the early 1950s.

shadowing methods to transcend technical limitations of the time, and to show definitively that these "spherical" virions possessed icosahedral symmetry (see figure from *Science* article). Such symmetry is now recognized as such a nearly universal principle of isometric virion structure and assembly that the icosahedron has



Structure of Small "Spherical" Viruses  
Paul Kaesberg  
(1956) *Science* 124:  
626-628

Fig. 2a (left). Electron micrographs of heavily shadowed turnip yellow mosaic virus. Because of the heavy shadowing and high contrast printing, the particle contours are much distorted; however, the particle shadows should be clearly delineated. (x about 150,000.) Fig. 2b (right). Icosahedral models of the particles of Fig. 2a.

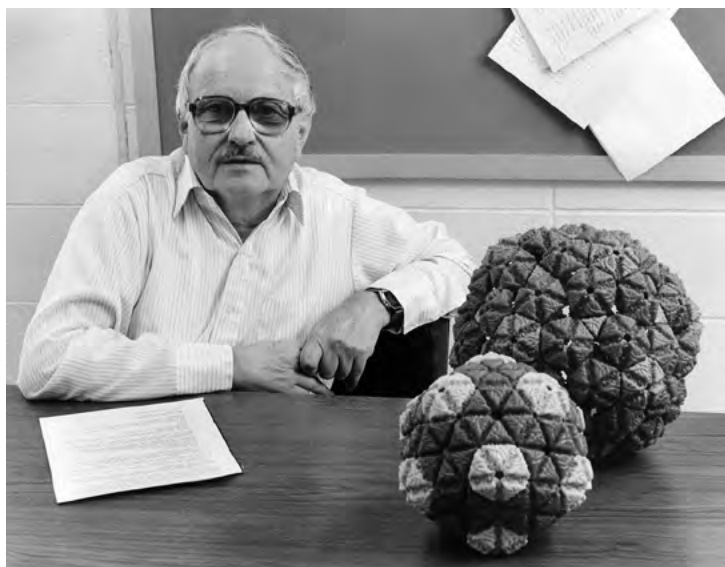
become a widespread symbol for viruses.

Paul complemented his physical studies with a variety of biochemical approaches, including diverse studies of RNA sequence, structure and function. In the course of these, his group advanced early RNA sequencing approaches based on ribonuclease fragmentation. Their results included the first demonstration by direct sequencing that the amber codon is UAG, and early oligonucleotide-based comparisons revealing closely related sequences in certain RNA bacteriophage. This latter work established an early foundation for the more global and sophisticated nucleic acid sequence comparisons that are now commonplace. Later, Paul's group published the first adaptation to RNA templates of Fred Sanger's powerful dideoxy-nucleotide-based DNA sequencing method, providing approaches broadly useful for direct studies of the sequence, structure, protein binding sites and other features of long RNA molecules.

In further studies of virion and viral RNA structure and function, Paul and his colleagues contributed to the recognition of multicomponent, divided RNA genomes, an important feature in the genetics of many viruses. Paul's group was also a pioneer in using *E. coli* and eukaryotic *in vitro* translation systems to study viral RNA coding capacity and expression mechanisms. Among other findings, their results revealed the strong general tendency of eukaryotes to efficiently translate only the most 5'-proximal open reading frames in mRNAs. As part of this work, Paul's group mapped and sequenced the first ribosome binding site from a eukaryotic mRNA, revealing its close linkage to the 5' end. He and his coworkers also demonstrated that in eukaryotic systems, downstream open reading frames in a mRNA are generally not translated, but become translatable when their initiation codon is linked to the 5' end by 5'-truncation of the mRNA.

In the course of his studies, Paul worked with many different viruses, always choosing for each research question one or more agents best suited to the particular biological issues and technical demands of the problem. Accordingly, his papers featured in aggregate a large variety of bacterial, plant and animal viruses. Nevertheless, in nearly all cases,





Paul in 1987-88 with models depicting progressively more complex virion structures with icosahedral symmetry.

the principles revealed by Paul's work have proven broadly relevant to a wide range of virus-host systems.

Among other honors, Paul was a member of the National Academy of Sciences, a Fellow of the American Academy of Microbiology, and a charter member and President (1987-88) of the

American Society for Virology. He was also a charter member of the Biophysical Society. In 1963 he obtained a lifetime NIH Career Award that paid much of his salary throughout his career.

One particularly memorable recognition for Paul and his family was his receipt in 1975 of

an honorary Doctorate of Science from the University of Leiden in the Netherlands. This honor was magnified because it was one of 13 honorary degrees specially awarded on the 400-year anniversary of that University's founding, an event intimately linked with the history of Leiden and The Netherlands. The elaborate week-long festivities included meetings with the

Queen and royal family, and culminated with a formal procession through the central streets of Leiden by the honorees, Leiden University officials and faculty, representatives of many other prominent world universities, and government officials. With all faculty in full academic robes representing the many colors of their disciplines and universities, the procession traveled to the presentation hall cheered by thousands of spectators and trumpet fanfare from adjacent roofs.

Paul's many interests evolved through his life and in later years included cosmology and bridge. A continuing passion was UW basketball. Paul was a season ticket holder for over 60 years and attended a Badger basketball game less than two weeks before his unexpected and peaceful passing. A devoted family man, Paul is survived by Marian, his wife of 57 years, his three sons Paul, James and Peter, two grandchildren, and many grateful students and postdocs. The memory of his accomplishments, humor and generosity will long be treasured by numerous colleagues around the world.

## As we went to press W.W. "Mo" Cleland passes away

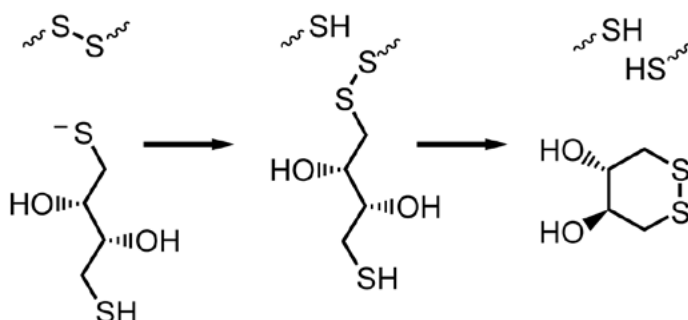


Mo Cleland died on March 6, 2013 as a result of injuries sustained in a tragic accident. Mo was a giant in enzymology. Among his many contributions was bringing about order to the field of multi-substrate kinetics and developing novel methods to examine enzyme mechanisms. He demonstrated the use of dithiothreitol – now commonly known as Cleland's Reagent – as an antioxidant in protein purification and stabilization.

Mo loved sailing on Lake Mendota, was a devotee of the Madison Symphony and Opera, and a serious and a nationally recognized philatelist. He was generous to colleagues and collaborators, and a dominant force in mechanistic enzymology and in our department.

The Department has voted to dedicate its next international Steenbock Symposium to Mo, with a focus on enzymology. A full memorial essay will appear in our next Newsletter. A description of the Steenbock Symposium to be held in his honor appears on page 47. A Fund has been established at the University of Wisconsin Foundation to honor Mo Cleland's contributions to the Department of Biochemistry (fund number 12157778). Although the exact use of these funds is yet to be defined, it is planned that they will reflect his great generosity of time towards graduate students and postdocs.

"Dithiothreitol: a new protective reagent for SH groups".  
Cleland, W. W. (1964) *Biochemistry* 3: 480-482



Reduction of a typical disulfide bond by Dithiothreitol (DTT) aka **Cleland's reagent** via two sequential thiol-disulfide exchange reactions.

## In Memoriam: Masayasu Nomura

Adapted from David Tennenbaum and Millard Susman



Normura while at UW-Madison

Masayasu Nomura, a molecular biologist and professor of Biochemistry and Genetics at UW-Madison between 1963 and 1984, passed away on Nov. 19 of 2011, at age 84 in California.

Nomura's scientific focus was the ribosome, a structure in the cell of all organisms that, under genetic control, assembles the proteins necessary for cellular chemistry and structure.

Using techniques that would be considered primitive today, Nomura performed the amazing feat of disassembling and reassembling the small subunit of the ribosome in a test tube. He discovered how mutations in this machine could make bacteria resistant to antibiotics, and dissected the pathways by which cells control growth through formation of proteins and RNA in ribosomes.

Nomura received his bachelor's and doctoral degrees from the University of Tokyo in the years when Japan was still emerging from the privations of World War II, and he thought he was destined to spend his life in hardscrabble labs working on projects related to agriculture or pharmacology, but his curiosity, scholarliness and bench smarts led to the opportunity to visit the United States in 1957 as a 30-year-old postdoctoral student. During a three-year sojourn in the U.S., Nomura worked with three towering figures in the burgeoning field of molecular biology: Sol Spiegelman, Jim Watson and Seymour Benzer. He came to Madison in the 60's to join the Genetics and Biochemistry

Departments, later as a member of the Institute of Enzyme Research.

Millard Susman, a past Chairman of UW Genetics (now retired), was hired in the same year as Nomura, 1963.

"After his arrival in Madison," Susman says, "he decided that although the ribosome field was very competitive and he wanted to avoid the rat race, he found they were irresistible, so he entered the field, and became Mr. Ribosome. He and his grad students deciphered the mechanism that allows the ribosome to make proteins, taking exact instruction from the genes."

"We occupied neighboring labs in genetics and had daily contact," Susman adds. "He'd talk about what was going on, and I would feel appropriately inadequate. He was really doing earth-shattering research."

"He was one of the most incredibly skilled and influential scientists, but he never got as much credit as he deserved," says Richard Burgess, a professor emeritus of oncology, who collaborated on several papers with Nomura. "He just had a

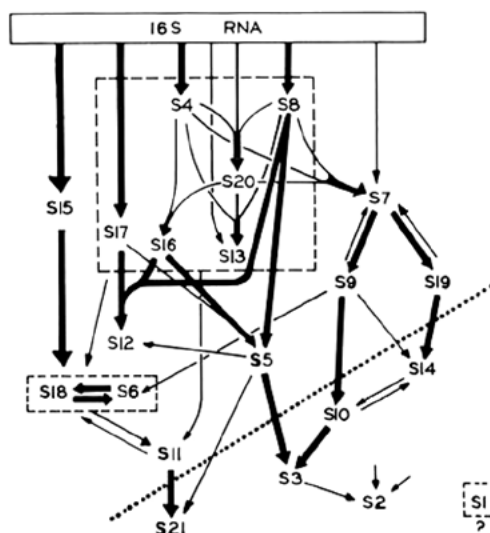


Figure 6. Revised assembly map of *Escherichia coli* 30 S ribosomal proteins.....  
image from:

"Assembly Mapping of 30 S Ribosomal Proteins from *Escherichia coli*". W.A. Held, B. Ballou, S. Mizushima and M. Nomura (1974) *Journal of Biological Chemistry*. **249**: 3103-3111.



Normura in 2009 visiting UW-Madison

fantastic ability to see what needed to be done, and do beautiful experiments to push knowledge forward, and kept going and kept going. I have huge respect for him, as a scientist and a person who was extremely generous and supportive of me when I was a young scientist."

Susman says Nomura, who emigrated from Japan after World War II, was "extremely hard working, he spent hours and hours reading the literature, and was amazingly brilliant at finding ways to answer scientific questions. He was a magical laboratory worker, and his productivity was just amazing. If he had been more assertive, he probably would have won a Nobel Prize."

Bill Reznikoff, a former Biochemistry faculty member, remembers Masayasu as a quiet but warm person. "At first, I wondered whether he was too reserved to teach undergraduates. Nevertheless, I asked him to give a lecture/demonstration in an undergraduate laboratory course in molecular genetics. It was a magical experience – both for the students and for me. He set up an experiment with his own hands and walked the students through the question being asked and the techniques used and then solicited their input in interpreting the results. It was a model in how to educate young students to be scientists."

While at UW, Masayasu helped nucleate a "Ribosome Group," which included Julian Davies, a Biochemistry

*continued, bottom next page*

### The Rosetta Stone

"Nomura's 'Assembly Map', which provided the instructions to assemble the 30S ribosome, was the Rosetta Stone for over 30 years. It was stunning that all the information needed to assemble the ribosome was present in the molecules themselves, and that the ribosome could spontaneously assemble. The question remained as to whether the process Nomura observed in the test tube was the same in a cell. Recent work has confirmed that this is indeed the case, but it is a testament to Nomura's pioneering research that it took over three decades of technological advances to make this leap."

-- Jamie Williamson (Scripps Institute)



## In Memoriam: Chris Raetz

By Professor Dave Nelson



Chris Raetz, a member of the UW Biochemistry Department from 1974-1987, died much too young, of anaplastic thyroid

cancer, on August 16, 2011. Chris was born in 1946 in East Berlin, the child of two industrial chemists who emigrated to Ohio when Chris was a boy. He attended Yale University, majoring in chemistry, then did his M.D. and Ph.D. work at the Harvard Medical School. In his Ph.D. research in the laboratory of Eugene P. Kennedy, he extended Kennedy's work on the synthetic pathways to phospholipids of the *E. coli* membrane, using thorough enzymology and very hard work. He spent a post-doctoral year with Herbert Tabor at the NIH, then joined UW Biochemistry in 1974.

While at the UW Chris began a long series of genetic and biochemical studies that led eventually to the elucidation of the entire ten-step pathway for the synthesis of lipid A, the core of the lipopolysaccharide endotoxin of *E. coli* and other Gram-negative bacteria. This (the Raetz pathway) and related problems occupied most of his attention for the rest of his career. He was a generous and supportive colleague, an enthusiastic teacher of undergraduates and mentor of graduate students, and a strong

proponent of careful genetics and rigorous enzymology. He set very high standards for his students and his colleagues, and he lived by these high standards.

Chris left Wisconsin in 1987 to take a position with Merck Research Laboratories, where he eventually became executive vice president for research in biochemistry and microbiology. In 1993 he accepted the chair of Biochemistry at Duke University, where he remained until his death. During the years at Duke, Chris extended his study of lipid biosynthetic enzymes to the crystallographic determination of their structures. He also made major contributions to the analysis of lipids and synthetic intermediates by mass spectrometry. When a consortium led by Ed Dennis of UCSD began the effort to determine the complete lipidome of a mammalian cell, Chris took a major role in that project.

Chris's exceptional qualities as a scientist were recognized with the ASBMB's Avanti Award in Lipids (in 2002), the van Deenen Medal from the University of Utrecht (2006), and his election to the National Academy of Science (2006), among other honors.

Chris produced more than 300 papers that were models of careful science and

good writing. He was a member of the editorial board of the *Journal of Biological Chemistry* and associate editor of the *Annual Reviews of Biochemistry*. The more

than 30 graduate students and 40 post-docs that Chris trained will carry on his tradition of good genetics coupled with good enzymology and critical thinking. But it won't be the same without him.



Chris Raetz while at UW-Madison

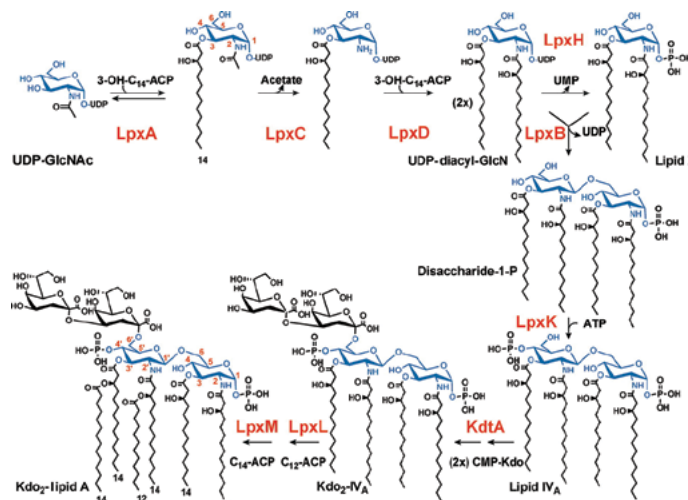


Figure 2. Constitutive pathway for biosynthesis of the Kdo2-lipid A portion of LPS in *E. coli* K-12 ..... image from: "Lipid A Modification Systems in Gram-Negative Bacteria" C.R.H. Raetz, C.M. Reynolds, M.S. Trent, and R.E. Bishop (2007) *Annual Review of Biochemistry* 76: 295-329.

### Nomura continued

faculty member. Julian recalls that it seemed unimaginable that Masayasu had succeeded in taking apart a ribosome and putting it back together again. He notes that "The fact that Masayasu was not awarded a Nobel Prize was a great injustice to one of the best scientists I have ever met."

In 1984, eager to live near more Japanese-Americans, the Nomuras moved to California, where Nomura became the Grace Bell Professor of Biological Chemistry at the University of California-Irvine.

Madison lost something irreplaceable when Nomura moved away. At Irvine,

Nomura continued to work on ribosomes, but he turned from bacteria to yeast. He continued to be a major force in ribosome research and was active in research until the very end, discovering that the molecular genetics of yeast ribosomes was significantly different from that of bacteria and rejoicing at all the surprises that he encountered.

At both universities, Nomura mentored generations of graduate and postdoctoral students. Nomura was much honored. He was elected to the National Academy of Sciences, the American Academy of Arts and Sciences, the American Academy of Microbiology, the Royal Netherlands

Academy of Arts and Sciences, and the Danish Academy of Arts and Sciences. In 2002, he received the Abbott-ASM Lifetime Achievement Award from the American Society for Microbiology.

Basic biology still benefits from Nomura's insights, Susman says. "Nomura showed that the 22 pieces of a ribosomal sub-unit could be put into a test tube and, under the right conditions, they would just glom together into a working structure. It was as if you put a bunch of gears and springs in a box, gave it a shake, and opened it to find that they had come together into a working cuckoo clock. Amazing."

## In Memoriam: Har Gobind Khorana

Adapted from Aseem Z. Ansari, Marsha Rich Rosner, and Julius Adler (*Cell*, 147. 12/23/11)



Gobind Khorana with Julius & David Adler in 1966 while at UW-Madison Biochemistry

Gobind Khorana traversed boundaries, both scientific and cultural. He pioneered the use of chemistry and physics to answer fundamental questions in biology. In particular, he helped decipher how RNA encodes protein, and how light is perceived. His research earned him the Nobel Prize in Medicine in 1968. Although deeply modest and unassuming, Gobind would often remark, “I only work on big problems.” Indeed, only such challenges were worthy of Gobind’s extraordinary intensity, creativity, and focus.

