

Biochemistry

UNIVERSITY OF WISCONSIN-MADISON

2006 NEWSLETTER



For friends of the Department of Biochemistry at the University of Wisconsin-Madison

Changes afoot, from Biochemistry Phase II to the New look of the Graduate Program...



From the Chair
Betty Craig

It is a pleasure to write my first “from the chair” dispatch for the Biochemistry Newsletter. It has been a busy and eventful year for the department, as well as for me personally, as I “learn the ropes” as chair.

I am pleased to report that the **Biochemistry Phase II Biostar Building Project**, our newest building to be centered on the present site of the 1956 wing, is moving forward. We are delighted that Flad and Associates, the designers of the 1998 Addition, have been chosen as the architects. The design process should take about two years, with groundbreaking anticipated in the spring of 2008. It will be a complex and challenging project, because of the many physical constraints on the site. The plan is to preserve the 1912 wing and parts of the 1937 wing to ensure the preservation of the Curry murals (*shown throughout this newsletter*). The safety of the vintage elm tree (aka Elmer) is also a priority.

The new building will have laboratories for 20-24 research groups. The remaining labs still located in the old Enzyme Institute building will be integrated into the new building, as will all the labs of the Biomolecular Chemistry Department. For the first time the biochemical sciences will be physically

together in contiguous space. The research space will include specialized areas for structural biology and chemical synthesis, allowing the department to stay at the forefront of emerging technologies. In addition, the building will include much-needed state-of-the-art lecture halls and teaching laboratories.

Another priority in the department has been the move towards a new graduate program - the **“Integrated Program in Biochemistry”** (to be called **IPiB**) - a joint venture with the Biomolecular Chemistry Department in the School of Medicine and Public Health. We think that the time for such a change has come. When the two departments first established doctoral graduate programs around the turn of the previous century, these independent programs satisfied the separate need for specialized training in plant and animal biochemistry in CALS, as compared to human biochemistry in the Medical School. But, in the ensuing decades, an understanding of the fundamental similarities of biochemical processes in cells of all life forms has blurred the boundaries between the research carried out by students in the two graduate programs.

So, the two departments crafted a plan for a new joint graduate program, capitalizing on the strong history of graduate training in both departments. Just weeks ago the two departments recruited the first class of students for this joint curriculum, as we continue to

negotiate the bureaucratic hurdles to establish an official new program. **Tom Martin** and **Sebastian Bednark**, working with **John Denu** and **Catherine Fox** from Biomolecular Chemistry, spearheaded the effort. I believe that IPiB represents an unprecedented step in cooperation and collaboration in the biochemical sciences at the UW.

I hope you like the new look of our Newsletter and find the articles inside informative. We would be glad to hear from you anytime, and visit us when you can, to meet with old friends and see the changes afoot in Biochemistry for yourself.

In this issue:

- A unique “hands-on” learning experience for undergraduates developed by **James Ntambi** that combines real-life experience with classroom learning (*page 3*).
- Establishment of two new professorships with a dual purpose – an opportunity to honor two of our emeritus professors, **Henry Lardy** and **Laurens Anderson**, and to help retain two of our faculty, **Laura Kiessling** and **Ron Raines** (*page 22*).
- Efforts by faculty, particularly **Mike Cox**, to address issues of science education in secondary schools (*page 24*).
- **“Hector DeLuca on Vitamin D”**, a talk sponsored by the Wisconsin Academy of Sciences, Arts and Letters (*pages 26 & 27*).

Richard Scheller, Executive Vice-President for Research, Genentech, Inc.

As a faculty, we all have a desire to help young students find and accomplish their life dreams. Some of our students come to the Department of Biochemistry without a clear idea of where they want to go intellectually and professionally, while others know that they are interested in Biochemistry and want to go on to be a scientist. **Richard (Rich) Scheller** is in that latter group.

“I think that there are a lot of very dedicated teachers at the University of Wisconsin. I thought that the classroom lecturing was generally outstanding. There were tremendous opportunities, even at a large state school, to do individual research and an honors undergraduate thesis.”

Rich came to the University of Wisconsin – Madison as a freshman in 1971. He had grown up in Milwaukee with a passion for science in general and biochemistry in particular. By some good fortune for me, he was assigned to me as an advisee. I do not know whether I had an impact on him, but I do remember that I thoroughly enjoyed the relationship. Rich was a very successful student who worked hard because he loved the adventure of science and he loved learning new things. He was a thoroughly fun person to interact with. He recently gave the University the best compliments that we could receive. “I think that there are a lot of very dedicated teachers at the University of Wisconsin. I thought that the classroom lecturing was generally outstanding. There were tremendous opportunities, even at a large state school, to do individual research and an honors undergraduate thesis.” Rich took advantage of the research opportunities open to undergraduates by first working in the laboratory of **Ray Brown** in the Oncology Department and then in the laboratory of **Muttaiya Sundaralingam** in our Department. Dr. Sundaralingam was the lead X-ray crystallographer in

Biochemistry at that time. Rich developed a deep appreciation of structural biochemistry from that experience and was a coauthor of a paper from Sunda’s lab (Sprang, Scheller, Rohrer and Sundaralingam. 1978. Journal of the American Chemical Society 100: 2867-2878).