Gobind is an icon for science sans frontiers. He was an early practitioner of what is now known as Chemical Biology. He pioneered new synthetic routes for nucleotide cofactors and oligonucleotides and then used these synthetic molecules to help elucidate the genetic code. He assembled the first synthetic gene, laying the foundation for Synthetic Genomes and Synthetic Biology. In 1971, after he joined MIT, he described the amplification of synthetic genes in a series of enzymatic steps. 15 years later, these were enhanced with a thermostable DNA polymerase, and became PCR. At MIT, Gobind took on lipids and membrane proteins, focusing on rhodopsins until his retirement in 2007.

**From India to UW.** The elegance of Gobind’s work has inspired generations of chemists and biologists around the

world, but has been singularly profound in India. There, Gobind symbolizes the fact that education and talent can overcome socioeconomic and intellectual boundaries.

Gobind began his education under a tree in a small village of a hundred families, who were mostly illiterate. Fortunately, his talent was recognized early, and he went on to Punjab University in Lahore. Although he almost became an English major, he graduated with a Masters in Chemistry and then won a rare fellowship to pursue a Ph.D. in organic chemistry at the University of Liverpool in England.

After obtaining his doctorate in 1948, Gobind enthusiastically moved to Eidgenössische Technische Hochschule (ETH) in Zurich to join the group of Vladimir Prelog, a chemist who won a Nobel Prize in 1975. In less than a year, he had to leave Zurich because his savings ran out. During his brief tenure at the ETH, however, Gobind serendipitously encountered the little known work of Fritz Zetzsche on carbodiimides, which later was crucial in Gobind’s synthesis of nucleotide cofactors and ATP.

Gobind failed to find a position in India, but then received a three-year fellowship with Alexander Todd at Cambridge University. There, Gobind learned of Sanger’s exciting advances in protein sequencing, Perutz’s and Kendrew’s breakthroughs in protein crystallography, and Todd’s own work on nucleic acids. This innovative environment drew Gobind, a synthetic organic chemist, to the newborn field of Molecular Biology.

In 1952, Gobind began his independent scientific career as a nonacademic researcher at the British Columbia Research Council in Vancouver, Canada. His seminal scientific contributions can be grouped into two phases. The first focused on nucleotides and nucleic acids, using carbodiimides to form pyrophosphate bonds, which eventually led to the first synthesis of coenzyme A and ATP. Soon, Gobind wrote to Van Potter, a leading cancer biologist at UW-Madison, asking if he would test his synthetic ATP in rigorous biochemical assays. Van Potter not only obliged with the experiments, but also succeeded in bringing Gobind to the

Institute for Enzyme Research, a vanguard of chemical biology at UW-Madison.

**UW and MIT.** From 1960 to 1970, Gobind was a member of our Department, and Co-Director of the “Enzyme Institute”. During this period, he generated and amplified synthetic oligonucleotides. Using the oligonucleotide CUCUCU, he discovered that the triplets CUC and UCU encode the amino acids leucine and a serine, respectively. Marshall Nirenberg had previously shown that UUU encoded phenylalanine, and Gobind, with characteristic humility, always noted that Nirenberg’s work inspired his own.



Khorana with Nirenberg during the 2009 Steenbock Symposium

Gobind next set his sights on synthesizing a complete gene. Ultimately, he synthesized the coding and regulatory regions of a tRNA gene, and demonstrated that it worked in bacteria. This tour de force defined a framework for biotechnology and, 40 years later, is still used to assemble synthetic genes and genomes.

The second phase of Gobind’s career began after he left Madison for MIT. There, he focused on the mechanism by which intrinsic membrane proteins function and how they interact with phospholipids in the lipid bilayer. His interests led him to bacteriorhodopsin and, eventually, mammalian rhodopsin.

The strategy he chose was a forerunner of contemporary systems biology: sequence the protein, mutate every residue, express and reconstitute the proteins in a native biological context, and then meticulously monitor the phenotypic perturbations. Gobind and his co-workers elucidated how bacteriorhodopsin, and latter mammalian



rhodopsin, pumps protons across the membrane when activated by light.

**The Khorana program.** Inspired by Gobind's story, UW-Madison launched the Khorana Scholars Program. This program places American and Indian students in leading laboratories in the other country, for a transformative summer research experience (see the article on page 20 of this newsletter). In 2007, the year Gobind retired from active research, Gobind generously lent his name to the program. During his last visit to UW-Madison, Gobind met the 2009 scholars. His joy at meeting the future generation of scientists and their passion for science was palpable.



Khorana with Khorana students  
2009 Steenbock Symposium

The respect and warmth felt by Gobind's academic family was readily evident in the periodic "Khorana



Masayasu Nomura and Hikoya Hayatsu with Gobind Khorana  
during the 2009 Steenbock Symposium

Symposia," which were held in various parts of the world. The last such gathering was in 2009 at the 33rd Steenbock symposium on Synthetic Gene to Synthetic Genomes. Many of the scientists that spoke, in describing their current work, noted how Gobind shaped their thinking and how his contributions continue to propel new fields, such as synthetic and chemical biology. As a tribute to Gobind, UW-Madison has made these talks publicly accessible at <http://www.biochem.wisc.edu/seminars/steenbock/symposium33>.

**A devoted family.** Gobind had a deep interest in nature and its beauty; he actively sought solitude in natural settings to think deeply and critically about science.

His beloved wife Esther, whom he lost in 2001, ensured that he was free to focus exclusively on science. Gobind tragically lost his daughter Emily in 1978 but is survived by his loving children David and Julia, who cared for him in his final years. Har Gobind Khorana pursued his work with a single-minded intensity but remained humble to the end. His innate curiosity and appreciation of life (as well as that quick laugh, that slight tilt as he craned his head to listen, and that quizzical look) will remain with those who were fortunate to be his friend. In a collection of his papers published a decade ago, he quoted from Otto Loewi, who could have describing Gobind himself: "We must be modest except in our aims."

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to papers authored with Khorana

(as well as the first two  
in the next issue)

## Honors & Awards

### Faculty

<b>Rick Amasino</b>	2011 American Association for the Advancement of Science Fellow
<b>Aseem Ansari</b>	2011 Romnes Faculty Fellowship 2012 Keck Foundation Grant
<b>Sebastian Bednarek</b>	2011 Vilas Associate Award
<b>Mike Cox</b>	2011 American Association for the Advancement of Science Fellow
<b>Paul Friesen</b>	2012 American Society for Virology Lifetime Membership Award
<b>Colleen Hayes</b>	2012 Scientific Researcher Award, National Multiple Sclerosis Society
<b>Hazel Holden</b>	2011 Kellett Award
<b>Laura Kiessling</b>	2011 WARF Named Professorship 2012 Murry Goodman Memorial Prize 2012 ACS Claude S. Hudson Award
<b>Judith Kimble</b>	2012 Elected to serve on National Medal of Science Award Comm.
<b>James Ntambi</b>	2012 FASBMB Teaching Award 2012 Elected to serve on AAS IOM Food and Nutrition Board
<b>Dave Pagliarini</b>	2011 Glenn Award 2011 Searle Scholar 2011 Ellison Medical Foundation New Scholar Award (declined) 2012 Shaw Scientist Award
<b>Ann Palmenberg</b>	2012 American Society for Virology has created 2 "Ann Palmenberg Junior Investigator Awards" to be given annually in her honor
<b>Wes Pike</b>	2012 Louis V. Avioli Award Recipient 2012 Career Award for Vitamin D Research
<b>George Phillips</b>	2012 American Association for the Advancement of Science Fellow
<b>Ron Raines</b>	2012 Finalist in Inaugural WARF Innovation Awards 2012 Chicago Clean Energy Challenge Award
<b>John Ralph</b>	2012 Fulbright Grant 2012 Stanford's GCEP (Global Climate and Energy Program) Distinguished Lecturer Award
<b>Ivan Rayment</b>	2012 WARF Named Professorship
<b>Mike Sussman</b>	2012 Named Bascom Professor
<b>Doug Weibel</b>	2012 NIH New Innovator Award 2012 Gates Foundation Grand Challenges Grant
<b>Marv Wickens</b>	2011 Elected to American Academy of Arts and Sciences

### Staff

<b>Dan Barnish</b>	Dept. Office	2012 Excellence in Higher Education Award
<b>Mark Meyer</b>	Pike	2012 ASBMR Young Investigator Award 2012 Vitamin D Workshop Travel Award
<b>Yuki Tobimatsu</b>	Ralph	2012 Best Research Poster Award Plant Cell Wall Gordon Research Conference 2012 ASPB Robert Rabson Award



## Postdoctoral Staff

Lars Renner	Weibel	2011 Paul Boyer Postdoctoral Excellence Award
Zak Campbell	Wickens	2012 Paul Boyer Postdoctoral Excellence Award

## Postdoctoral Fellowships

<b>2011</b>	J. Kyle Friend	Kimble	American Cancer Society
	Thomas Ream	Amasino	Life Science Research Foundation
	Chen-Yu Wang	Attie	American Diabetes Association Mentor Based Fellowship
	Zachary Campbell	Wickens	NIH Ruth L. Kirschstein National Research Service Award
	Paul Grimsrud	Pagliarini	NIH Ruth L. Kirschstein National Research Service Award
	Matthew Kotlajich	Landick	NIH Ruth L. Kirschstein National Research Service Award
	Nicholas McGrath	Raines	NIH Ruth L. Kirschstein National Research Service Award
	Langdon Martin	Raines	NIH Ruth L. Kirschstein National Research Service Award
	Jamie Verheyden	Kimble	NIH Ruth L. Kirschstein National Research Service Award
	Tonya Zeczycki	Cleland	NIH Ruth L. Kirschstein National Research Service Award
<b>2012</b>	Sarah Brenner	Weibel	Hartwell Postdoctoral Fellowship
	Matthew Bruss	Attie	Trainee on the Molecular and Applied Nutrition T. G.
	J. Kyle Friend	Kimble	American Cancer Society
	Thomas Ream	Amasino	Life Science Research Foundation
	Hannah Seidel	Kimble	Life Science Research Foundation
	Scott Aoki	Kimble	NIH Ruth L. Kirschstein National Research Service Award
	Zachary Campbell	Wickens	NIH Ruth L. Kirschstein National Research Service Award
	Kevin Desai	Raines	NIH Ruth L. Kirschstein National Research Service Award
	Paul Grimsrud	Pagliarini	NIH Ruth L. Kirschstein National Research Service Award
	Matthew Kotlajich	Landick	NIH Ruth L. Kirschstein National Research Service Award
	Matthew Kraft	Kiessling	NIH Ruth L. Kirschstein National Research Service Award
	Nicholas McGrath	Raines	NIH Ruth L. Kirschstein National Research Service Award
	Jamie Verheyden	Kimble	NIH Ruth L. Kirschstein National Research Service Award
	Tonya Zeczycki	Cleland	NIH Ruth L. Kirschstein National Research Service Award

## Graduate Students

<b>2011</b>	Brittany Albaugh	Denu	2011 IPiB Graduate Teaching Excellence Award
	Matthew Copeland	Weibel	2011 IPiB Graduate Mentoring Award
	Michael Goren	Fox	2011 Sigrid Liermo Memorial Award in Biochemistry
	Angela Gruber	Cox	2011 Keystone Symposia Travel Scholarship
	Audrey Klingele	Cox	2011 Graduate School Vilas Travel Award
	Matt Mead	Hull	2011 Travel Award
	Jonathan Mitchell	Friesen	2011 American Society for Microbiology Student Travel Award
	Asher Page	Cox	2011 Graduate School Vilas Travel Award
	Asher Page	Cox	2011 Vilas Research Travel Award
<b>2012</b>	Ben Knowles	Record	2012 IPiB Graduate Teaching Excellence Award
	Hannah Tuson	Weibel	2012 IPiB Graduate Mentoring Award
	Kelly Hoadley Manthei	Keck	2012 Sigrid Liermo Memorial Award in Biochemistry
	Nathaniel Byers	Friesen	2012 American Society for Virology Student Travel Award
	Ben Knowles	Record	2012 Gordon Biopolymers Conference Graduate Best Poster
	Maggie Strable	Ntambi	2012 Cell Metabolism Oral Presentation Award
	Josue Baeza	Denu	2011-2012 Biological Scholars Award
	Michael Bellecourt	Landick	2011-2012 Biological Scholars Award
	Lucas O'Neill	Ntambi	2011-2012 Biological Scholars Award
	Ian Windsor	Raines	2011-2012 Biological Scholars Award
	Matthew Zmudka	Holden	2011-2012 Biological Scholars Award

**Graduate Students**

**Graduate Fellowships**

<b>2011</b>	Nathan Bruender	Holden	CALS Wisconsin Distinguished Graduate Fellowship
	Matthew Copeland	Wiebel	WARF Scholar
	James Ellinger	Markley	Sam C. Smith Graduate Fellowship
	Ye Jin (Jenna) Eun	Wiebel	Senator Robert Caldwell Graduate Fellowship Award
	Amy Jancewicz	Rayment	2010-2011 Advanced Opportunity Fellow
	Sean Johnston	Raines	Autism Speaks Fellowship
	Douglas Knowles	Record	Arnold & Catherine Denton Graduate Fellowship
	Christopher Lapointe	Wickens	Biochemistry WARF Research Assistant Award
	Khanh Van Ngo	Cox	Genentech Graduate Research Fellowship
	Juan Rodriguez-Molina	Ansari	Jerome Stefaniak Graduate Fellowship
	Sohel Shamsuzzaman	Pike	Ahmad Scholar
	Rebecca Phillips	Rayment	NSF Graduate Research Fellow
	Johnnie Walker	Fox	NSF Graduate Research Fellow
	Darryl Wesener	Kiessling	NSF Graduate Research Fellow
	Jordan Burke	Butcher	Wisconsin Distinguished Graduate Fellowship
	Sean Newmister	Rayment	Wisconsin Distinguished Graduate Fellowship
	Asher Page	Cox	Wisconsin Distinguished Graduate Fellowship
<b>2012</b>	Justin Acheson	Fox	CALS Wisconsin Distinguished Graduate Fellowship
	Joshua Carson	Pagliarini	American Heart Association Fellowship
	Joseph Esquibel	Martin	2011-2012 Advanced Opportunity Fellow
	Sean Johnston	Raines	Autism Speaks Fellowship
	Douglas Knowles	Record	Denton Fellowship
	Christopher Lapointe	Wickens	Genentech Graduate Fellow
	Manohary Rajendram	Wiebel	Mao Wisconsin Distinguished Graduate Fellowship
	Hillary St. John	Pike	DeLuca Fellowship in Biochemistry
	Jonathan Stefely	Pagliarini	NIH Ruth L. Kirschstein National Research Service Award
	Johnnie Walker	Fox	NSF Predoctoral Fellowship
	Josue Baeze	Denu	NSF Graduate Research Fellow
	Virginia Kincaid	Kiessling	NSF Graduate Research Fellow
	Corey Nemic	Ansari	NSF Graduate Research Fellow
	Chrissy Petzold	Keck	NSF Graduate Research Fellow
	Rebecca Phillips	Rayment	NSF Graduate Research Fellow
	Erin Ronayne	Cox	NSF Graduate Research Fellow
	Kelly Stecker	Sussman	NSF Graduate Research Fellow
	Amelia Still	Pagliarini	NSF Graduate Research Fellow
	Darryl Wesener	Kiessling	NSF Graduate Research Fellow
	Kate Helmich	Ralph	WARF Research Assistant Grad Fellow
	Loren LaPointe	Senes	WARF Research Assistant Grad Fellow

**Training Grant Awards**

<b>2011</b>	Nathaniel Byers	Friesen	Trainee on the Madison NIH Virology T. G.
	Matt Mead	Hull	Microbes in Health and Disease T. G.
	Benjamin Mueller	Senes	Computation and Information in Biology and Medicine T. G.
	Maggie Strable	Ntambi	Trainee on the Molecular and Applied Nutrition T. G.
	Robert Presler	Raines	Trainee on the Biotechnology T. G.
	Elena Sorokin	Kimble	Trainee on the Biotechnology T. G.
	Kristen Andersen	Raines	Trainee on the Chemical Biology Interface T. G.
	Christine Bradford	Raines	Trainee on the Chemical Biology Interface T. G.
	Darryl Wesener	Kiessling	Trainee on the Chemical Biology Interface T. G.
	Lauren Michael	Butcher	Predoctoral Trainee on Molecular Biophysics T. G.
	Johnnie Walker	Fox	Predoctoral Trainee on Molecular Biophysics T. G.
	Jordan Burke	Butcher	Trainee on the Molecular Biosciences T. G.
	Lindsay Hoover	Craig	Trainee on the Molecular Biosciences T. G.
	Angela Manlick	Cox	Trainee on the Molecular Biosciences T. G.
	Jonathan Mitchell	Friesen	Trainee on the Molecular Biosciences T. G.
	Katherine Rank	Rayment	Trainee on the Molecular Biosciences T. G.
	Erin Ronayne	Cox	Trainee on the Molecular Biosciences T. G.