Rich’s interest in structural biology led him to go to the California Institute of Technology so that he could work with **Richard Dickerson**. It was during this time that he manifested key features of his career; his great interest in exciting science and his ability to collaborate with a variety of investigators. During his graduate training at Cal Tech, Rich worked with **Art Riggs**, **Keiichi Itakura** and **Herb Boyer**. He made his mark at the time as one of originators of key recombinant DNA techniques, but later worked with **Eric Davidson’s** lab as his interests changed to using the technology to study developmental biology questions using the sea urchin as a model organism.

Rich then went on to work with **Richard Axel** and **Eric Kandel** at Columbia University – Physician and Surgeon’s Medical School for a postdoc. Rich was the molecular biology bridge that led these two labs to use recombinant DNA technology to start studying molecular neurobiology using the marine snail *Aplysia* as a model organism. This is the field that he continued to pursue as a professor at Stanford University, at first in the Biology Department, and then in the Department of Molecular and Cellular Physiology and the Howard Hughes Medical Institute.

In 2001, Rich became the Director of Scientific Research at Genetech. Currently he is the Executive Vice President for Research. His scholarly contributions have been recognized by numerous honors including his election to the American Academy of Arts and Sciences and to the National Academy of Sciences. All those who know Rich, know him as an exciting, fun person who still loves science.



Genentech, Inc.

IN BUSINESS FOR LIFE

Study Abroad in Uganda – International Health and Nutrition

by Professor James Ntambi

Billions of people face pressing health and nutrition issues that seldom confront most Americans. **James Ntambi**, Professor of Biochemistry and of Nutritional Sciences, College of Agricultural and Life Sciences (CALS), has initiated a program to help educate UW students about these world-wide problems. He does so by taking a group of students from UW-Madison to Uganda, “The Pearl of Africa,” to learn first hand about the many health and nutrition issues faced by people in a developing country. The “Uganda Study Abroad: International Health and Nutrition” program offers exciting opportunities to learn about these issues from a classroom perspective and through real world experiences.

The program is the outgrowth of a partnership between CALS and Makerere University (Uganda’s premier institution of higher education) in Kampala, Uganda. Professor Ntambi, the program’s creator and leader, hopes that as future health care providers, these participants will some day lend their expertise to addressing these problems. He believes this exposure will make them better health care providers, whether they eventually work overseas or in Wisconsin. As Professor Ntambi states, “You cannot experience a situation like Uganda and not become a more caring and therefore more effective health care provider!”

Professor Ntambi, along with John Ferrick, CALS International programs office, work closely with colleagues at Makerere University and in particular the Institute of Public Health (MUIPH) on course content and in developing the experiential learning opportunities during the 3-week field study in Uganda. During the fall course that precedes the winter break overseas experience,



2006 students

students develop a better understanding of the many health and nutrition issues that confront most Ugandan's. These questions then form the framework for the course as well as the 3-week field experience in Uganda. Examples of some questions students consider are: What are common nutritional deficiencies in developing countries? Why do people have vitamin deficiencies? How do economics affect health? What are the impacts of the HIV/AIDS epidemic? Why has Uganda been so successful in its fight against this disease? What are the relationships between nutrition and infectious diseases – most specifically related to children?

In Uganda, Professor Ntambi and his colleagues at MUIPH arrange learning visits to rural health centers, Mulago Hospital (the National referral hospital), HIV/AIDS clinics, child nutrition centers and homes in rural villages. Professor Ntambi also makes a strong connection to the relationships between health and food; how it is grown, stored, and consumed. Field-trips to agricultural research stations, farms, and local markets highlight these relationships.

The program began in the fall of 2003 with twelve students and has grown to fifteen. In response to needs identified by students returning from Uganda, the program now includes a service-learning component that is helping to address the lack of access to clean water—a significant problem in Uganda. With Professor Ntambi as their faculty advisor, in 2005 students formed a 501(c) 3

not-for-profit student organization called the Village Health Project-VHP (www.villagehealthproject.org) and applied and obtained two Wisconsin Idea Undergraduate Fellowship grants from the Morgridge Center for Public Service to help implement rural water projects. VHP also works with an AIDS support organization to purchase ribbons for sale back here at UW-Madison, with the proceeds supporting HIV/AIDS positive clients and other health related activities in Uganda.

With his colleagues in Uganda and at UW-Madison, Professor Ntambi has created a program that is making a difference for UW students interested in health careers. The program really makes “the world their classroom,” and clearly demonstrates that UW-Madison is not only a world-class, but also a world-involved university! It is the Wisconsin Idea gone international.

If you wish to contribute to this program, please see page 31 for more information.



John Kakitahi
Makerere University

James Ntambi
Dept. of Biochemistry

John Ferrick
CALS International
Programs Office



2006
Village Health Project
University of Wisconsin-Madison, USA
COBIN and
Institute of Public Health, Uganda

Completed water tank with homeowners

Dedication plaque

Faculty Research Spotlight

by Aseem Ansari

Simple synthetic molecules orchestrate a genomic symphony



Starting as a single fertilized cell, a human being made of billions of very different cells eventually takes form. All cells contain the same genome, but "specialize" to acquire diverse shapes and functions. The genome itself is an inert repository of information, an extremely large encyclopedia written with just four letters. How is the information read to orchestrate such a complex and precise transformation?

The genomic encyclopedia is selectively accessed, and the information guides the fate of cells. Different parts of the encyclopedia define different fates and numerous cues impinge on the cell to direct it to utilize information in specific chapters. These cues instruct regulatory proteins to bind specific sites in the genome and to regulate the expression of target genes. Thus, these regulatory proteins, known as transcription factors, play a central role in cellular physiology. The importance of their roles is clear in all organisms. In humans, their malfunction underlies numerous diseases, including cancer and diabetes.

My lab is focused on understanding how transcription factors stimulate the transcription of targeted genes. As a post-doctoral fellow, I began to dissect transcription factors using chemical and biological methods. Our work, and that of other labs, showed that the factors were amazingly modular - lego blocks that can be mixed and matched in many combinations.

Now, we try to recreate functional molecules using synthetic counterparts. Our reasoning is that if we truly understand how the proteins work,

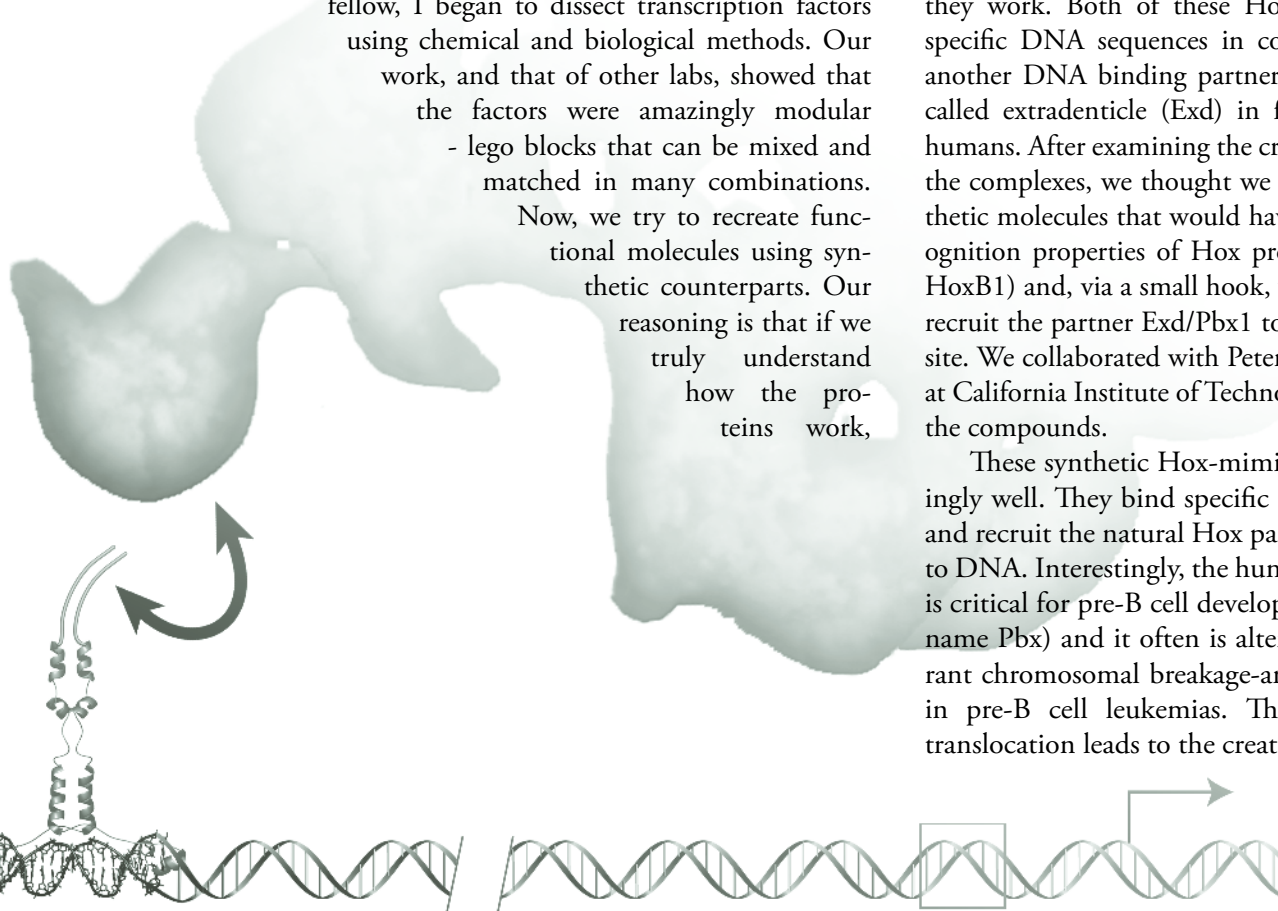
we should be able to reassemble a live transcription factor from simple synthetic modules.