## Training Grant Awards *continued*

	James Vasta	Raines	Trainee on the Molecular Biosciences T. G.
	Paul Wrighton	Kiessling	Trainee on the Molecular Biosciences T. G.
	Kristen Andersen	Raines	Trainee on the Molecular and Cellular Pharmacology T. G.
	Alex Carlson	Pike	Trainee on the Molecular and Cellular Pharmacology T. G.
	Neil Daily	Martin	Trainee on the Molecular and Cellular Pharmacology T. G.
<b>2012</b>	<b>Christine Bradford</b>	Raines	Trainee on the Chemical Biology Interface T. G.
	<b>Nathaniel Byers</b>	Friesen	Trainee on the Madison NIH Virology T. G.
	<b>Matt Mead</b>	Hull	Microbes in Health and Disease T. G.
	<b>Benjamin Mueller</b>	Senes	Computation and Information in Biology and Medicine T. G.
	<b>Juan Rodriquez-Molina</b>	Ansari	Trainee on the Genomic Sciences T. G.
	<b>Tucker Carrocci</b>	Hoskins	Trainee on the Biotechnology T. G.
	<b>Robert Newberry</b>	Raines	Trainee on the Biotechnology T. G.
	<b>Douglas Porter</b>	Kimble/Wickens	Trainee on the Biotechnology T. G.
	<b>Robert Presler</b>	Raines	Trainee on the Biotechnology T. G.
	<b>Jan Windsor</b>	Raines	Trainee on the Biotechnology T. G.
	<b>Jordan Burke</b>	Butcher	Trainee on the Molecular Biosciences T. G.
	<b>Angela Manlick</b>	Cox	Trainee on the Molecular Biosciences T. G.
	<b>Paul Wrighton</b>	Kiessling	Trainee on the Molecular Biosciences T. G.
	<b>Rachel Barkley</b>	Rayment	Trainee on the Molecular Biosciences T. G.
	<b>Michael Bellecourt</b>	Landick	Trainee on the Molecular Biosciences T. G.
	<b>Laura Bond</b>	Ntambi	Trainee on the Molecular Biosciences T. G.
	<b>Trish Hoang</b>	Raines	Trainee on the Molecular Biosciences T. G.
	<b>Sean Johnston</b>	Raines	Trainee on the Molecular Biosciences T. G.
	<b>Molly McDevitt</b>	Pagliarini	Trainee on the Molecular Biosciences T. G.
	<b>Jonathan Mitchell</b>	Friesen	Trainee on the Molecular Biosciences T. G.
	<b>Lucas O'Neill</b>	Ntambi	Trainee on the Molecular Biosciences T. G.
	<b>Jarred Renvold</b>	Pagliarini	Trainee on the Molecular Biosciences T. G.
	<b>Katharine Schulz</b>	Harrison	Trainee on the Molecular Biosciences T. G.
	<b>James Vasta</b>	Raines	Trainee on the Molecular Biosciences T. G.
	<b>Kelly Werner</b>	Pagliarini	Trainee on the Molecular Biosciences T. G.
	<b>Brendan Floyd</b>	Pagliarini	Trainee on the Molecular and Applied Nutrition T. G.
	<b>Maggie Strable</b>	Ntambi	Trainee on the Molecular and Applied Nutrition T. G.

## Undergraduate Majors

### *2011 Hilldale Undergraduate Research Fellowship:*

<b>Grant Barber</b> (Pagliarini)	<b>Lauren Buckley</b>
<b>Zeeshan Haq</b> (Record)	<b>Ian Johnson</b>
<b>Michael Kerins</b> (Record)	<b>Austin Krejci</b>
<b>Mark Kraemer</b> (Record)	<b>Michael Montenero</b>
<b>Joel Prince</b> (Raines)	<b>Katherine Omernick</b>
<b>Sonia Trevino-Dopatka</b> (Weibel)	<b>Brian Rekoske</b>
<b>Sang Joon Won</b> (Cox)	<b>Christopher Schmitz</b>

### *2011 ASM Undergraduate Research Fellowship:*

**Sonia Trevino-Dopatka** (Weibel)

### *2011 University Book Store Academic Excellence Awards:* **Desmond Chan**

### *2011 Undergraduate Nucleic Acids Best Poster Award in the Research Poster Competition ASBMB Annual Meeting:* **Joseph Piechura** (Cox)

### *2012 Hilldale Undergraduate Research Fellowship:*

<b>Amy Davis</b> (Raines)	<b>Lauren Hoffer</b>
<b>Brandon Hernandez</b> (Kiessling)	<b>Amy Yan</b>
<b>Athavi Jeezanathan</b> (Pagliarini)	
<b>Benjamin Knight</b> (Mitchell)	
<b>Kellie Kolb</b> (Landick)	
<b>Nathan Menninga</b> (Adler)	
<b>Ryan Sacotte</b> (Weibel)	
<b>Yuliang Leon Sun</b> (Hoskins)	
<b>Michael Voss</b> (Landick)	

### *L&S Honors Program Research Scholarship:*

**Alison Huckenpahler** (Record)  
**Dana Bellissimo** (Record)

### *Trewartha and Mark Mensink Senior Thesis Award:*

**Wenting Cai** (Mitchell)

### *Khorana Program Fellowship:*

**Athavi Jeevananthan** (Pagliarini)

### *SCORE Program Fellowship:*

**Grant Barber** (Pagliarini)

## Great Lakes Bioenergy Research Center

*A cross-campus center for innovative research to produce fuel from biomass includes four Biochemistry faculty.*

By Professor Rick Amasino



The Great Lakes Bioenergy Research Center (GLBRC) was founded in 2008 with the support of the Department of Energy (DOE). There are two other such centers,

the Joint BioEnergy Institute ([jbei.org](http://jbei.org)) in the San Francisco Bay Area, and the BioEnergy Science Center ([bioenergycenter.org](http://bioenergycenter.org)) headquartered in Oak Ridge. This year the DOE renewed all three Bioenergy Research Centers at the same rate of funding as in the previous 5-year award – \$25 million total costs per year for 5 years. The goal of these centers is to perform basic research that will enable the production of transportation fuels from biomass.

Our center is headquartered at University of Wisconsin-Madison and our major partner is Michigan State University. The lead PI for the center is Tim Donohue, a professor in the Bacteriology Department at the UW and our Chief Scientific Officer is Ken Keegstra, a professor in the Department of Biochemistry & Molecular Biology at MSU. Tim and Ken are joined on a management team by nine faculty members from UW and MSU who represent the four scientific areas of the center: 1) improving plant biomass, 2) deconstructing biomass, 3) converting biomass to energy, and 4) fostering sustainable bioenergy practices. (Descriptions of the four research areas are at <http://www.biochem.wisc.edu/newsletters/2008/glbrc.aspx>).

Four Biochemistry faculty currently

serve on the management team: Rick Amasino, Brian Fox, Bob Landick, and John Ralph.

In addition to working in the area of improving plant biomass, I serve as the management team member representing our education and outreach efforts. Our center has devoted a portion of our funding to educating the public about energy issues. Two of my GLBRC colleagues, John Greenler and Leith Nye, work full time on education and outreach, and we collaborate with other education experts such as Hedi Baxter-Laufer (UW) and Charles “Andy” Anderson (MSU). Our efforts include developing classroom materials and conducting workshops for K-12 teachers in the use of these materials, summer research programs for undergraduates that focus on minorities and students from small colleges, and developing computer games that educate in the area of energy in collaboration with a group at the Wisconsin Institute for Discovery (<http://discovery.wisc.edu/home/wisconsin/research/education-research/>). You can peruse many of our materials at <http://www.glbrc.org/education/>.

Presently, most of the ethanol used in fuel comes from corn grain because the starch in corn grain is readily converted to sugar. In biomass, most of the sugar that one hopes to utilize is in cell walls—structures that have, for obvious reasons, evolved to be quite resistant to breakdown. The goal of the deconstructing biomass area is to break down biomass into sugars in an efficient and economical manner which is a major challenge in converting biomass into liquid fuels. One highlight from the Center’s deconstructing biomass

efforts is the discovery of how to use ionic liquids in the break down of biomass into sugars without the need for enzymes or pretreatment steps. This work was done in Ron Raines’ group, and resulted in Ron founding the first start-up company based on GLBRC research. The company, called Hyrax Energy (<http://hyraxenergy.com>), won the 2012 Clean Energy Challenge sponsored by the Clean Energy Trust of Chicago.

This year the Wisconsin Energy Institute (WEI) building opened. The WEI, which is located east of the Enzyme Institute on the corner where University Avenue and Campus Drive meet, is a campus-wide “meta-center” that will bring together many energy-related efforts in research, education and service. It is distinct from, but will interface with, the GLBRC. Areas of focus in the WEI include: liquid fuels for transportation systems; thermal and electrical energy storage and utilization; carbon neutral electricity; policy, economics and societal impact of energy challenges; and energy outreach and service programs. You can read about the WEI at <http://www.energy.wisc.edu>. My GLBRC colleagues in education and outreach will move into the first floor of the building to become part of a larger educational effort, and John Ralph will move his research group into beautifully designed lab space in an upper research floor.

We look forward to another 5 years of working in the important area of sustainable, carbon-neutral fuel production. Follow our progress at <http://www.glbrc.org>.



**Wisconsin Energy Institute**  
UNIVERSITY OF WISCONSIN-MADISON



# From the Emeritus Faculty



**Julius Adler**

My great interest is to find out what is in charge of an organism (if anything!). I pick my research projects to try to get an answer to that.

In charge of a person and of other primates appears to be the prefrontal cortex. That was discovered about 40 years ago by Aleksandr Luria. In fruit flies the analog of the prefrontal cortex seems to be the central complex. We study the fruit fly's central complex

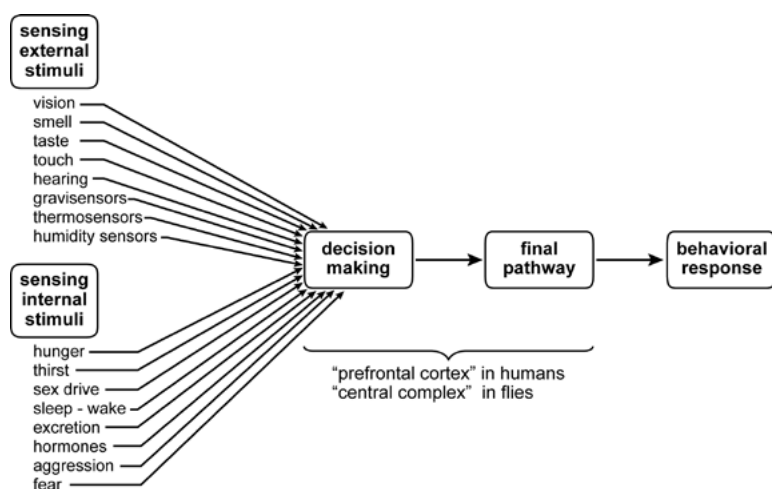
by means of biochemistry and genetics to get at the mechanism involved here, with hope to ultimately expand this knowledge to all other organisms including people.

Some thirty mutants (obtained from Martin Heisenberg, Roland Strauss, and Douglas Armstrong) are now known that are defective somewhere in the fruit fly's central complex but the nature of the defect in each is not yet known. Eight undergraduates and I are trying to find that out. We have shown that five of these thirty are defective in sending a message to the fly's legs and wings. These are the ones we study to find out how "thinking" is translated into "action".

Another approach to this same subject is to study mutants we ourselves have isolated. Normal flies avoid going to an attractant mixed with overpowering repellent. The undergraduates here have found mutants that can't decide what to do ("Towards finding out how a decision gets made: The response of *Drosophila* to conflicting stimuli and the isolation and study of decision mutants", manuscript about to be submitted). Also, normal flies run away from repellents and go instead to attractants. The undergraduates have found mutants that don't know what to do ("*Drosophila* mutants that are motile but fail to respond to any sensory stimuli", manuscript about to be submitted). The defect in each of these mutants will be discovered in order to learn how the central complex functions.

The above thoughts are included in the figure at left.

Recently one of my postdoc heroes (1979!) returned to Madison to visit me, **Marty Springer**. We enjoyed Babcock chocolate hot fudge sundaes. The same will be provided to any of you, please come. Oops! also chocolate sundaes went to visitors **Joe** and **Maddie Sanfilippo**, now graduate students at Indiana.



**Perry Frey**

Research in the Perry Frey Group continues on a smaller scale with departmental support for supplies on two capstone projects. **Dawei Chen** is working part-time on these

projects, with the additional assistance of **Laurie Reinhardt** of the Cleland group, while pursuing other interests. Positive initial results on either project would represent significant progress. Perry continues to collaborate with Professor Shyue-Chu Ke at the National Dong Hwa University, Taiwan on the characterization of free radical species at the active site of lysine 5,6-aminomutase. The most recent advance has led to the identification of a third radical generated from lysine analogues. The collaborative research

includes one of the capstone projects in Madison and continuing research in Taiwan.

Perry resigned as Associate Editor of Biochemistry after 20 years of service. He resigned his last Editorial Board membership with Bioorganic Chemistry, after 25 years of service. Perry also resigned as a member of the Advisory Council to the Redox Biology Center at the University of Nebraska after 12 years of service. He derived satisfaction in these roles but felt that it would be best to make way for younger scientists. Perry has continued to review research papers and has recently written Perspective and Review articles for publication.

Wisconsin alumni of the Frey group are in transition at academic institutions and companies. **Glen Hinckley** moved from Elmhurst College to Farmingdale State College, SUNY. **Kuo-Hsiang Joseph Tang** is developing his productive

research program as Assistant Professor of Chemistry at Clark University in Worcester, MA. **Phil Schwartz** recently moved from Pfizer Research to Takeda California in San Diego. **Kafryn Lieder** operates The Well Tempered Word, LLC in Madison. **Dawei Chen** is in transition while exploring small business opportunities in Madison.

In retirement, Perry is pursuing a new challenge. Never having learned music in his youth, he decided to learn music in his "second childhood" as a student of the piano. After taking lessons for three years, he now regards himself as an intermediate student of the piano, with aspirations to become as proficient as a typical teenaged student. He might reach that level within two or three years. This activity keeps him occupied many afternoons and evenings, year-round. It gives him great pleasure.

The Reznikoff pseudo retirement:



**Bill Reznikoff**

In writing this short report from a Professor Emeritus (*merit = deserve, e = out*; therefore I deserve to be out) I want to thank Marv for asking me to write this document.

Cathy and I doing the same things that we described before – only more so. Cathy has a real passion for working with a Ugandan NGO that serves a whole slum community with a school, a clinic, a credit union, etc. Thank you James Ntambi for introducing us to Uganda and for helping us, particularly Cathy, in our efforts. These efforts include donations of shoes, clothing, computers, etc. that James' study abroad program takes to Uganda; and financial donations that we send on our

own. We were again in Uganda a year ago and had a wonderful and rewarding time.

I am the Director of Education and also of Housing and Conferences at the MBL. I thought that I was retiring from writing grant proposals but now I do it almost continually – but it is worth it. Because the students that I meet who take our research immersion courses come away with career changing experiences. In between the grant proposals I try to help course directors arrange their courses and I have to deal with all sorts of little problems. It keeps me busy and out of trouble.



Rez returns to his youthful hangout - MBL

How long will I continue to do it? I am considering three more years if my health allows.

Speaking of health (and we are in pretty good shape), one problem with aging is that you discover lots of little things that are not quite functioning at an optimal level – like my right knee that doesn't like me to bicycle. But they are small.

I am really sorry to hear that Mo has died. He was an amazing institution in the Department. He did not like molecular biology (until he had to accept the title in order to pick up a student with molecular biology training grant support) but he could be really entertaining and if one needed a volunteer to help undergraduates, he was right there to do it (although what "it" was, was not quite clear). Too bad too sad.

Give us a call if you happen to come to Cape Cod. We would love to see you.



**Roland Ruckert** Splitting birch logs

It's been 16 years since I retired from academia and reinvented myself as a forest manager. Marv Wickens suggests it's time for a progress report. First, we moved two years ago, after 43 years on West Lawn Ave., to Fox Ave two blocks away. Ruth "hated" the north-facing kitchen and leaky windows. I had imagined we'd find a single story house with a double garage where I could shelter my Subaru from the elements during the winter. Ruth

couldn't imagine leaving our neighborhood where there are no such houses. We found the south-facing kitchen she "always wanted" with a sun room overlooking a sheltered back yard perfect for birds and other loveable critters. Ruth loves puttering in "her" garden which is fine with me as I love to putter in "my" woodlands. She has converted the basement into a potting center and laundry. So, as we enter our eighty years of life, we still live in a two-story with

basement and attic and a single garage with my Subaru still facing ice and snow every winter. And we can still walk to Trader Joes, our bank, pharmacy, library and perhaps most importantly, the Laurel Tavern. Oh, the house is tight, warm and requires one-third the amount of energy to heat and air condition.

Meanwhile I spend half my life in our woodlands, a 3 ½ hour drive north to 2374 Rueckert Road, about 5 miles, as the crow flies, southeast of Rhinelander

in Oneida county. Headquarters is a two-bedroom cottage which includes a garage so that in Rhinelander I do not have to scrape snow and ice from my Subaru. On the other hand I have a lot more snow shoveling to do in the front yard. That is actually fortunate because, except for pine pruning, I don't do much forest work in the winter. First, because heavy winter clothing taxes my stamina as I grow older and second because of a wolf pack prowling in my vicinity intimidates me. Paul DeLong, Wisconsin's chief forester assures me there is no record of a wolf attacking a human but that provides him greater assurance behind his desk than it does me when I am alone in the deep snow.

But I digress from my forest manager activities. Our woodland is 310 acres of mixed conifer and hardwood growing in poor to good soil, undulating glacial till presenting a variety of biomes. One hundred acres I inherited from my father; the rest we acquired over the years beginning when I was a student in 1957. Since my retirement at the end of 1996 I have been learning how to manage it. Management, in this case, doesn't mean planting trees. It is more a matter of



selecting “desirable” trees by removing those less so. In the hills and eskers I favor long-lived white and red pine and oak at the expense of short-lived balsam fir which grow like grass but make lovely aromatic Christmas trees. The wet lowlands are dominated by sedge marshes which, the biologist say, have been that way since the last glaciers receded. The drier lowlands are dominated by spruce, fir and tamarack whose roots can survive the anaerobic soil conditions.

When the trails are clear of snow much of my time is occupied by keeping the roads cleared of fallen timber, my source of firewood. I patrol my three miles of logging trails on a sturdy all-terrain vehicle (ATV) carrying necessary tools - chain saw, pole saw, pruning saw, lopping

shears and pruning shears, as the case may be. Bucking the trees into segments, splitting them and piling the firewood is invigorating in the dry cool fall, but sweaty and disagreeable during the humid mosquito season. I also work on esthetics, keeping brush from taking over on trails. But the heavy lifting of forest management is done, not by me, but by a logger. I have, in the last fifteen years had five harvests; each has been overseen by a DNR (Dept of Natural Resources) state forester. His services are paid by a 5% state tax imposed on the harvest. I have been fortunate in selection of my logger, Dennis Schoeneck who happens to be a neighbor, and who this year was selected Wisconsin State Tree Farmer of the Year. After each harvest the woods looks healthier.