Our early results were extremely encouraging. By linking a small DNA-binding ligand to a short designed peptide, a molecule emerged that specifically recruits the transcriptional machinery, thousand times the size of our synthetic molecule, to a targeted promoter. Using this same logic, we now want to manipulate genes that are of central importance in human development and disease. We have begun by focusing on the Homeobox (Hox) family of transcription factors.

Hox proteins have a DNA binding domain that is conserved from bacteria to man. In nearly all multicellular organisms these proteins control genes and regulatory networks that are critical for axial patterning and segmentation of the organism. In humans, several Hox proteins also play a role in hematopoiesis and their malfunction is thought to facilitate the onset of several leukemias.

We chose to focus on two key members of this family, Ultrabithorax (Ubx) from the fruit fly *Drosophila melanogaster*, and HoxB1 from humans, because they are critical biologically, and because a great deal is known about how they work. Both of these Hox proteins bind specific DNA sequences in combination with another DNA binding partner. This partner is called extradenticle (Exd) in flies and Pbx in humans. After examining the crystal structure of the complexes, we thought we could build synthetic molecules that would have the DNA recognition properties of Hox proteins (Ubx and HoxB1) and, via a small hook, would be able to recruit the partner Exd/Pbx1 to a specific DNA site. We collaborated with Peter Dervan's group at California Institute of Technology to generate the compounds.

These synthetic Hox-mimics work surprisingly well. They bind specific DNA sequences and recruit the natural Hox partners Exd/Pbx1 to DNA. Interestingly, the human Hox partner is critical for pre-B cell development (hence its name Pbx) and it often is altered due to aberrant chromosomal breakage-and-reattachment in pre-B cell leukemias. The chromosomal translocation leads to the creation of an abnor-



mal protein that is a potent transcriptional activator of genes that trigger unbridled cellular proliferation. When these genes are expressed in an unregulated manner they lead to the onset of acute lymphocytic leukemia. We now are trying to create artificial transcription factors to combat this oncogenic form of Pbx1. This is a significant challenge: the molecules must traverse the cellular membrane, enter the nucleus, and act as we command. What is more, they must not only be potent, but specific.

A key facet of transcription factors is their cooperative assembly on specific DNA sites. We have learned new rules that govern these interactions, including the role of allosteric modulation of DNA structure in cooperative assembly of several factors. Using a new microarray-based approach that was developed in our lab, and named CSI:Madison by my students, we can comprehensively define the DNA recognition properties of our synthetic molecules as well as that of the natural proteins. Such textured

information provides invaluable insight toward the design of synthetic molecules that function with high degree of precision.

In the long term, we hope to generate molecules that can trigger different genes and networks in a pre-ordained manner. Along the way, we surely will need to manipulate their potency and specificity, and learn what networks they activate and how. As our understanding of these process increases, we hope to design molecules that trigger specific differentiation pathways. The basic approach could be used to guide the fates of stem cells and treat several terrible diseases. The applications to personalized therapeutics and tissue engineering are far off, but in getting to that distant target we will also gain significant insights into regulatory networks that govern cell fate. Ultimately, we hope to engineer cell fates by choreographing transcriptional networks. We want to design precision-tailored chemicals that read desired articles of the genomic encyclopedia, and direct cell fate in a predetermined manner.

In Memoriam: 2006

Arnold, Aaron

(PhD 1937 Elvehjem)

October 29, 2004

Hankes, Lawrence Valentine

(PhD 1949 Elvehjem)

December 16, 2004



by Donna Troestler and George Phillips

The Center for Eukaryotic Structural Genomics (CESG) was founded by John Markley, Brian Fox, and George Phillips and is in its 5th year, and Phase 2, of the the NIH's Protein Structure Initiative (PSI). During the five-year pilot phase of PSI, the \$270 million given to nine U.S. centers resulted in more than 1,100 solved protein structures, of which more than 700 were unique, and numerous technical advances (*see PSI Pilot Phase Selected Technical Advances at the end of this article*).

During the pilot phase, CESG received a four-year, \$17 million grant, and its primary efforts were centered on setting up a protein production pipeline with requisite staff and equipment. With essential support from Biochemistry Department staff and collaborators, CESG successfully implemented a pipeline, and went on to solve 61 structures, primarily from *Arabidopsis thaliana*. The second phase of the NIH project, PSI-2, supports four large-scale and six specialized U.S. centers. The four large-scale centers are expected to generate between 3,000 and 4,000 structures. CESG has become a "Specialized Center," with the explicit mission of developing novel methods for quickly determining structures of proteins that traditionally have been difficult to study. This effort has received \$20 million of support from NIH.

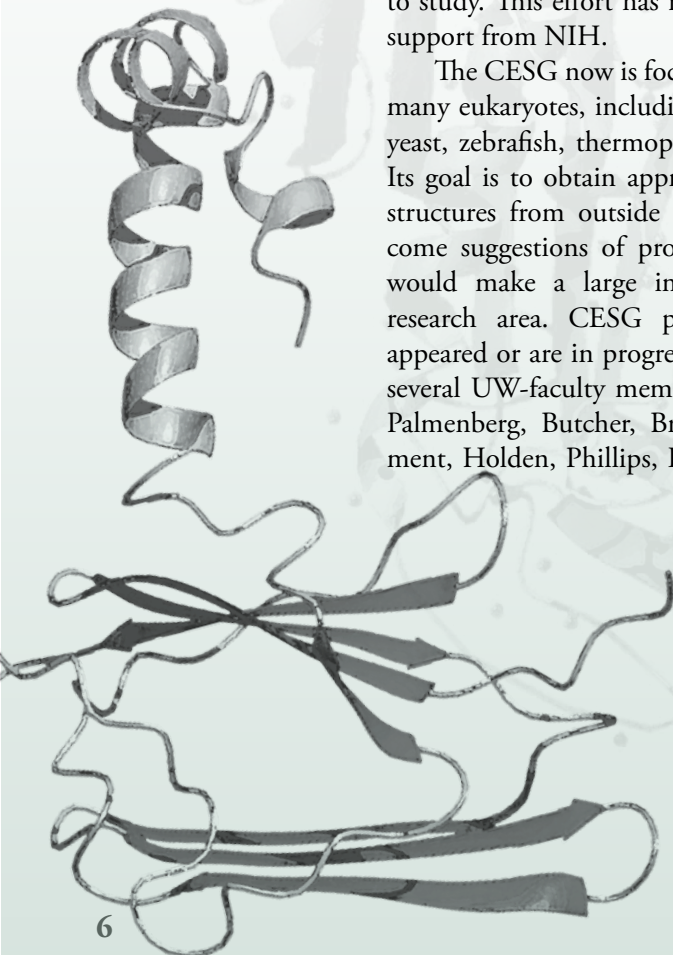
The CESG now is focusing on proteins from many eukaryotes, including human, mouse, rat, yeast, zebrafish, thermophilic algae, and others. Its goal is to obtain approximately 20% of our structures from outside requestors, so we welcome suggestions of proteins whose structures would make a large impact on a particular research area. CESG publications that have appeared or are in progress include as coauthors several UW-faculty members, including Raines, Palmenberg, Butcher, Brow, Denu, Frey, Rayment, Holden, Phillips, Fox, and Markley from

Biochemistry and Biomolecular Chemistry and Shen and Thorson from Pharmacy. Collaborations with other faculty members are underway. Currently, we are collaborating with Prof. James Thomson to solve structures of proteins he and others identify as potentially playing key roles in the differentiation of human stem cells. We are already nearing the end of our first year of PSI-2, and to date we have deposited an additional 21 structures (91 total) into the Protein Data Bank (PDB).