I alluded above to wolves. These woodlands are also inhabited by deer, bear, coyotes, bobcat, raccoons, mink, ferret, beaver, muskrats and just recently, I’m assured by locals, by cougar and moose. As for flora I have so far catalogued 142 species, some of which are coveted enough to merit visits by a local nursery which has cloned some of them.

Finally I should mention that we put our woodland under a permanent conservation easement with the Northwoods Land Trust a few years ago. They monitor the land each year to insure it is being managed to their standards. If you are visiting the northwoods, be sure to stop by and visit. I’d be happy to show you what I am doing. 2374 Rueckert Road, Rhinelander WI 54501 (715) 362-4324

### **Steenbock Symposium on Enzyme Structure and Function**

will be held at The University of Wisconsin-Madison, May 22-24, 2014. This symposium is hosted by the Department of Biochemistry, and is in honor of the life of W. W. Cleland, our colleague and friend. The symposium will bring together leading scientists in the field to discuss their most recent research activities, and how they have been influenced by Professor Cleland’s remarkable contributions to enzyme chemistry.

The speaker list includes:

Karen Allen – Boston University  
Richard Armstrong – Vanderbilt University  
Vahe Bandarian – University of Arizona  
John Blanchard – Albert Einstein College of Medicine  
Squire Booker – Penn State University  
Debbie Dunaway-Mariano – University of New Mexico  
Paul Fitzpatrick – Texas A&M  
Judith Klinman – University of California – Berkeley  
Tom Meek – GlaxoSmithKline  
Frank Raushel – Texas A&M  
Nigel Richards – Indiana University – Purdue University, Indianapolis  
Vern Schramm – Albert Einstein College of Medicine  
JoAnne Stubbe – MIT  
Wilfred van der Donk – University of Illinois  
Grover Waldrop – Louisiana State University

Session chairs include:

Perry Frey – University of Wisconsin  
Rowena Matthews – University of Michigan  
Dexter Northrup – University of Wisconsin  
George Reed – University of Wisconsin  
Peter Tipton – University of Missouri  
Chris Walsh – Harvard University

The banquet talk will be given by Professor Paul Cook from the University of Oklahoma, who will tell us about another side of Mo – namely his stamp collecting activities.

The symposium promises to be both a great scientific experience as well as a chance for friends to come together to celebrate the life of our “mechanistic hero.” Organizers for the symposium are Debbie Dunaway-Mariano, Hazel Holden, Frank Raushel, Ivan Rayment, and Nigel Richards.

# From the Labs

## Calling all Past Members of the Department of Biochemistry

We want to hear from you!!!! Let us know what you have been up to. Please remind us of the faculty or facility you worked with and approximately when.

Send updates to:

E-mail: [alumnineews@biochem.wisc.edu](mailto:alumnineews@biochem.wisc.edu) or regular mail in care of the department.

Keep in touch!! Like the Department on Facebook

[facebook.com/UWMadisonIPiB](https://www.facebook.com/UWMadisonIPiB)



### Butcher lab

Greetings from the Butcher Lab! 2012 was a busy and exciting year for us. We purchased the department's first small angle X-ray scattering (SAXS) instrument, which allows us to determine the low-resolution shapes of macromolecules in solution. This instrument is now housed in NMRFAM and has been very popular. **Jordan Burke** demonstrated the power of a combined SAXS and NMR approach by solving the structure of a complex of U2 and U6 spliceosomal RNAs. These RNAs are major components of the spliceosome active site, and among the largest RNA structures ever determined in the solution state. Check out her 2012 paper in RNA, and look for an

even more exciting follow up paper in 2013. Jordan successfully defended her thesis, did a brief postdoc in NMRFAM and then moved on to UCSF where she is a postdoc with Hiten Madhani. **Katie Mouzakis** produced another research highlight for us by investigating the mechanism of ribosomal frameshifting in HIV. This work was recently published in Nucleic Acids Research. Katie defended her Ph.D. and is gearing up to move to beautiful Durango, CO where she has accepted a tenure-track position as an Assistant Professor at Fort Lewis College.

**Ashley Hoggard** and **Lauren Michael** graduated this year with Master's degrees. Ashley gave birth to Albert Elmer Hoggard, a healthy boy born this year on July 18th. Lauren is working on campus at the Center for High-Throughput Computing.

We've had an awesome team of undergrads working in the lab this past year:

**Andrew Lang**, **Preston Easterday**, **Hong Hong Liao** and **Alex Blume**. Andrew and Preston have graduated and Andrew is a medical student at UW-Madison. Preston is currently in the process of applying to medical school. Hong Hong continues to be an energetic and enthusiastic researcher. Alex got off to a strong start and is currently studying abroad in Sweden.

Finally, we welcomed the newest members of the Butcher Lab, **Allison Didychuck** and **Eric Montemayor**. Allison is a very bright first year biophysics graduate student. Eric is an outstanding postdoc from the University of Texas Health Sciences Center at San Antonio and will split his time between our group and David Brow's group in Biomolecular Chemistry. Both Allison and Eric will be working on the spliceosome project, our long-standing collaboration with Dave Brow.



### Cleland lab

*Some time after the following letter was written, on March 6th 2013 Mo Cleland passed away. Mark and I will always remember Mo fondly for his mentorship and his great generosity in sharing his vast knowledge with others. We will also miss stopping in his office to hear a story about some past escapade, the storyline from an opera or old movie he just watched, or some advice on just about anything. Mo lived his life doing what he loved to do everyday.*

In January, **Mo** attended and spoke at the Isotopes in Chemistry and Biology GRC held again in Galveston, Texas. In December, Mo joined a family gathering for Christmas in California. Afterward, he attended the 23th Enzyme Mechanisms Conference held in Coronado Bay, California in early January 2013.

In June post-doc **Tonya Zeczycki**,

scientist **Laurie Reinhardt** and Mo again hosted our collaborators, John Wallace and Paul Attwood from Australia, Sarawut "Yui" Jitrapadkee from Thailand and former Rayment post-doc, Martin St. Maurice from Milwaukee. We discussed our individual results and planned future experiments for our pyruvate carboxylase project. It's always an intense, productive, and enjoyable few days. In addition to the pyruvate carboxylase project, Laurie is continuing to study the mechanism of the reaction of NAD<sup>+</sup> Synthetase (*M. tuberculosis*) and its mutants.

In the summer we warmly welcomed Professor John Marlier from Cal Poly again to come and perform research in our lab. He is working on his project about thioester hydrolysis funded by NSF with co-principal investigators Dr. Kristen Meisenheimer, Emily Fogle, and Lori Robbins.

In addition to John, Associate Professor Mark Snider from the College of Wooster in Ohio came to our lab to perform research this summer. We've known Mark since he was a graduate student (Ph. D '01)

with Richard Wolfenden at North Carolina at Chapel Hill and it's always a pleasure to see and work with him. He is collaborating with scientist **Mark Anderson** on the kinetic isotopes effects of the reactions of enzymes maleamate amidohydrolase and 6-hydroxynicotinate 3-monooxygenase. Mark and Brian Smith (Denu Lab) published their work on nicotinamidase. Mark is continuing their work on Sir2. **Anna Rutkowski** is an undergraduate who now works with Mark on these projects.

**Tania Soerianto**, an undergraduate working with Laurie, was awarded a paid internship at Nostrum Laboratories Inc. in Kansas City, Missouri for the summer 2012. She graduates in May 2013.

There's good job news concerning Tonya! In July, Tonya started as an assistant professor at the school of medicine of East Carolina University in Greenville, North Carolina. She is in the Department of Biochemistry and Molecular Biology. Ann Menefee, who completed her Ph. D. ('09) with George Reed, has joined her lab as a post-doc/lab manager.





## Cox lab

a 6 month sabbatical in the first half of 2012, and used it in part to complete the 6th edition of the Lehninger text. That text was printed just before Thanksgiving. We have some very interesting initiatives going in the lab, and I am looking forward to an exciting 2013. I miss you all and hope you are all in store for a happy and healthy year to come.

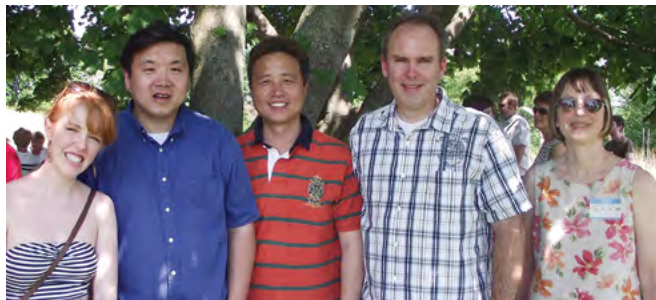
Warmest regards, Mike

## More News:

September 2012 **Rose Byrne** was selected to participate in the ASBMB Public Affairs Advisory Committee's sponsored Fall Student Hill Day in Washington D.C. During this time, students and postdocs from around the country come to Washington D.C. to meet with their own congressional representatives to describe their research and advocate for NIH funding. Rose met with Elizabeth Swartz of Senator Ron Johnson's office and Representative Rehberg of Montana.

(<http://asbmbpolicy.wordpress.com/2012/09/14/a-busy-week-for-asbmbs-public-affairs-office/>)

September-October 2012 **Dmitry Baytin**, **Irina Bakhlanova** and **Alexandra Dudkina** arrived in Madison to work in the Cox lab on an ongoing collaboration that initially began with Dr. Vladislav Lanzov. All three previously travelled to Madison to work in the lab as part of that collaboration.



Mike and Beth Cox had a party at their home in May 2012 and Qun Shan, Xiao-hong Qian and Brian Webb came to help celebrate Mike's birthday along with current lab members Erin Ronayne and Liz Wood.

Hi all,  
It has been a big year here. Perhaps most important, I have recovered almost completely from my very scary 2011 bout with Guillain Barre Syndrome. I had

All are from B.P. Konstantinov Petersburg Nuclear Physics Institute, Department of Molecular and Radiation Biophysics, National Research Centre "Kurchatov Institute", St. Petersburg, Russia.

## Arrivals:

**Stefanie Hartman Chen** joined the lab in November 2012 as a postdoc. She received her B.S. at Virginia Tech in 2005 and her Ph.D. at Duke University in 2012. Her thesis advisor was Dr. Tao Hsieh.

## Goings:

**Audrey Klingele, Khanh Ngo** and **Asher Page** all received PhDs. Audrey is now working at Lucigen. Khanh is a postdoc at UCSF – Mission Bay in the lab of Maria Barna. Asher plans to join the Michael Eck lab at the Dana-Farber Cancer Institute in early 2013.

**Charles Dulberger** left the lab in July 2011 to pursue graduate school at the University of Chicago in the fall. He's now at University of Chicago in the Molecular Biosciences cluster, Biochemistry & Molecular Biophysics.

## Awards:

**Mike Cox** was elected to the rank of AAAS Fellow.

**Erin Ronayne** received the 2012 National Science Foundation Graduate Research Award.

**Asher Page** received the 2011-2012 Wisconsin Distinguished Graduate Fellowship Award.

**Angela Gruber** received the 2011 Keystone Symposia Travel Scholarship to attend the "DNA Replication and Recombination" meeting in Keystone, Colorado. **Asher Page** and **Audrey Klingele** both received a 2011 Graduate School Vilas Travel Award to attend the same meeting.

**Asher Page** also received a Vilas Research Travel Award to work in the lab of Dr. Peter McGlynn at

the University of Aberdeen, Scotland in December 2011.

**Joseph Piechura** received a 2011 Nucleic Acids Best Poster Award in the Undergraduate Student Research Poster Competition at the ASBMB Annual Meeting in Washington, D.C.



Mike had dinner with a few Cox lab alums (Khanh Ngo, Xiao-hong Qian, Sarita Jain, Leslie Waite and Qun Shan) in Albany, CA, summer 2012.

## Past Lab News:

**Sarita Jain** sent news that she joined XenoPort as Senior Director, Business Development. XenoPort is a biopharmaceutical company focused on developing therapeutics for the treatment of nervous system disorders, including neuropathic pain, spasticity and Parkinson's disease.

**Lisa Iype** sent news that she's working for the Institute for Systems Biology in Seattle as a Bioinformatics Scientist.

**Cédric Norais** sent news from France that he's enjoying teaching biology to engineering students and is doing research on the *E. coli* CRISPR system.

**Lukas Bane** is now a graduate student and has joined Dr. Rachele Gauder's lab at Harvard and has been working on determining the structure of an integral membrane divalent metal transporter.

**Joseph Piechura** is now a grad student and has joined the Dr. Erin O'Shea lab at Harvard. He's exploring signal integration into the cyanobacterial circadian clock.

## Engagements:

**Asher Page** and Rachel Fried became engaged the October weekend immediately following Asher's defense.

## Weddings:

**Angela Manlick** and Ben Gruber were married 9/24/11, **Marielle Gruenig** and Falk Eichhorn were married 10/1/11, and April 2012 **Vessela Petrova** and Luke Ensberg were married.

## Babies:

**Akiko Sakai** sent us news from Japan that she and her husband, Ryo Sakasai, had a baby girl (Chihiro).

On July 14, 2012, **Marielle Gruenig-Eichhorn** and Falk Eichhorn had a baby

girl (Fiona Maya Eichhorn).

On August 18, 2012, **Dennis Harris** and Yeajin Song had a baby girl (Naleigh Ann Song).

On October 18, 2012, **TaeJin Kim** and his wife, Yejoong, had a baby boy (Ethan

Dongwook Kim).

November 2012, **Julie Eggington McLachlan** and Adam McLachlan had a baby boy (Michael Robert McLachlan).



## Craig lab

Greetings from the Craig Lab. Much has happened since the last dispatch from the lab. Many comings and goings, and many babies. We welcomed six Craig Lab newborns over a 16 month period, as well as Betty's new grand-child!! A record?? Congrats to the lab's new parents: Amy, June, Sanjith, Jeanette, Hyun-Young and Ji-Yoon.

## THE NEWS:

The big news is that after working half-time for two years **Willy Walter** really did retire. For his retirement party many lab alums sent their memories and amusing anecdotes that made us all laugh. **Tom Ziegelhoffer** joined the lab (again) taking over many of Willy's roles and jumping into the world of cytosolic J-proteins, along with **Hyun Young Yu**.

Two PhD students graduated. **Jeanette Ducett** (nee Waltner) moved on from the world of "what does a ribosome-associated chaperone do when it's not on the ribosome" to the world of "real prions" (not those yeast ones). **Masaya Hayashi**

whose interest in evolution helped lead the Craig lab in that exciting direction has returned to Japan for his postdoc.

Several postdocs are off to new places and new jobs. **Takashi Higurashi** joined the Biotech company EVEC in Sapporo, Japan, a move which had the added benefit of being in the same city that his wife had a job! **June Pais** moved to Boston. As a postdoc at New England Biolabs she is in enzymology heaven (no, we don't get a discount on enzymes). **Justin Hines** is now an assistant professor of chemistry at Lafayette College in Pennsylvania, keeping up his interest in yeast prions. **Chandan Sahi**, who claims to greatly miss the Wisconsin winters, joined the faculty of the Indian Institute of Technology, Bhopal.

**Ji-Yoon Song** has returned to Seoul; both she and her husband snagged coveted jobs at the Samsung Advanced Institute of Technology. Her Fe-S cluster/proteolysis project (how is it and why is it that *Isu*'s half-life can vary from 15 min to two hours) has been picked up by **Szymon Ciesielski**, who recently joined the lab as a postdoc from Gdansk, Poland. Our University of Gdansk connections remain strong. Not only does **Jarek Marszalek** come to the lab for several months each

year as a visiting professor, two visiting students (**Julia Majewska** and **Michal Rogaczewski**) will arrive in March for a year to continue their work on our joint Fe-S cluster biogenesis projects.

**Brenda Schilke** (master geneticist and molecular biologist) continues to bridge all the mitochondria projects, from Fe-S cluster biogenesis to mitochondrial import. IPIB grad student **See-Yeun Ting** has joined the import project. Brenda and See-Yeun make a good team working to understand the amazing complexities of the mitochondrial import motor.

**Amy Prunuske** moved north, leaving the ribosome-associated chaperones and pleiotropic drug resistance behind, and has settled into her new job as assistant prof in the University of Minnesota-Duluth Medical School. **Lindsey Hoover** and **Peter Kuhn** and a new (as of Jan 2012) IPIB graduate student **Kanghyun Lee** now form the core of the ribosome-associated chaperone group (aka "B" group). **Sanjith Yeruva** has also left the lab, returning to India. But **Om Shrestha** who joined the lab (and "B" group) in 2012 continues the same enthusiasm for structure that Sanjith and Jeanette brought to the lab – so the Craig lab's baby steps in that direction will hopefully continue!



## Fox lab

Hello from 141B Biochemistry Addition and 4th floor of Old Genetics. This updates from 2010 to present. In the Biochemistry Addition, the current people, sorted by their lab bay south to north are **Johnnie Walker**, **Taichi Takasuka**, **Justin Acheson**, **Lai Bergeman**, **Chris Bianchetti**, **Mike Mbughuni**, **Kirk Vander Meulen** and **Shishir Chundawat**. The undergraduates working in the lab are

**Ryan Aschenbrener**, **Malak Benslimane**, **Connor Harmann**, **Albert Kim**, **Amy Lim**, **Ben Prom**, **Sung-Soo Kim**, **Cameron Seiser**, and **Taylor Tighe**.

**Justin** is solving structures of toluene monooxygenase and other proteins. During his graduate career, he solved structures of product bound states, has the first crystal structure of toluene bound in the active site of a diiron enzyme, solved the structure of the reductase, and also the hydroxylase-ferredoxin complex at 2 Å resolution. Justin is not afraid of shaking, baking, slicing or dicing any protein in order to get to structure.