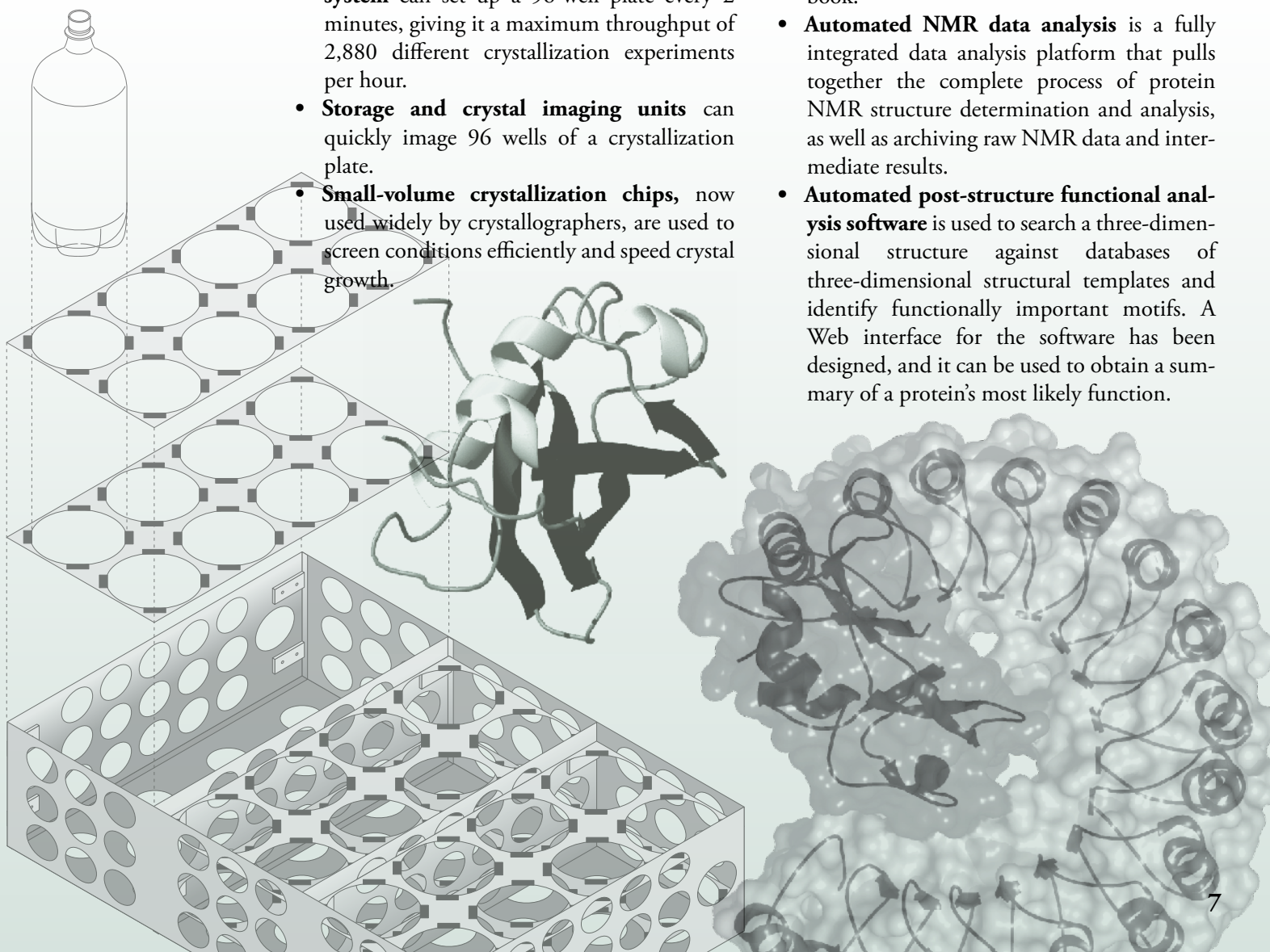
Later this year, for space and planning purposes, CESG's protein production laboratory will move to the old Genetics building on Henry Mall. We will occupy the entire fourth floor of the building, and a large portion of the 3rd floor. It has been a lengthy process to clear out the areas we will occupy and to prepare the space for CESG labs, as the rooms and labs were outdated and in need of many repairs. We hope to move by the end of summer, 2006. CESG's X-ray crystallography team will remain located at the Phillips Lab, and the NMR teams will remain located at the Markley Lab and in Prof. Brian Volkman's laboratory at the Medical College of Wisconsin.

CESG is conducting a workshop with NMRFAM this summer. The **2006 CESG/NMRFAM Wheat Germ Cell-Free Protein Production Workshop** will be held from July 30, 2006, to August 4, 2006, and will offer 25 participants a unique opportunity to obtain hands-on experience with cell-free protein production from wheat germ extracts. It will cover various aspects of small-scale expression screening and large-scale production of labeled proteins for NMR spectroscopy or crystallization screening. Both manual and automated procedures will be covered.

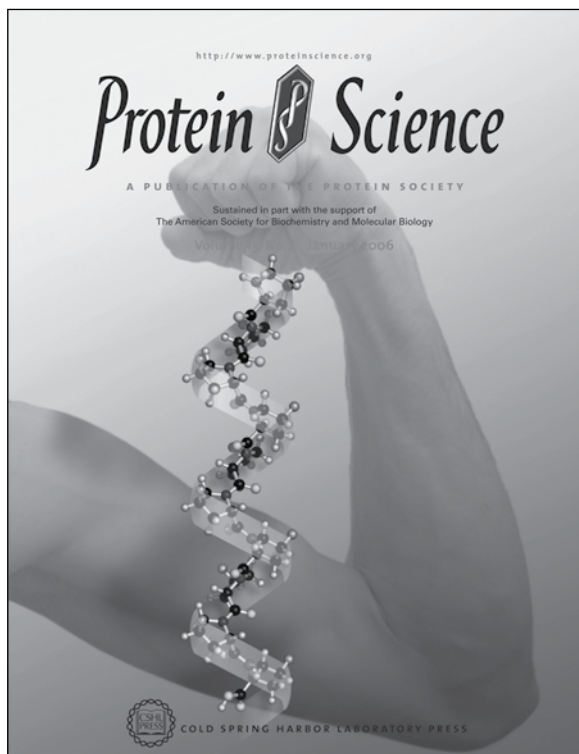
For more information on the workshop, CESG, and CESG structures, visit our website at: <http://www.uwstructuralgenomics.org>



- The “Sesame” Laboratory Information Management System allows users to enter, process, view, and extract relevant data from any location using a series of Web-base applications.
- **Auto-induction protocols** allow automatic induction of bacterial protein production. These protocols produce 10 times more protein per volume of culture than traditional methods.
- **Custom expression vectors that provide target protein fusions** that promote total expression, enhance solubility, and permit rapid detection by fluorescent tags. These vectors can be used to engineer proteins to improve their folding and solubility.
- **Auto-induction protocols** allow automatic induction of bacterial protein production. These protocols produce 10 times more protein per volume of culture than traditional methods.
- A **fully integrated robotic crystallization system** can set up a 96-well plate every 2 minutes, giving it a maximum throughput of 2,880 different crystallization experiments per hour.
- **Storage and crystal imaging units** can quickly image 96 wells of a crystallization plate.
- **Small-volume crystallization chips**, now used widely by crystallographers, are used to screen conditions efficiently and speed crystal growth.
- **Incorporation of a wheat germ cell-free expression system** (*developed at CESG in collaboration with Prof. Y. Endo, Ehime University and Cell Free Sciences, Yokohama, Japan*) holds the promise of increasing the production of proteins from higher organisms.
- **Automated software for X-ray crystallographic structure determination** can carry out fully automated determination of three-dimensional protein structures from X-ray diffraction data.
- **Automatic crystal mounting and crystal screening robots** use computational processes to automatically screen crystals for quality or for contiguous collection of multiple data sets.
- The interaction between various pieces of lab equipment, a bar code writer, and a personal digital assistant through a wireless computer network allows for inexpensive, small-scale automation of a lab environment and can replace the old-fashioned laboratory notebook.
- **Automated NMR data analysis** is a fully integrated data analysis platform that pulls together the complete process of protein NMR structure determination and analysis, as well as archiving raw NMR data and intermediate results.
- **Automated post-structure functional analysis software** is used to search a three-dimensional structure against databases of three-dimensional structural templates and identify functionally important motifs. A Web interface for the software has been designed, and it can be used to obtain a summary of a protein's most likely function.



Ron Raines



Poly (2S-proline) forms a left-handed helix that is the most stable structural element attainable with a natural polypeptide. The stability of this polyproline type II helix is enhanced by installing an electron-withdrawing substituent in the R configuration at C γ of the proline residues, as in this model of [(2S,4R)-4-fluoroproline]₁₀ (photography by Robin Davies, image design by H. Adam Steinberg).

Alan Attie



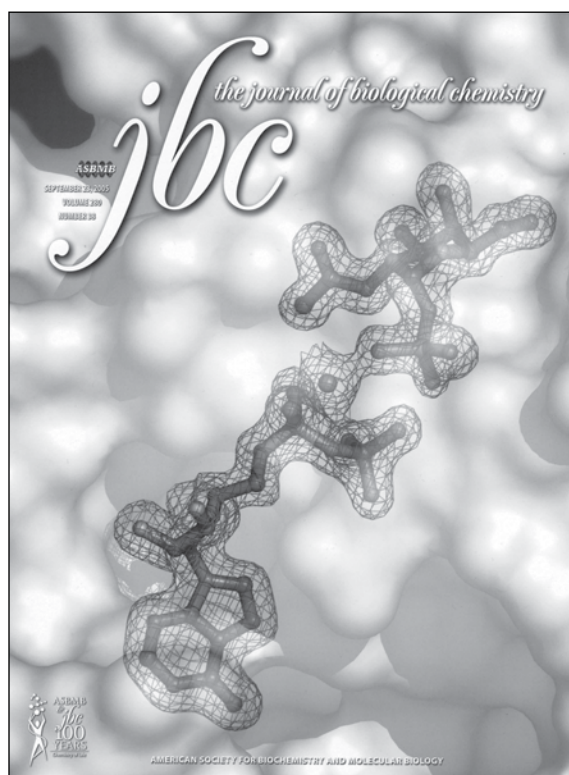
Electron-microscopic image (40,000x) of a pancreatic β -cell (upper left) and a fenestrated endothelial cell forming the wall of a micro-capillary. Insulin-containing secretory granules can be observed in the β -cell, with one showing evidence of a recent fusion with the β -cell surface membrane resulting in the dispersion of insulin into the extracellular space (photography by Ben August, image design by H. Adam Steinberg).