**Johnnie**, **Taichi**, **Lai**, **Chris**, **Mike**, **Kirk** and **Shishir** are working on various

biofuels enzymes and their reactions and structures. **Chris**, **Mike**, **Kirk** and **Shishir** joined the lab since my last newsletter contribution. **Chris** is a crystallographer who trained with George Phillips on cellulase structure and function. **Mike** is an enzymologist who trained with John Lipscomb in Minnesota. He is an expert on oxygenases. **Kirk** is a bioinformatics/enzymologist who trained with Sam Butcher. **Shishir** is a chemical engineer who trained with Bruce Dale at Michigan State. Combined with the protein engineering, biochemistry, and molecular biological skills provided by Johnnie, Taichi and Lai, this is a really strong, diversely talented research team. We have

been working on engineered cellulases from thermophilic bacteria and the natural enzyme system produced by a *Streptomyces* isolated by Cameron Currie's group from a microbe/insect symbiotic culture. Seems that wood wasps intentionally inoculate a highly cellulolytic mixture of microbes and fungi into the pine tree when they lay their eggs. This microbial community degrades the wood, contributing to the invasive nature of the insect attack. We have found a number of interesting enzymes that contribute to this natural destructive capability, solved some crystal structures of new enzymes, and have begun to understand the basis of their function in the microbial community.

In the Old Genetics building, CESG transformed itself into PSI: Biology include the Transmembrane Protein Center (TMPC, myself as PI) and the Mitochondrial Protein Partnership (MPP, John Markley and Dave Pagliarini as PI and Co-Investigator) and from Houston, the Natural Products Partnership (NPP,

George Phillips, as PI). Collectively, we make sure that University of Wisconsin maintains their decade-long contributions to the Protein Structure Initiative. The current CESG crew includes **Dave Aceti, Emily Beebe, Craig Bingman, Don Drott, Ronnie Frederick, Andy Geisor, Kashia Gromek, Shin-Ichi Makino, John Primm, Donna Troestler, and Russell Wrobel**. The undergraduates working in CESG are **Marley Crews-Hill, Alexander Declene, Aidan Holmes, Jo Holder, Otto Kletzien, Jessica Liu, Hannah Meddaugh, Kylie Moyer, Trang Nguyen, Kayla Olson, Rachel Schwanz, and Fabian Suchy**.

TMPC is a collaborative project. We identify researchers with interesting membrane proteins that can provide biological and functional insights, and then TMPC discovers how to make the proteins for collaborative studies on structure and function. Some of our collaborators that you may recognize include Katrina Forest (UW Bacteriology), Jay Bangs

(formerly UW Medical Microbiology and Immunology, now SUNY Buffalo), Arnie Ruoho, Baron Chanda and Cynthia Czajkowski (UW Neurosciences), Alessandro Senes (UW Biochemistry), and Celia Goulding (UC Irvine). We have membrane proteins in crystallization screening trials and our project Scientific Advisory Board meeting is coming in a month or so. It is an exciting time, as we are learning many new things about membrane protein structure and function.

I have been Director of the UW Biotechnology Training Program since 2008, and hear about the exciting research of graduate students from four of the colleges on campus. I still teach Biochemistry 625 every spring, with special guest lectures from Mo Cleland and George Reed coming this spring.

To you, the reader of these brief comments, best wishes for the coming year. Please stop into the lab if you are in Madison for a visit. We would be happy to see you.



**Friesen lab**

remain one of five research groups of the Institute for Molecular Virology (IMV) here at U.W.-Madison. Our main research interest continues to be the biochemistry of host-virus interactions by using baculoviruses as a model system. We focus primarily on the virus-mediated events that trigger apoptosis in baculovirus-infected cells. Most recently that interest has led us into a study of the host DNA damage response. We have discovered that not only do baculoviruses induce the DNA damage response in their host but they also encode genes that modulate the response to enhance and expedite aspects of virus replication. How viruses manipulate the host DNA damage response is a hot topic in virology of late.

I have heard from many past members of our research group, several of whom

Greetings to all! I hope that this newsletter finds everyone in good health and happy. The PDF lab is still functioning well from the 7th Floor of R.M. Bock Laboratories. We

I visited with at the annual meeting of the American Society for Virology. These virologists include **Rianna Vandergaast** (IPiB) - a postdoc at the University of Maryland, **Nadine Dalrymple** (IPiB) - a postdoc at Stony Brook University (New York), and **Kim Schultz** (CMB) - a postdoc at Johns Hopkins University. **Doug LaCount** (Biochemistry) is also a regular ASVer - he is professor at Purdue University and recently received tenure there - congratulations! Another very recent visitor to the lab was **Susan Mendrysa**, who with her two young boys stopped by to say hello on their way to visit grandparents near Green Bay. Susan is a professor at Purdue and as you know is also married to Doug. In other alumni news, **Erica Lannan** (MDTP) is now an assistant professor at Prairie State College (near Chicago) and **Becky Cerio** (MDTP) recently accepted a job in the Office of Scientific Program and Policy Analysis at the National Institute of Diabetes and Digestive and Kidney Diseases at NIH. **Erik Settles** (MDTP) is a new Senior Scientist at Pan Genome Systems here in Madison. **Duy Tran** is an IRTA Fellow of Developmental Glycobiology at National Institute of Dental and Craniofacial

Research (NIH). **Mike Guy** is postdoc at the University of Rochester-Medical Center (New York) and **Dave Taggart** is a postdoc at Ohio State University - the school that took the Big Ten Tournament basketball title away from our Badgers this year! I also hear from **Diccon Fiore** and **Melinda Brady-Osborne**, who were our faithful research specialists in the lab. Just last summer, **Kathy Zuehlke** (Hajek) visited the lab as she attended the 50th Anniversary Celebration of the CMB Program here. Kathy is an award-winning science teacher in the greater Atlanta area. Lastly, I look forward to **Steve Pullen's** Christmas card every year - Steve is a longtime Senior Principal Scientist at Boehringer-Ingelheim (Connecticut).

Among current PDF lab members, **Nate Byers** (IPiB) won a position on the U.W.-Madison Virology Training Grant and **Jonathan Mitchell** (IPiB) just finished his stay on the Molecular Biosciences Training Grant. Nate is working on baculovirus IAPs and DNA damage. He'll give his first talk at ASV this summer. It was Jonathan who made the recent discovery that our virus both induces and manipulates the DNA damage response. He recently accepted a postdoc position



with the Lemon group (working on HCV) at North Carolina University. Jonathan is working on his thesis now – and he already has writing cramps!

Anna and I are doing well. I was recently elected as Chair of the IMV so my administrative duties have increased. In addition, I am the principal instructor and administrator for U.W.'s only undergraduate virology course (Biochem/MMI 575). With about 100 students in this information-packed course, I keep busy meeting with students who want letters of recommendation for medical school and students who think I will tell them what will be on the next exam. In reality, I enjoy the teaching and especially the interaction with those students who love virology. Anna continues teaching classes in Pilates and Zumba all the while working at the flower shop as a floral

designer. Our crew of Brittany spaniels at home is now up to three – they keep us busy with healthy walks, hunting, and canoeing on the Wisconsin River on weekends. In between, I have also taken up the marksman's game of skeet. In addition to organizing charity competitions for the American Cancer Society and the Multiple Sclerosis Society, I have even won several WI State championships – who would have thought?

Another labor of love for me has been serving as local host and organizer of the ASV meeting when it is held here in Madison (Monona Terrace Convention Center) every five years. I was commander and chief at the 25th Anniversary Meeting of the ASV in 2006 and took over the 31st annual meeting this past summer for our infamous local host Ann Palmenberg, who had serious health problems last year.

I am happy to report that Ann recovered in time for the meeting and is still doing well – our combined efforts made the 2012 Madison meeting one of the best ever with respect to record attendance (more than 1,500 virologists all in one building), income earned for the Society (student travel grants), extraordinary science, quality Madison brews served, and most important – plenty of fun! Just ask someone about "Virolympics"!

It was good to see old friends at ASV – it seems like half of the virologists in the world have trained or worked in Madison at one time or another. Consequently, one of the highlights of the Madison meeting is always the Badger reunion, wherein all virologists connected to Wisconsin share beer, brats, and stories. Hope to see you there sometime.

Until then, God Bless.



### Kiessling lab

The Kiessling Group has been as busy as ever the past two years, publishing a total of eleven papers between the five project teams (*Chemotaxis*, *Sugar*, *Stem Cell Lounge*, *B Cell Bombers*, and *Multivalency*). While performing this innovative and collaborative research, we still managed to have lots of fun along the way.

Kiessling Group members have received numerous prestigious awards since publication of the last newsletter. For outstanding contributions in the field of carbohydrate chemistry, **Laura Kiessling** received the Hudson Award, the highest honor given by the carbohydrate division of the American Chemical Society. Laura was also recognized for her exceptional communication skills in the classroom by winning the James W. Taylor Excellence in Teaching Award. Kiessling Group graduate students have received significant recognition for excellence as well: **Darryl Wesener**, **Nitasha Bennet**, **Valerie Winton**, and **Virginia Kincaid** were awarded NSF Graduate Research Fellowships while **Heather Hodges** and **Joshua Fishman** were recipients of the Chemical Biology Interface Training

Grant. Additionally, **Samira Musah** received a Graduate Peer Mentor Award from the University of Wisconsin.

Travelling the globe to share recent results from the lab and promote the benefits of working at the interface of chemistry and biology has kept Laura busy. Excitingly, Laura co-chaired the first ever Keystone Symposium on Chemical Biology, entitled "Chemical Biology and Novel Tools in Pharmacology". Several members of the Kiessling Group, as well as other UW-Madison faculty, attended the Santa Fe conference. Everyone, including Laura, found their way to the dance floor at the end of the meeting to celebrate the successful and highly impactful gathering. To stay informed about exciting opportunities like this and innovations in the field of chemical biology, join Laura's 1000+ Twitter followers ([www.twitter.com/chemicalbiology](http://www.twitter.com/chemicalbiology)).

Back in beautiful Wisconsin, the Kiessling Group has not been letting Laura have all the fun. This past summer, the entire lab spent the day paddling down the mighty and majestic Wisconsin River. Inspired by her days on the water at MIT, Laura and daughter Kyra quickly jumped to an early lead and headed the pack. Though it was quite hot and several scary spiders were encountered, everyone safely reached the end of our journey enjoying good laughs and intellectual conversation

along the way. The trip epitomized what the Kiessling Group is all about: working hard, going with the flow (literally in this case), and collaboration with good company.

In lab news, *Team Sugar* continues to do sweet science. Sadly, **Matthew Levensgood** and **Kenzo Yamatsugu** finished their postdoctoral training. Matt has taken a position at Seattle Genetics, and he and wife, Sheeny, recently welcomed a beautiful baby girl to their family. Kenzo is the newest faculty member in the Department of Chemistry at the University of Tokyo. Helping to lead *Team Sugar* is **Matthew Kraft**, our newest postdoc. Matt has already gained renown for his skills in the lab and in science writing, winning an NIH Postdoctoral Fellowship. With the departure of graduate students **Christopher Brown** and **Becca Splain** there were large shoes to fill on *Team Sugar*. Graduate students **Valerie Winton**, **Virginia Kincaid**, and **Philip Calabretta** have accepted the challenge. With **Darryl Wesener** and **Mario Martinez** passing their prelims and becoming dissertators, *Team Sugar* is posed to maintain its sugar high.

In the *Stem Cell Lounge*, love is in the air! Lab alum **Lingyin Li** got married over the summer, while current students **Paul Wrighton** and **Samira Musah** both got engaged. Congratulations! Samira

will defend soon and will be heading to Harvard Medical School to work with Donald Ingber. **Joseph Klim** is already at Harvard in the Eggan Group starting his postdoctoral training. New IPiB student **Yefim Zaltsman** and senior grad student **Paul Wrighton** have been active in sharing the importance of stem cell research with the public through Wisconsin Stem Cell Roundtable outreach programs. Rounding out the team is **Pun Wangkanont**, a former undergrad in the group who has returned to the nest.

*Team Chemotaxis* said goodbye to **Margaret Wong** as she defended her thesis and took a postdoctoral position with Novartis in Boston. Graduate student **Heather Hodges** has picked up the reigns, bringing youthful exuberance to the project. Heather recently adopted a kitten, Tugsly, who is quickly becoming a lab mascot. The Kiessling Group sends our best wishes to former chemotaxer **Anthony Fowler**.

The *B Cell Bombers* added another dissertator to the team last spring as **Nitasha Bennet** passed her prelim. B cell big brother **Adam Courtney** wrapped up his PhD and is now a postdoc in Art

Weiss's group at UCSF. San Francisco is a big change from Adam's small-town Canadian roots, but he seems to be enjoying the beach, working on his tan, and soaking up the big city life. Senior graduate students **Daniel Zwick** and **Rachael Sheridan** continue to be the microscopy and flow cytometry gurus of the lab, while newcomer **Joshua Fishman** brings a strong background in polymer synthesis to the team. We bid farewell to Postdoctoral Fellow **Jonathan Hudon** as he moved overseas to further his training with Peter Seeberger in Germany.

**Team Multivalency** continues to gain insight into the function of DC-SIGN using glycomimetics. **Lynne Probst** finished her tenure as a Postdoctoral Fellow in the Kiessling Group and is now an instructor for the capstone undergraduate biochemistry laboratory course here at UW-Madison. We're elated she moved only one building away and can still visit the lab from time to time! Since receiving his PhD this summer, **Shane Mangold** has returned west to work with Bob Grubbs at CalTech. **Joseph Grim** is holding down the fort and excited to further elucidate the role of DC-SIGN in immunity.

Collaborations between the project teams have been occurring inside and outside of the lab. **Paul Wrighton** and **Virginia Kincaid** performed at the IPiB Art Show last spring with their graduate student band, the Pearl Snaps. The Biochemistry Addition has never rocked so hard! Kiessling Group yoga has become a favorite activity the past few months, involving taking classes at lab members' favorite studios around Madison. Namaste!

In other news, we welcomed **Kayte Cunningham** to the group as a coordinator for the Chemical Biology Interface Training program. **Becca Splain** began her postdoctoral work in the Van Der Donk laboratory at the University of Illinois-Urbana/Champaign. The Kiessling Group wishes the best of luck to **Libby Schmidt** as she finishes her undergraduate degree and ventures out into the world. We'll miss you, Libby!

If you were not mentioned above, it may be that we haven't heard from you in awhile. If you are a former group member, we'd love to learn what you are up to. Please drop us a line and stay in touch. The Kiessling Group looks forward to another highly successful and fun-filled year.



**Kimble lab**

The Kimble lab has seen many significant events since our last newsletter contribution in 2010. Five graduate students have completed their Ph. D. degrees and moved on. **Kyung Won (Kai) Kim** finished her lovely analysis of GLD-2/RNP-8 and its regulation of the oocyte program, and is now doing her postdoc with Dr. Yishi Jin at the University of California in San Diego; **Johan Jeong** integrated the network controlling germline stem cell (GSC) stem cells with the cell cycle machinery and then moved to Stanford University for a postdoc with Dr. Thomas Rando; **Dyan Morgan** laid the foundation for understanding GSCs in XO males and then returned to her home state of Kansas to work with Erik Lundquist in a postdoc that combines research and teaching; **Josh Snow** discovered FOG-3

cell cycle effects with key similarities to its human Tob/BTG homologs and has now joined a Madison biotech company; and **Clint Morgan** completed his innovative analysis of chemical reprogramming the sperm-oocyte decision and then returned to med school to complete his clinical training — he officially gets his Dr. title in June 2013 when he also completes his M.D. We've just learned that he has matched with a residency in surgery here at UW-Madison and so we won't have to say good-bye for a few years!! In addition to those graduate students who left, **Aaron Kershner** completed his Ph. D. degree with ground-breaking work on FBF targets of self-renewal, but then broke the mold and decided to stay on to analyze *lst-1* and *sygl-1*, two new and mysterious genes that he discovered towards the end of his thesis research. These new genes are major regulators of GSC self-renewal and very exciting!! The one other departure has been **Dr. Jamie Veryheyden**, a postdoc who made important contributions to the sperm-oocyte decision, and then moved

across the street as a Senior Scientist in the Genetics Department with Xin Sun.

Despite all the departures and transitions, the lab remains a lively and fun place to be. Some people are continuing and making great progress, while others have just arrived and are finding their feet. Three dissertators are well on their way towards that golden moment of getting their degree: **Elena Sorokin** is making progress toward completing her genomic analysis of sperm-oocyte reprogramming; **Dan Noble** is midstream in his analysis of how FOG-1 and FOG-3 proteins regulate the sperm fate; and **Heiji Shin** joined Aaron Kershner and quickly became a central player in our analysis of *lst-1* and *sygl-1*. In addition, two graduate students started their journeys towards a Ph.D.: **Aman Prasad** began the research phase of his M.D./Ph.D. degree in fall 2012, and **Kim Haupt** joined the lab at the end of the year. It will be fun to see how their thesis projects evolve.

Kimble lab postdocs are also making great strides. Senior postdoc **Dr. Kyle**

**Friend** completed a terrific piece of work showing that PUF and Ago proteins work together in both worms and humans to regulate translational elongation. And now Kyle has secured himself a position for next year on the faculty of Washington and Lee University in Lexington Virginia!! Congratulations Kyle!! In addition, **Dr. Amy Groth**, who is working on Notch transcriptional controls, has accepted a position on the faculty of Eastern Connecticut State University in Willimantic, Connecticut!! Congratulations Amy!! Three other postdocs have joined the lab since the last newsletter: **Dr. Scott Aoki** did his graduate work at Harvard University, working on protein structure, and is now tackling macromolecular complexes that control *C. elegans* germ cell fates; **Dr. Hannah Seidel** did her graduate work at Princeton University working on *C. elegans* evo/devo and has now turned to

the analysis of environmental effects on physiology, including effects of starvation on germline stem cells; and **Dr. Erika Sorensen-Kamakian** did her graduate work on Notch signaling in mammalian cells at the University of Minnesota and is now tackling similar questions in vivo with *C. elegans*.

We've also had a number of talented undergrads in the lab. **Tram Lai, Taylor Bailey** and **Hannah Gemrich** each worked here for a summer, while **Tyler Hansen** and **Andrew Krawczyk** have projects that will develop into senior theses. In addition, **Marco Ortiz** from the Undergraduate Program on Genomic Sciences [National Autonomous University of Mexico (UNAM) in Cuernavaca] was in lab for a year to do a senior thesis project, which he did with **Dan Noble**. After a few months at home to defend his thesis, visit his family and get his visa, Marco has now rejoined us to complete that project and

start his own independent project.

In addition to these comings and goings punctuated by terrific scientific progress, we've also seen a lot of action on the baby front. Is there something in the lab water supply again? In 2011, we welcomed Nathan Friend in October, Anthony William Noble in November and Nathan Geoffrey Kamakian in December; in February 2012, Ethan Myung Wan Aoki arrived and in February 2013, Anika Mohantey was born. Lab parties are lively if a bit hectic!!

**Sarah Crittenden, Anne Helsley, Jadwiga Forster** and **Peggy Kroll-Conner** are also still making miracles happen, each in her own way, to keep the lab happy and thriving. And me (**Judith**)? I'm still hanging in there. That's it for now -- this is obviously the short version of news from the Kimble lab, so please stop by to say hello and get caught up if you are in the neighborhood!!



#### Moving onward and upward:

Four graduate students completed their PhD degrees: **Kuang-Lung Hsueh** in Fall 2011. He is now at the Academia Sinica in Taipei as

#### Markley lab

a postdoc and is applying for academic positions in Taiwan. **Jin Hae Kim** and **Jimmy Ellinger** in the summer of 2012. Jin married recently and is staying on as a very productive postdoc. Jimmy moved to Minnesota in December 2012 to take up a post-doctoral position in the laboratory of Claudia Schmidt-Dannert in the Dept. of Biochemistry, Molecular Biology & Biophysics at the University of Minnesota. **Ziqi Dai** completed his PhD at the end of 2012, has married, and is now working at Epic Systems, a healthcare software company located in Verona.

**Dr. Kiran Sagarapu** and his family have returned to India where Kiran is a Ramanujan Fellow at the Center for NMR and Structural Chemistry, Indian Institute of Chemical Technology, Hyderabad, India. They reported the birth of a baby boy in July 2012.

**Dr. Kaifeng Hu** and his family left

in May 2012 to return to China where Kaifeng is the Principal Investigator of the NMR Group at the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Kunming, Yunnan, China.

**Dr. Arash Bahrami** was recruited to a California start-up company, NetSeer Inc. (Contextual Advertisement Targeting), where he is a Senior Data Scientist.

**Dr. Roger Chylla** resigned his position after becoming lured away to become the Chief Technology Officer at HealthMyne Inc., a Madison-based company developing innovative medical imaging and analytics systems for health care providers.

**Dr. Jordan Burke**, after completing her Ph.D. with Sam Butcher at the end of 2012, joined the staff of NMRFAM as a short-term postdoc. She trained NMRFAM staff members and users in SAXS data collection and analysis for about four months before leaving for a postdoctoral position at UCSF.

**M. Francisca Jofre** has left her part-time job with BMRB and NMRFAM to work full time as an Outreach Specialist in the College of Letters and Science.

#### New graduate students:

**Tala Suidan** a graduate student in the Biophysics Program, joined the lab in

2012.

**Hesamaddin (Hesam) Dashti** another Biophysics student, also joined in 2012.

#### New postdocs:

**Dr. Jameson Bothe** was recruited from the University of Michigan, where he completed his Ph.D. with Hashim Al-Hashimi. Jameson is working on the thermodynamic properties of the IscU system.

**Dr. Jaime Stark** joined from the University of Nebraska, Department of Chemistry, where he completed his Ph.D. with Robert Powers. Jamie is collaborating on metabolomics projects and setting up a small molecule protein screening platform.

**Dr. Vincent Chen** came from Duke University, where he trained with Jane and David Richardson. Vincent has experience in developing software to visualize and validate NMR structural constraints and is splitting his effort between BMRB and NMRFAM.

#### Visiting professors at NMRFAM:

**Prof. Valerie Copie** from the department of Chemistry & Biochemistry at Montana State University is spending part of her sabbatical at NMRFAM during the month of April.

**Prof. Oleg Dmitriev** from the



department of Biochemistry at the University of Saskatchewan, Canada plans to spend a sabbatical at NMRFAM from July 1, 2013, to June 30, 2014. Oleg has been a long-term NMRFAM user starting with his days with Bob Fillingame.

**Prof. E. Sonay Elgin** will be spending a sabbatical in the lab from August 1, 2013, to July 31, 2014. Sonay received her Ph.D. here in 2002.

#### News from former lab members:

**Brian Volkman** and Kristin have a daughter (Emi) born in time for their Christmas card.

**Ian Lewis** and Jen have a second son (Soren) born in March 2013.

#### Grants and Equipment:

**Accelerated Renewable Energy Consortium.** John served as the “corresponding PI” on a grant application to the US Biomass Research and Development Initiative along with UW professors from Ag and Applied Economics, Biological Systems Engineering, Soil Science, and Extension and Soil Net, a small local business. In July, 2012, the group received a \$7 million 4-year grant from the USDA and partnered with Maple Leaf Dairy in Cleveland, WI, which provided a 20% in-kind match. Their project, Accelerated Renewable Energy, has the goals of utilizing cow manure to produce bio-products, reducing the environmental impact of manure, and sustainably maintaining cropland fertility. Technology developed by Wisconsin businesses (Soil Net, Braun Electric, and

FEECO International) will be installed and tested at UW and at Maple Leaf Dairy. Saleable products to be produced from manure include garden mulch, fertilizer pellets, cellulosic ethanol, and protein for animal feed or bacterial culture media. The project also will produce biodiesel from oilseed grown on at Maple Leaf Dairy. For information, see <http://www.ave.wisc.edu/>.

**Mitochondrial Proteome Project (MPP).** We are now into the third year of this project, supported by the PSI:Biological Program of NIH National Institute of General Medical Sciences (NIGMS). MPP is paired with the Northeast Structural Genomics Consortium headed by Guy Montelione. Dave Pagliarini (MPP Co-PI) and John (PI) are attending a “Mid-Course Review” by an external panel at Rutgers in early April. The MPP has over 20 collaborating biologists and biochemists who have nominated targets for structure/function studies. The project is paying off with interesting structures and functional results (<http://www.mitoproteins.org/>).

**NMRFAM.** With the demise of the NIH National Center for Research Resources, the NMRFAM grant was transferred to NIGMS. The Bruker 700 MHz NMR spectrometer on loan from the Great Lakes Bioenergy Research Center, has been moved to part of John Ralph’s space in the new Bioenergy Research Building at the intersection of Old University and Campus Drive. A Bruker Nanostar SAXS system (product of a shared instrumentation grant that Sam Butcher wrote) has been installed and

is now working well and is fully booked by users. See the website (<http://www.nmrfam.wisc.edu>) for information on new NMRFAM software.

**BioMagResBank (BMRB).** The NIH National Library of Medicine (NLM) has funded BMRB since it was founded in 1990, but NLM support will terminate in September, 2014. We met with potential funders (NSF, NIH, and DOE), but none of them provided a positive response. The concern of the biological NMR community over the future of BMRB led to a supportive publication (*Nat Struct Mol Biol.* 2012 19:854-60). We were informed subsequently that NIGMS would consider a “R01” grant application in support of BMRB. John and Eldon submitted a grant application in February, 2013. The BMRB website (<http://bmrw.wisc.edu>) has been revamped and now has greatly improved search capabilities.

#### Meetings and travel:

Several lab members attended the XXVth ICMRBS meeting in Lyon, France last August.

Several lab members will attend the Gordon Research Conference on Computational Aspects - Biomolecular NMR, May, 2013. We look forward to seeing **Ian Lewis**, who has been invited to give a talk there.

#### Late breaking news:

**Woonghee Lee** successfully defended his Ph.D. thesis on April 5, 2013, becoming #43 on the Markley lab Ph.D. list.



**Mitchell lab**

This was a great year for the Mitchell lab! Following excellent results in a CAPRI assessment on classifying *de novo* designed interfaces able to bind, we achieved another

highly competitive result in a blind assessment for predicting mutagenesis effects on protein-protein interactions. Mitchell lab alumni also landed two choice postdoctoral positions. **Xiaolei Zhu** accepted a position with Daisuke Kihara in the Departments of Biological Sciences and Computer Sciences at Purdue University. **Omar Demerdash** completed the MD portion of his MD/PhD work and

will soon begin his postdoctoral work with Teresa Head-Gordon in the Departments of Chemistry, Bioengineering, and Chemical & Biomolecular Engineering and the University of California at Berkeley.



## Ntambi lab

With more hands at the bench, we are expanding our areas of research. In addition to continuing to unravel the role of stearoyl-CoA desaturase-1 (SCD1) in lipid metabolism, we are now investigating the functions of the other mouse isoforms, SCD2-4.

Since 2011, we have said goodbye to **Lacmbouh Ade**, **Matthew Flowers**, and **Xueping Liu**. **Ade** was using tissue culture and mouse models to investigate the effects of SCD1 deletion in skin. After two years in the Ntambi lab, he has moved on to attend medical school here at UW. **Matt** was a postdoctoral fellow in our lab and now is an Assistant Scientist for Jon Levine in the Department of Neuroscience. **Matt** recently published a paper that concluded that combined adipose and liver deletion of SCD1 does not protect mice from obesity. **Liu**, who was also a postdoctoral fellow in our lab, is now working as a research scientist at Regulus Therapeutics located in San Diego. Regulus Therapeutics is a biotech company that uses miRNA technology to design new treatments for diseases such as cancer and diabetes. Before **Liu** left, he finished a project investigating the role of SCD1 deficiency in one-carbon metabolism.

**Ahmed Aljohani** is a new graduate student in the Endocrinology and Reproductive Physiology Program (ERP). He is interested in discovering the mechanism by which SCD1 deficiency protects against high carbohydrate or high fat diet-induced obesity. This work

is directed toward exploring the role of DNA and histone methylation in *de novo* lipogenesis.

**Laura Bond** is a second year graduate student in IPiB. She hails from Rochester, MN and received her B.A. in chemistry from St. Olaf College. **Laura's** project focuses on SCD isoform 3 and fatty acid transport between tissues. **Laura** is mentoring two senior undergraduates, **Tamin Rajakumar** and **Samir Joshi**. **Tamin** is studying another unexplored SCD isoform, SCD4. For her senior thesis project, she is characterizing the SCD4 knockout mouse that our lab has recently generated and aims to determine the effects of deletion of this heart-specific SCD isoform on cardiac fatty acid content. **Samir Joshi** is a senior biochemistry major and has been optimizing genotyping of our newer mouse lines. He graduated in December and will pursue a career as a physician assistant.

**Sabrina Dumas** is a first year Nutritional Sciences graduate student and all of us are excited to welcome her on board. **Sabrina** is originally from Trinidad and Tobago and completed her B.S. in Nutritional Sciences at the University of Arizona. She is interested in studying the ketogenic activity of SCD1 deficient mice. When not in lab, **Sabrina** can usually be found eating pizza, watching movies or running.

**Lucas O'Neill** is a second year graduate student in IPiB. He is originally from Pittsburgh, PA and received his B.S. in Biology at The University of Pittsburgh at Greensburg. **Lucas** is fond of the great restaurant scene in Madison and he loves to spend his time off traveling to places like Noah's Ark and Mall of America. In the lab, **Lucas** is focused on determining the role of SCD2 in a tissue specific manner. Moreover, he is interested in how monounsaturated fatty acids produced by SCD2 affect various physiological functions such as glucose clearance, bone development,

and brain function. Currently, **Lucas** is mentoring two undergraduates **Kyung Kim** and **Jia See**. **Kyung** is a senior and she is investigating the role of SCD2 in smell. **Jia** is also a senior and is studying how fatty acids affect the path of pre-adipocyte differentiation.

**Maggie Strable** is a fifth year Nutritional Sciences graduate student. Her primary research project focuses on understanding the potential differences in the metabolic effects of the hepatic monounsaturated fatty acids oleate and palmitoleate. **Maggie** has two excellent undergraduate biochemistry students working with her, **Nick Friedlander** and **Kristin Harrington**. They investigate the metabolic role of SCD1 in extrahepatic tissues such as the skin and brain. Although **Maggie** is busy with her research projects, she is looking forward to going to Uganda this year with the annual study abroad program lead by Dr. Ntambi and John Ferrick.

**Dr. James Ntambi** continues to teach and lead a study abroad program entitled "International Health and Nutrition" for undergraduates that come from several disciplines across campus. **Ntambi** and his colleague **John Ferrick** teach students in a seminar style course focusing on education, agriculture, culture and healthcare system in Uganda. This is followed by a three week trip to Uganda, during the winter break where the students work in the villages and see nutritional, environmental, and public health problems first-hand. They visit rural health centers, HIV/AIDS clinics, and child nutrition centers. While in Uganda, the students utilize what they have learned in the course to complete a project on resolving an issue of their interest. In addition, the students periodically receive hands-on experiences by participating in the construction of water tanks to provide clean water to the rural communities they visit. Students describe their experience



as unique and transforming. Please take a moment to visit the Uganda program's webpage: <http://www.biochem.wisc.edu/uganda/>.

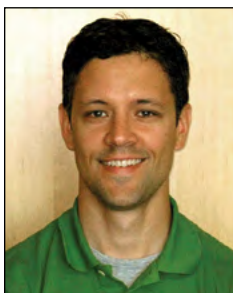
Dr. Ntambi also serves as an advisor for the Village Health Project (VHP). Established in 2005 by his Uganda study abroad students, the organization seeks to aid people by supporting sustainable projects that improve sanitation, nutrition,

and education in rural Uganda; and to facilitate collaboration between the University of Wisconsin-Madison students and Ugandan grassroots organizations in working for this cause.

Dr. Ntambi's involvement with Uganda does not stop there. He is also helping to advance basic research in global health education and training in Africa. As a result of Dr. Ntambi's accomplishments

in scientific research, he has been awarded the American Society for Biochemistry and Molecular Biology (ASBMB) Award for Exemplary Contributions to Education.

You are always welcome to stop by and talk with the members of our lab - our doors are always open. More information about our research and publications can be found on our website: <http://www.biochem.wisc.edu/faculty/ntambi/>



**Pagliarini lab**

Hello from the Pagliarini Lab on the 4th floor of the Biochemistry Addition! This is our first official "Letter From the Lab," having first introduced ourselves in a New Faculty Profile in the last Newsletter. Since that time, we have continued to grow into a diverse and vibrant group of 10 graduate students, 2 postdoctoral fellows, a senior technician and a great team of 6 undergraduates. Together, we continue to study mitochondria – the tiny metabolic machines that comprise 10% of our bodies – and the biochemical underpinnings of mitochondrial dysfunction in both rare and common human diseases. It has been a real privilege to build a research program like this in Madison, where there is a long and rich history of world-class metabolic and mitochondrial research. In particular, our group has developed three focus areas:

**1. Rapid mitochondrial modulation by posttranslational modifications (PTMs).** It's long been known that cells use PTMs for tweaking protein function and for an array of signaling processes. However, the nature and importance of PTMs for regulating mitochondrial function has remained unclear. We believe that PTMs are widely important for properly altering mitochondrial activity to maintain homeostasis, and that elucidating the signaling processes at play could lead to novel therapeutics for metabolic disorders. To that end, we recently published a paper in *Cell Metabolism* – led by postdoc **Paul Grimsrud** and CMB graduate student **Josh Carson** – that describes the dynamic nature of mitochondrial reversible phosphorylation

from the livers of mice following both acute and chronic perturbations. IPiB graduate students **Amelia Still** and **Brendan Floyd** are preparing a manuscript that similarly evaluates mitochondrial reversible acetylation – a PTM whose prevalence and importance now rivals that of phosphorylation. These studies are part of some exciting and productive ongoing collaborations with the Coon, Attie and Denu groups on campus.

**2. Mitochondrial adaptation to nutrient stress.** Changes in nutrient availability often require more drastic alterations to the mitochondrial infrastructure, involving transcription and post-transcriptional processes. In a manuscript recently published in *Cell Reports* – led by CMB graduate student **Jarred Rensvold** – we described the widespread mitochondrial remodeling that occurs when cells are deprived of iron. Our work suggests that mitochondrial dysfunction may be a central problem in iron deficiency, which is the #1 nutritional disorder worldwide.

**3. Functional investigations of mitochondrial proteins mutated in human diseases.** As a postdoc, I led an integrative genomics and proteomics study to define the protein composition of mammalian mitochondria. Four years later, hundreds of proteins in this so-called MitoCarta list have no known function, including many that are associated with human diseases. A long-term goal of my group is to elucidate the biochemical activities of these proteins as a first step toward devising therapeutic approaches for their associated diseases. Toward that goal, I co-direct (along with John Markley) the Mitochondrial Protein Partnership (MPP), a structural genomics consortium that is part of the NIH's larger Protein Structure Initiative (PSI). Members of my group,

including IPiB students **Jon Stefely** and **Andrew Reidenbach**, work closely with the protein biochemists and crystallographers of the MPP to elucidate the structure and function of these key proteins. Jon and Andrew, along with crystallographer **Craig Bingman**, senior technician **Adam Jochem** and undergraduates **Jaclyn Saunders** and **Grant Barber** (now at Harvard Medical School), among others, are preparing a manuscript that describes the structure and function of a novel mitochondrial kinase that is mutated in a cerebellar ataxia.

Fortunately, our early work has helped us to receive multiple honors and awards during the past few years that help to fund our program. **Dave** received Searle Scholar, Glenn Foundation and Shaw Scientist awards. **Paul Grimsrud** received an NIH F32 postdoctoral fellowship. **Amelia Still** received an NSF graduate fellowship. **Jon Stefely** received an NIH F30 Physician Scientist award. **Josh Carson** received an American Heart Association predoctoral fellowship. Undergraduates **Grant Barber** and **Athavi Jeevananthan** received Hilldale awards. Grant and Athavi were also selected to participate in the SCORE and Khorana programs, respectively. **Amelia Still**, **Jarred Rensvold**, **Molly McDevitt** and **Kelly Werner** are funded by the Molecular Biology Training Grant (MBTG), **Brendan Floyd** is funded by the Molecular and Nutritional Sciences Training Program (MANTP), and **Danielle Lohman** is funded by the Biotechnology Training Program (BTP). Last, we are also grateful for our funding from the NIH (NIDDK and NIGMS) and the USDA.

We hope to report exciting new stories from each of our research themes in the next Newsletter. In the meantime, check out our lab website ([www.pagliarinilab.org](http://www.pagliarinilab.org)) for the latest news and publications!





### Palmenberg lab

Hello Biochemistries and other Team Palmenberg alumni! This past year was quite interesting to say the least, and it's time to bring you up to date. **Marchel**, as always has been shepherding students, grant funding and purchasing to keep the lab humming. **Kelly Watters**, **Holly Basta**, **Ryan Petty**, **Valjean Bacot-Davis** and **Jessica Ciomperlik** are all now dissertators and well on their way to respective degrees. **Kelly** had an excellent paper published in *JVI* last year on the rhinovirus 2A proteases, and **Ryan** just had a neat *EMCV* Leader:Ran biochemistry story accepted there as well. About 5 more papers involving various combinations of the whole cast are in the works (as usual, Ann is the slow part) and these include a wonderful modeling story for the rhinovirus C capsid (**Holly**), Leader:kinase interactions (**Jess**), and NMR structures and biochemistry of Leader:Ran (**Valjean**). **Yury Bochkov** is

now working out at the UW hospital with Jim Gern, and collaborating on many facets of the rhinovirus C directions. A major cooperative team project between Jim, Ann and John Yin (UW Engineering), linking rhinovirus biochemistry with asthma exacerbations, was just funded, so picornaviruses will live on for quite some time in the lab. It's a very productive time experimentally, primarily catalyzed by great students, Marchel and local collaborative faculty support.

As perhaps you've heard, **Ann** was diagnosed with an aggressive form of lymphoma in the fall of 2011, and spent about 7 months out of the lab in treatment and rehab. But she's now baaack... mostly full time, mostly mobile, and picking up the pieces. Remission is a good thing! During the dark days, Paul Friesen stepped in like a champ, both to run the day-to-day functions of the Virology Institute, and to complete preparations for the American Society for Virology annual meeting, held July 21-25, 2012 at the Monona Terrace. Ann was semi-functional by then, but she mostly schmoozed with friends and rode around on a little red scooter to save (her) energy. In truth, phenomenal kudos are

really owed to Paul for the Herculean job he did in Ann's absence, to bring together what is widely acknowledged as the best ASV ever (our 5th in Madison). During the meeting (1600 virologists) **Jean-Yves Sgro** and **Adam Steinberg** taught a mini-course on bioinformatics. Students from all the campus virology labs organized and ran the first ever "Virolympics," a series of virus-related brain-teaser and physical games that were part of the meeting entertainment package, and the Hepatic Lesion Band (herpes virologists) also played, to the delight of everyone. Who knew virologists were so talented? Ann has now permanently retired from ASV planning (the 2017 Madison meeting will be run by Kristen Bernard), and Paul is now the official director of the IMV. Lots of changes, but all for the good! Ann, now free from many campus and national committees (dropped when she was sick), is continually getting stronger and now "free" to focus on the fun part of science. Many thanks to all of you who wrote, called or beeped to give your support over the last year. Friends and colleagues are what make this all worthwhile.



### Phillips lab

Big changes in the Phillips laboratory. Several folks successfully completed their Ph.D.'s since the last update, including **Chris Bianchetti**, **Aram Chang**, **Aaron Bryden**, and **Crane Zhang**. But the

big news is that **Professor Phillips** has 'retired' from UW, and is now Professor Emeritus. This does not mean he's quit working however, as Rice University hired him back as the Looney Professor of Biochemistry. The lab at UW will keep on keepin' on for a while as **Kate Helmich** is still working on her Ph.D at UW. UW grad student **Jerry Wang** has moved to Rice to complete his studies, but that still leaves **Kate**, **Bob Smith**, and

Scientist **Craig Bingman** holding down Phillips Lab North. Phillips Lab South is now fully functional and we regularly have joint Skype lab meetings with both sites involved. **Drs. Hongnan Cao** and **Ragothaman Yennamalli** moved to Rice with Dr. Phillips and have been continuing to work on projects started at UW-Madison.



### Pike lab

The Pike laboratory has been active over the past year using genome-wide methodologies to explore both the process of cellular differentiation and the actions of vitamin D in cell types that play a central role in bone metabolism. To this end, we have discovered that the extensive transition from mesenchymal stem cells to mature osteoblasts and then osteocytes involves widespread, yet specific, qualitative and quantitative changes in numerous epigenetic histone marks that define specific chromatin states at genes known to highlight each specific cell type. These marks, together with *de novo* binding and/or displacement of bone cell transcription factors such as RUNX2 and SP7, and their regulatory complexes appear to orchestrate the changes in gene expression that are observed during the differentiation process. Interestingly, exposure to the vitamin D hormone at specific times during this transition results in unique cellular responses at both the DNA as well as RNA output levels. Further studies at the level of specific vitamin D target genes *in vitro* and *in vivo* have identified mechanisms whereby the hormone regulates biological processes that include bone resorption, bone mineralization, stress responses, and growth control, among others. These ongoing studies have been exceedingly fruitful; many of these discoveries have been selected for presentation at national meetings held during the past year.

**Dr. Mark B. Meyer** has now been promoted to Associate Scientist in the laboratory, and directs both our DNA sequencing and bioinformatics efforts to explore the mechanisms that are involved in differentiation and gene regulation. He has been aided in this endeavor by **Ms. Nancy A. Benkusky**, who was recently employed as an Assistant Researcher in the lab. She has rapidly learned the methods that are a prelude to conducting deep sequencing analysis, and many additional analyses that are central to our research effort as well. Mark also has a number of biological projects that are ongoing, including an analysis of the mechanisms

that determine the differentiation of precursors into either osteoblasts or adipocytes. Mark received an award from the 15th Vitamin D Workshop to travel to Houston, Texas in June of 2012 and a 2012 Young Investigator Award from the American Society of Bone and Mineral Research (ASBMR) in Minneapolis, MN in October of 2012 for his work in these research areas. These studies are supported by the NIH.

**Dr. Seong Min Lee** was recently promoted to Assistant Scientist for his work that has focused upon the mechanisms that underlie the regulation of the vitamin D receptor (VDR) gene in bone and other cell types. These studies have identified regulatory regions within the VDR gene that play a central role in auto-regulation by the vitamin D hormone in bone cells and in the gene's regulation by PTH as well. In unique studies, Seong Min has deleted individually these regulatory enhancers within the context of a large segment of DNA that contains the entire expression and regulatory locus and introduced them stably into cell lines and as transgenes in mice. These studies are among the few that explore the role of regulatory regions both *in vitro* and *in vivo*. They appear to confirm our view that these regions are critical for VDR gene regulation. Additional studies ongoing include an examination of the effects of mutant VDRs introduced into the global VDR-null mouse. These and other studies are supported by the NIH and were presented in scientific sessions at the ASBMR meeting in Minneapolis in 2012.

**Dr. Chang-Hun Lee** is now completing his 4th year in the laboratory. Chang has focused during the past year on a study of the transcription factor SP7, a transcription factor induced by the RUNX2 bone cell master regulator and which is essential for the formation and differentiation of osteoblasts. A genome-wide analysis of binding sites for this transcription factor has provided a larger view of the genes that are regulated by this factor and is providing clues as to its central role in osteoblastogenesis.

**Dr. Melda Onal** has recently joined our group as a Research Associate, having obtained her PhD in Professor Charles O'Brien's laboratory in Little Rock where she worked on the regulation of

expression of the gene for Rankl (*Tnfrsf11*). There, she focused specifically upon the consequence to the skeleton of deleting one of at least 7 of the enhancers that control the expression of this gene. To extend this work, we prepared three mouse strains each of which contained a unique Rankl enhancer deletion. Dr. Onal is now exploring the consequences of these deletions on the immune system, the skeleton and in other tissues where Rankl plays a role. Her work now confirms that our molecular approach using ChIP-seq analysis to define the nature and scope of a regulatory gene locus is a useful one to identify key regulatory regions both *in vitro* and *in vivo*. She has been aided in this project by **Ms. Allison Danielson**, who is an undergraduate student in Biochemistry at the University. A renewal for this work was recently funded by the NIH.

**Hillary St. John** is a third year graduate student in the IPiB Biochemistry Program at the University of Wisconsin, and holds the Hector F. Deluca Fellowship Award for the second year in a row. Hillary is interested in bone cell differentiation and together with **Dr. Katie Bishop** initiated a project aimed at understanding the molecular basis for the osteoblast to osteocyte transition. Osteocytes, derived from the osteoblast lineage, represent the most predominant cells of bone, and in recent years have become the focus of intense research as they play both a central role in bone remodeling and an endocrine role in the production of the phosphate homeostatic hormone FGF23. Having identified a unique cell line capable of the osteoblast to osteocyte transition, Hillary is exploring the changes that occur to the transcriptome as well as the underlying changes that occur to the epigenome on a genome-wide scale. She is aided in this endeavor by **Ms. Sydney Hansen**, an undergraduate student in Biochemistry who has proven skillful in the numerous molecular cloning efforts that are also part of this project. Numerous surprising observations have been made that highlight the osteocyte transition and the genes that are either suppressed or upregulated. The role of vitamin D in osteocyte biology is also being explored. We anticipate an extensive understanding of the molecular changes that occur to this cell during its differentiation into this

unique functioning cell type. This work has been presented in numerous venues at the University of Wisconsin and at the ASBMR meeting in Minneapolis in 2012.

**Alex Carlson** is a third year graduate student in the Molecular and Cellular Pharmacology Program at the University. His work is focused on the endocrine function of the osteocyte, having observed that the phosphate hormone FGF23 is expressed in the cell line used by Hillary and that it is regulated by the vitamin D hormone, PTH, and surprisingly, by the heterodimer PPAR $\gamma$ /RXR. Extensive histone modification and transcription factor binding analysis using ChIP-seq has identified a series of regulatory enhancers that play a role in FGF23 expression. Alex is exploring these regulatory regions for their contribution to FGF23 expression. As FGF23 plays a central role in vitamin D metabolism and in chronic kidney disease, clarification of the regulation of this hormone is central to our understanding of both mineral homeostasis as well as disease.

**Sohel Shamsuzzaman**, MS, is a third year graduate student in the IPIB Biochemistry Program who currently holds the Kamaluddin Ahmad Distinguished Graduate Scholarship. Soheli is interested in the mechanisms that underlie smooth muscle cell reprogramming to the osteochondroprogenitor phenotype that plays a role in the calcification of atherosclerotic plaques and the mechanisms through which the vitamin D hormone, perhaps via Rankl, influences this process. Accordingly, he has studied the ability of osteogenic cocktails to induce this reprogramming process to cells with an osteoblast-like phenotype and the changes in gene expression that accompany

this process. Using a series of transgenic mice compromised for VDR, Rankl and ApoE expression or double nulls, Soheli is exploring the contribution of these factors in arterial calcification.

**Amber Mael** is a recently hired Senior Research Assistant who comes from the Morgridge Institute. Amber has extensive skills in cell culture, particularly as it relates to the preparation of induced pluripotent stem cells (iPS cells). To this end, she has prepared a series of human fibroblast- and smooth muscle cell-derived iPS cell lines for our studies aimed at understanding the early role of RUNX2 in the mesenchymal/preosteoblast phenotype. Amber is also involved in numerous additional projects, including those involve the preparation of bone marrow-derived mesenchymal cell lines from our many genetically altered mouse lines. She is aided in these projects by **Ms. Tori Osinski**, an undergraduate in the Biochemistry Program at the University.

**Erin Riley** is an Associate Research Assistant who is responsible for our rapidly increasing mouse colony. It is safe to say we have over two dozen different strains of mouse, most arising from our efforts to characterize the regulatory regions of genes *in vivo*, but also from our efforts to explore the role of the VDR and other gene products in unique cell types *in vivo*. Erin has played an essential role in our exploration of the VDR gene with Dr. Seong Min Lee, the Rankl gene with Dr. Melda Onal, and more recently in our exploration of the *Cyp24a1* and *Cyp27b1* genes and others as well. Erin seems able to keep everything under control while at the same time producing the genetically modified mice that are needed for our extensive biological studies. It is clear that

Erin is central to our successful foray into genetically modified mouse studies.

**Drs. Rob D. Nerenz** and **Kathleen A. Bishop** have left the laboratory over the past year or more, **Rob** to an additional Clinical Chemistry Postdoctoral position at Wash U St Louis and **Katie** more recently to a Postdoctoral position with Professor Clifford Rosen in Maine. Their founding efforts in the laboratory were considerable and they are missed. **Dr. Paul D. Goetsch** obtained his PhD in December of 2012 and has moved on to the University of California at Santa Cruz where he is working in the laboratory of Professor Susan Strome studying the embryogenesis of *C. elegans*. Paul's work in this laboratory focused upon the contribution of homeobox gene products such as *Pbx1* and *Meis2* to the regulation of specific gene targets by vitamin D.

We continue to make new and unexpected discoveries. As with all scientific endeavors, while many of our working hypotheses have been confirmed, an equal number of them have not. This, together with the emerging literature, continues to lead us down research paths that are totally unanticipated. Thus, the excitement continues unabated. As a laboratory leader, I consider it a privilege to participate in this renaissance in transcription research, facilitated largely by the phenomenal technical advances highlighted by massively parallel DNA sequencing together with the development of highly sophisticated bioinformatics analyses. This type of research is certainly one of the big post genomic payoffs that has emerged following the sequencing of the human genome and as happens frequently in science was completely unpredicted.





### Raines lab

**Amit Choudhary** became the 25th Junior Fellow in chemistry at Harvard University. **Greg Ellis** remains on campus as a postdoctorate with Professor Tim Bugni at UW-Madison, following his marriage to fellow IPiB student **Nicole Beauchene**. **Sayani Chattopadhyay** is working at Champion Technologies, a specialty chemical company in Houston. **Ben Caes** is applying his knowledge of cellulose at ink manufacturer Siegwerk USA in Des Moines. Finally, we bade farewell to three M.D./Ph.D. students: **Mike Levine**, **Nadia Sundlass**, and **Mike Palte**. They are completing their M.D. training at various Wisconsin medical centers and making plans for residencies in surgery, dermatology, and pathology, respectively. Mike also married IPiB student **Rachel Kubiak**.

Two postdoctorates also left us – **Katrina Jensen** is an Assistant Professor at Black Hills State University, and **Langdon Martin** is an Assistant Professor at Warren Wilson College. And, the group celebrated the marriage of **Caglar Tanrikulu**.

### Departures

Since the publication of the last departmental newsletter, seven graduate students earned their Ph.D. degrees in our laboratory.

### Arrivals

Though we miss the seven graduate students who left us, we are excited that seven new graduate students have joined us. **Kalie Mix** and **Ian Windsor** are in the IPiB program; **Matt Aronoff**, **Aubrey Ellison**, **Robert Newberry**, **Thom Smith**, and **Kaylee Underkofler** are graduate students in the chemistry department.

Three postdoctorates have also joined us. **Raso Biswas** came from the University of Berne, where he worked with Professor Jean-Louis Reymond. **Kevin Desai** was at Florida State University with Professor **Brian Miller**, who himself was once a postdoctorate with us. And, **Brett VanVeller** joined us after obtaining his doctorate at MIT with Professor Tim Swager.

Several undergraduates are working with us as well: **Amy Davis**, **Spencer Peh**, **Steve Leeb**, **Chin Leng Cheng**, **Kevin Walters**, **Kelly Wallin**, **Tia Chitwood**, and **Alex Peterson**.

As you can imagine, our team of thirty (16 graduate students, 6 postdoctorates, and 8 undergraduates) engenders a highly stimulating and productive environment!

### Current Events

- **Kristen Andersen**, **Trish Hoang**, **Sean Johnston**, **John Lukesh**, **Rob Presler**, and **Jim Vasta** have become dissertators and continue to progress towards their doctoral degrees.
- **Mike Palte**, **Ian Windsor** (in goal),

and the rest of the Warthogs ice hockey team won the recreation C-league championship.

- **Trish Hoang** and her husband bought their first house.
- **Jim Vasta** won first place in his age group in the Zoo Run Run 5K race.
- In August 2012, at the annual Protein Society meeting in San Diego, alumni **Steve Fuchs**, **Chiwook Park**, **Ken Woycechowsky**, **Jason Horng**, and **Nick Panasik** had an impromptu reunion.
- As the holiday party ornament-design winners in 2010 and 2011, the group rested their creative energies in 2012 and plan for a spirited reentry in 2013.

We always keep our webpage up-to-date. Please keep up with us by adding a bookmark to [www.biochem.wisc.edu/labs/raines](http://www.biochem.wisc.edu/labs/raines). There, you can read about our latest research and learn the whereabouts of all 44 doctoral and 23 post-doctoral alumni.

Although there is continual turnover in the lab, we still maintain a collegial atmosphere that fosters creativity and independence. Please stop by if you are in town – we always enjoy seeing you!



Renowned red heads Mike Bruesewitz (WI men's basketball player, 6'6") and Sean Johnston (IPiB student/Raines group, 6'5").





## Ralph lab

The last year or so has been pretty exciting in the Ralph Lab, where students, postdocs, and researchers are involved in a range of often collaborative studies on plant cell wall biochemistry. On the way to attempting to engineer plant lignins to

be more readily degradable (to improve biomass conversion energetics), the group has been involved in: discovering the first monolignol acyltransferase and successfully downregulating it in grasses; discovering new types of lignin monomers and an entirely new natural homopolymer from the 'missing monolignol', caffeyl alcohol (*PNAS* cover article and *Science* highlight); discovering a new lignin monomer from an alternate biosynthetic pathway, the flavone triclin (which has

basic and practical implications – the compound is quite useful!); establishing a new 'zip-lignin<sup>TM</sup>' approach (cover article in *ChemSusChem*); delineating the role of a 'domain of unknown function' gene involved in xylan biosynthesis (cover article in the *Plant Journal*); developing fluorescence-tagged monolignols that are receiving considerable interest; and on and on – it has been a very productive and exciting time!



Three journal covers from our cover articles. Two of them are from Yuki Tobimatsu's articles – we are thinking he should write all the Lab's papers from now on (or at least submit them)!



## Record lab

We're thriving in our new space in the Biochemical Sciences Building, and are delighted to have visitors! One focus of our research is on determining the mechanism by which the RNA polymerase molecular machine puts promoter DNA in the active site cleft, opens it using binding free energy, and then stabilizes the initial unstable open complex by folding and assembly of mobile regions of core polymerase on the downstream duplex. We're now able to ask more detailed questions about what regions of polymerase carry out these steps, and how they are regulated. IPiB student **Amanda Drennan**, who obtained her PhD last summer, characterized the dramatic consequences of deleting a mobile region of core polymerase or an in-cleft region of the specificity (sigma) subunit for the kinetics of both early and late steps of this process, and on the properties of the final open complex. Amanda and

**Ted Gries** (former lab member and '10 IPiB PhD, now a Chemistry professor at Beloit College) recently became the proud parents of daughter Winifred. IPiB student **Sara Heitkamp**, who also obtained her PhD last summer, characterized the series of large conformational changes needed to insert the promoter DNA in the cleft. Sara is now a Scientific Development Program Fellow with Beckman Coulter. Chemistry graduate student **Emily Ruff** and Biophysics graduate students **Raashi Sreenivasan** and **Jan Murray** are studying the roles of other polymerase elements, promoter sequence variants and transcription factors in these key steps of transcription initiation. Undergraduate Biochemistry majors **Dana Bellissimo** (now in the MD-PhD program at Penn), **Mark Kraemer** (now at UW Medical School) and **Kristin Zorn** (now in Sarah Ades' laboratory at Penn State), mentored by Amanda, Sara, and Emily, were quick learners and contributed a lot to these projects while doing their senior theses on this challenging system.

The second focus of our research is on quantifying noncovalent interactions of individual biochemical functional groups

in water, of relevance for understanding how biochemical solutes like urea and osmolytes interact with proteins and nucleic acid as well as for understanding the contributions of various noncovalent interactions to protein and nucleic acid self-assembly processes. IPiB student **Ben Knowles** is studying polyols and ethylene glycols, in order to understand both the chemical interactions of these solutes with proteins and nucleic acids and the physical effects (excluded volume effects) of polyethylene glycols, which of course are widely used to crystallize proteins or assembly multi-subunit complexes. Chemistry graduate student **Emily Guinn** is quantifying interactions of urea, osmolytes, Hofmeister salts and other solutes with functional groups of proteins and nucleic acids, to determine why urea is a protein and nucleic acid denaturant while most osmolytes are protein stabilizers (though not of nucleic acids), and why the stability of protein-nucleic acid complexes is increased so greatly, particularly at high salt concentration, by replacing the laboratory salt KCl by the physiological salt KGlutamate. Ben and Emily will obtain their PhD degrees this semester.



Both have been assisted in their research by many very capable Biochemistry or Chemistry undergraduates and senior thesis students, including **Michael Kerins** (now at Kimberly-Clark), **Tyler Wied** (now at Johns Hopkins), **Zeeshan Haq** (now at UW Medical School), as well as **Roger Diehl, Chau Phan, Hyo (Mike) Cha, Rachel Wong, August Melcher** and **Audrey Hartzler**, all of whom are now applying to graduate or medical school.



**Weibel lab**

Highpoints and a summary of the Weibel lab from the past year:

**Former High School Students:** Congratulations to former research assistants **John**

**Ntambi** and **Norah Ntambi** who graduated from West High School and currently attend the University of Wisconsin (John: Whitewater; Norah: Madison).

#### **Former Undergraduate Students:**

**Sonia Carey** (née Treviño-Dopatka) received a B.S. in Biochemistry from UW-Madison in May 2012, got married, co-authored a paper in *Journal of Bacteriology*, and moved to Boulder, CO where she is currently teaching. **Nate Cira** received a B.S. in *five* majors (including Biochemistry) from UW-Madison in May 2012, and is currently a graduate student in Bioengineering at Stanford. In his last semester as an undergrad, Nate published a first author paper in *Lab on a Chip*, co-authored a paper in *PLoS One*, and was a co-inventor on a patent. **Kelsey Thornton** received a B.S. in Biochemistry from UW-Madison in 2012, co-authored two papers (*ACS Medicinal Chemistry Letters*; the second is submitted), and started graduate school in Biochemistry at The Ohio State University. **Zhou Zhong** received a B.S. in Biochemistry from UW-Madison in May 2012, is currently a research assistant in our lab and with Walter Goodman (Entomology), and is preparing for graduate school in 2013.

#### **Former Graduate Students:**

Matt Copeland received a Ph.D. in

Senior lab members are **Mike Capp** (who is pioneering the development of solutes as probes of coupled folding in protein and nucleic acid processes, including transcription initiation) and **Irina Shkel** (whose speciality is computational analysis of chemical and physical (coulombic, excluded volume) effects of solutes on biopolymer processes). Postdoctoral research fellow **Rogério Sassonia** returned to Brazil and a position

Biochemistry and is currently a Postdoctoral Fellow with Brian Pfeleger at UW-Madison studying bioenergy production. Matt is engaged to a former member of the Weibel lab (Abbey Vangeloff). **Marie Foss** received a Ph.D. in Biochemistry and is currently a Postdoctoral Fellow with Georgiana Purdy at Oregon Health Science University where her research focuses on *Mycobacterium tuberculosis*. **Jack Ho** received a M.S. in Biomedical Engineering and is currently employed at Epic (Middleton, WI). **Daniel Pauw** received a M.S. in Cellular and Molecular Biology 2 and is exploring graduate school in Information Sciences. **Hannah Tuson** received a Ph.D. in Biochemistry and is currently a Postdoctoral Fellow with Julie Biteen at the University of Michigan.

#### **Former Postdoctoral Fellows:**

**Lars Renner** is currently a Group Leader in Molecular Nanosensors at the Technical University Dresden. Lars received the Boyer Postdoctoral Excellence Award from the Department of Biochemistry, UW-Madison.

I repeated the experiment from 2011, and asked current members of the lab to write a short summary, which you can find below. In the few cases where people were too busy with research to write something, I improvised.

**Tristan Abbott** (Freshman, Biochemistry) characterizes the interaction of RecA with the anionic phospholipid, cardiolipin in collaboration with Manohary. Tristan competes in triathlons and recently finished the Racine half-ironman.

**George Auer** (4th year Graduate Student; Biomedical Engineering) studies the assembly of the bacterial cell wall. George has a remarkable likeness to the

in Chemistry at UNESP (Sao Paulo State University). Scientists **Ruth Saecker** and **Laurel Pegram** have also left the laboratory; all are greatly missed. Laurel and husband Demian Riccardi (now at Oak Ridge National Labs, previously a UW PhD with Qiang Cui in Chemistry) recently also became proud parents of a daughter (Ada).

That's an update on us; let us know about you.

famous chess player, Bobby Fisher (when he was young and before he went crazy).

**Katie Brenner** (Postdoctoral Fellow; Ph.D., Caltech) recently joined the lab and is working on a diagnostic device for detecting necrotizing enterocolitis. She is the recipient of a Postdoctoral Fellowship from the Hartwell Family Foundation. When not on campus, she can be found building forts and playing games with her kids.

**John Crooks** (2nd year Graduate Student, IPiB) develops tools to track the distribution of lipids within bacterial cells to understand how lipid domains affect bacterial physiology and behavior. John has a passion for playing musical instruments.

**Jenna Eun** (6th year, Graduate Student, IPiB) defends her Ph.D. dissertation in December 2012 and will be a Postdoctoral Fellow with Ethan Garner at Harvard. Jenna uses small molecules to study bacterial cell biology. During summer 2012, Jenna improved science curriculums for elementary and middle school students in Mexico. She is grateful to biochemists that donated time & resources to make the trip successful.

**Katie Hurley** (3rd year, Graduate Student, Pharmaceutical Sciences) joined the lab in May and passed her preliminary exam in July. She is developing inhibitors of chromosome segregation and maintenance in bacteria to study these mechanisms. Katie is a ballroom dancer and creates beaded jewelry.

**Piercen Oliver** (Postdoctoral Fellow; Ph.D., Lehigh) images lipid domains in bacteria and studies their influence on local biochemistry. He recently received a Postdoctoral Fellowship from the National Science Foundation. Piercen tinkers with electronics, enjoys cycling, and recently became a father (Luther Oliver).



**Manohary Rajendram** (4th year Graduate Student, IPIB) studies protein-lipid interactions in bacteria and is having a terrific and productive time in the lab. She recently achieved her goal of participating in a Taekwondo competition and finished first in an individual form event.

**Madhusudan Rajendran** (Sophomore, Biochemistry and Math) recently joined the lab through the Biochemistry Scholars Program. He is conducting research in collaboration with Thiago to study polar localization of proteins in *E. coli*. He enjoys playing soccer with his friends.

**Pedro J. Resto** (Postdoctoral fellow, Ph.D. UW-Madison) recently joined the lab from Biomedical Engineering. He is developing a point-of-care DNA detection system to identify bacteria. Pedro has been a Hoofers instructor in sailing, windsurfing, and snow kiting for the past four years and divides his attention between two children: a daughter (4 years) and a newborn son.

**Ryan Sacotte** (Senior, Biochemistry) collaborated with Matt and Hannah on the motility behavior of *Proteus* cells through the Biochemistry Scholars Program. He spent last summer working at Harley Davidson.

**Hannah Sandock** (Junior, Biochemistry) collaborates with Earl on the structure and composition of bacterial membranes. She misses her former mentor, Lars.

**Thiago Santos** (2nd year Graduate Student, MDTP) studies molecular

mechanisms of protein localization in bacteria. He had an amazing time teaching an undergraduate microbiology lab course in 2012 and is passionate about science, baking bread (including the Brazilian pão de queijo; Ed: Weibel Lab members have never tasted it before), and is contemplating organizing a lab trip to Brazil in the coming year(s). World Cup 2014?

**Earl Yoon** (2nd year Graduate Student, MDTP) studies the relationship between phospholipid composition and cell morphology. He is not a hockey fan.

**Peter Vander Velden** (Junior, Biochemistry) has worked on several projects, including biofuels production in bacteria and behavior that protects bacteria from predation. His interests include the environment, science, energy, Science Olympiad, reading, and building chocolate fountains (Ed: the Weibel lab has never tasted one of his chocolate fountains).

**Zhou Zhong** (Research Assistant) is developing microfluidic devices to study bacterial chemoaxis and is collaborating with Jenna to study small molecular regulators of bacterial biochemistry. Zhou is from Southwest China and loves snowboarding.

**Maoquan Zhou** (Postdoctoral Fellow; Ph.D., West Virginia) joined the lab in May, 2012. A synthetic chemist by training, he has been working on several projects, including the development of potent antibiotics and chemical biology probes. He enjoys his family, playing

badminton and table tennis, hiking, good food, beer, and music.

**Doug Weibel** (PI) feels privileged to participate in research and education with tremendously talented undergraduate and graduate students and postdoctoral fellows. Outside of work, Doug spends time with his family: Gina (spouse), Xander (12 yr.), Guy (9 yr.), Zoe (7 yr.), and Clementine (3 yr.).

#### Other Notable News:

**Jean-Marie Swiecicki** (Ecole Normale Supérieure) returned to the lab to finish up his bacterial motility project and manuscript during his graduate school vacation (yes, vacation in the lab!). **Sergio Lopez Aristabal** (University of San Paulo, Brazil) spent approximately six months in our lab working on several bacteria motility projects, returned to Brazil to graduate, then returned recently for two weeks to finish up one of his projects. **Melissa Hemling** was a summer intern in 2011 and 2012 as part of the NSF-sponsored Research Experience for Teachers Program at UW-Madison. Melissa is a chemistry and biology teacher at Beaver Dam High School in Wisconsin who developed an approach to use microfluidics to teach chemistry concepts to her classroom.

We hope you will visit us at <http://www.WeibelLab.org> to find out recent news about our group. If you are in the area, please consider stopping by so we can give you a tour through the lab.



#### Wickens lab

Greetings from the Wickens lab! Since the last newsletter, we have been focusing on how RNAs are controlled, and how networks of mRNA control are assembled and integrated. Let's start by talking about the people who are now in the lab; then those who've left; then a quick tour of our science; and a final few comments about Marv. And a plea to stay in touch!

#### Current lab members....

**Zak Campbell**, from U Arizona, has joined us as a post-doc, and has been

focusing on RNA-protein interactions, and developing ways to create designer proteins for new purposes. **Melanie Preston**, a post-doc from University of Rochester, has joined the group to work on uridylation and its role in RNA regulation.

Among the PhD students, **Chris Lapointe** works on enzymes that control RNAs by adding untemplated nucleotides; **Douglas Porter** and **Daniel Wilinski** are trying to define networks of RNA control by proteins, and understand how they work, control key events, and evolve. **Cary Valley** has concentrated on RNA-protein interactions, trying to enhance their affinity and specificity. **Shruti Waghray** has been studying proteins involved in mRNA regulation, trying

to figure out how a protein recruited by many regulatory proteins turns down translation of specific mRNAs.

Four undergrads now assist us: **Markus Neville**, **Sam Disalle**, **John Nielsen** and **Mike Harte**. Markus has been working on control by PUF proteins, with tutelage from Daniel, and at the same time and is training Sam to take care of our frog colony. John and Mike are keeping lab running smooth by providing basic support. John is also starting to do research with Chris' help and advice.

**Natascha Buter** continues as our lab technician – ordering, maintaining, advising, training, and at the same time, doing experiments with a new entry into the lab menagerie – *Neurospora*, a fungus with filamentous predilections. Natascha

keeps the lab running smoothly and greases our collective skids.

**Carol Pfeffer**, Marv's administrative assistant, keeps Marv writing, signing, executing, declining and accepting on schedule – not to mention, correctly – well, mostly. She keeps a mean and effective calendar, and is a great shield as well. You cannot overestimate the value of good insulation.

### Departures...

**Amy Cooke** has left for EMBL after defending her thesis, and now is a post-doc in Matthias Hentze's group. **Yvonne Koh** now is a post-doc as well, working with Sydney Brenner in Singapore. **Jacque Baca** (now Legendre) lives in Livermore, California (near Berkeley) and is applying for positions there. **JJ Chritton** lives near Madison and is working at Epic, a prominent software company. **Alana Beadell** moved to the University of Chicago. Among our ex-undergrads, **Caitlin Bell** graduated this past December and is now working at St. Mary's hospital in Madison, while **Eric Mortensen** is finishing his BS this spring and applying for jobs at local biotech companies.

### In the lab, but hardly human...

Molecules and creatures from quite different branches on the evolutionary tree have found comfortable homes with us. Three main families of molecules live in the lab. Some – the PUF proteins and certain nucleotidyl transferases – were discovered here and have remained. They sometimes sit quietly in the corner, and sometime stand boldly front and center; but they always occupy our collective cortex, drawing on our energy in a happy synergy. **The PUF proteins** have become a paradigm for proteins that bind and control mRNAs. We continue to study how they do so, and to use their remarkable scaffold for studies of molecular remodeling. Our aim is to use them manipulate RNAs by design. Certain **nucleotidyl transferases**, including poly(A) and poly(U) polymerases, regulate RNAs through the

addition of untemplated nucleotides. We now want to know how they find their RNA substrates and to manipulate their specificities for multiple purposes. **Deadenylases**, such as human CNOT8, not only remove poly(A), but also repress translation completely independent of that activity. Since the same deadenylases are recruited by many different RNA-binding molecules, their mechanisms of action are of central importance.

In addition to the humans and molecules that live here, multiple creatures bright and beautiful join us in our cohabitation. Each species provides something special. The yeast, ***S. cerevisiae***, continues to permeate work in the lab, due to the ease with which molecular genetics can be done. Most of us at least have a dalliance with yeast; some have full-fledged affairs, and try to understand its networks of RNA control. A distant fungal relative, ***Neurospora***, has recently joined us as well, provoked by similar interests. The South African clawed toad, ***Xenopus laevis***, provides oocytes and embryos that can readily be injected to analyze the behavior of specific molecules, and determine how they affect mRNAs. ***C. elegans***, a small nematode worm, provides powerful genetic and molecular analyses that we try to bring to bear on molecules we love. To do so, we often collaborate with the Kimble lab, which concentrates on this organism. At the moment, we are not working with ***Drosophila*** as we have in the past, but the lure of its nervous system still beckons. And don't be surprised if other creatures join us.... dreams are afoot in Marv's restless cortex....

### Wrapping up, a final human or two...

Marv is pretty much the same – or at least so it seems to him. Since the last Newsletter, he was elected to the American Academy of Arts and Sciences, in the same election that brought in Bob Dylan, Paul Simon and Helen Mirren. Bob, Paul and Helen were deeply disappointed that Marv was unable to attend the induction

ceremony in the fall. But as it happened, Marv then was on sabbatical for the academic year of 2011/2012, living and working in central London. During that period, he wrote a substantial NIH grant, which since has been funded; co-wrote a collection of papers with members of the lab; and continued to develop the programs he created that send UW undergrads to Cambridge and Oxford. At the same time, he created new programs for Heidelberg and Barcelona. He also became a balletomane, however contrary that may seem to his apparent agility and morphology. In December of 2012, Marv was thrilled to join his post-doc mentor, John Gurdon, in Stockholm, for his receipt of the Nobel Prize – a wonderful and unforgettable experience. Marv also continues to teach the graduate class in Methods that he created, which he enjoys tremendously, in large part because it enables him to meet grad students and post-docs throughout the department as they work to develop and give their lectures. For an update on **Judith**, you will have to look at her Letter from the Lab. But lest you have any doubt whatsoever – which you shouldn't – we remain happily and covalently linked. **Zach**, our son, is now a third-year graduate student at Cal Tech in Bob Grubbs' group, doing synthetic organic chemistry. Amazing – he now writes papers and grants, gives talks – and seems to be thriving and enjoying it. We are more than a little happy for him. And if you want to embarrass him, tell him you read the nice essay about him in Cal Tech News (<http://www.caltech.edu/content/beginning-life-science>) or read one of his papers...

There is not enough room here to share what you all are doing, but we would very much like to keep in touch. Please do come and visit when you have a chance. Or at least drop a line and let us know what you are up to.... Or, just maybe, we should contrive to all meet somewhere and have a darn good time together.

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