Marv Wickens

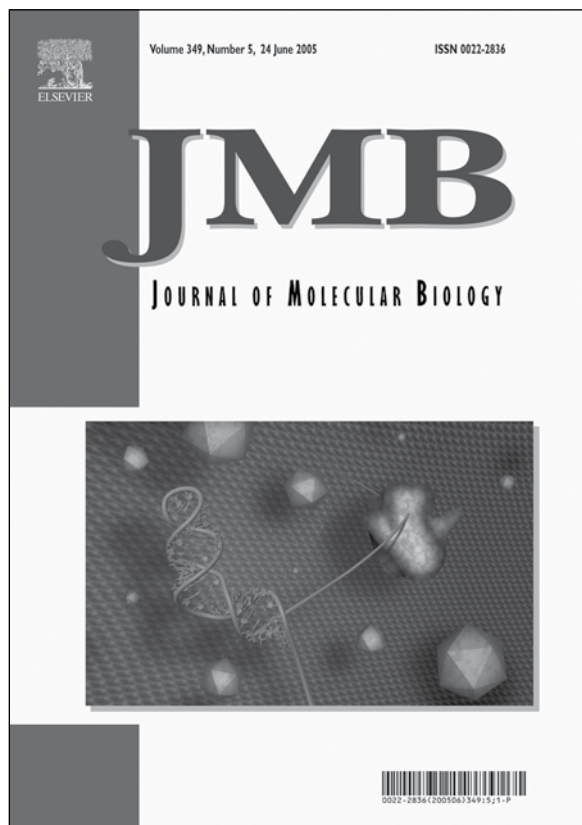


The specificity of a regulatory protein in the *C. elegans* germline (photography by Sarah Crittenton, image design by H. Adam Steinberg).

Hazel Holden



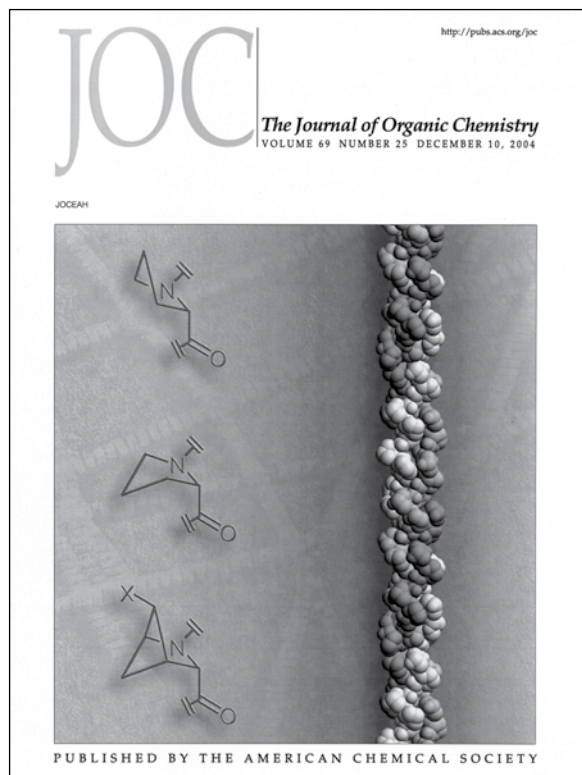
N-acetyl galactosamine kinase (GalNAc kinase) is an ATP-dependent enzyme that catalyzes the production of GalNAc-1-phosphate. Crystals of the human enzyme were grown in the presence of its substrates, MgATP and GalNAc. As can be seen from the electron density (mesh), the enzyme is active in the crystalline state and the products of the reaction, MgADP and GalNAc-1-phosphate, are observed in the active site (image design by H. Adam Steinberg).



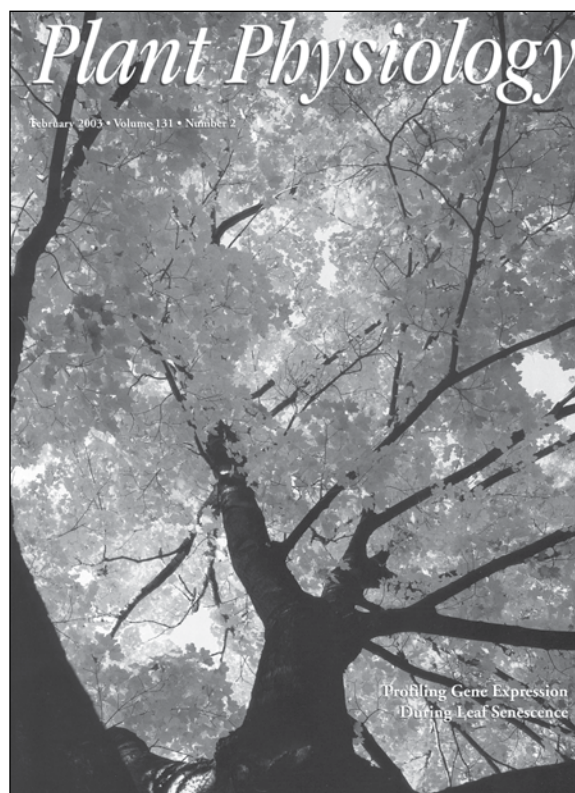
Structure of the HIV frameshift site RNA (PDB ID 1Z2J) with artistic rendering of an approaching ribosome (image design by David Staple and H. Adam Steinberg).



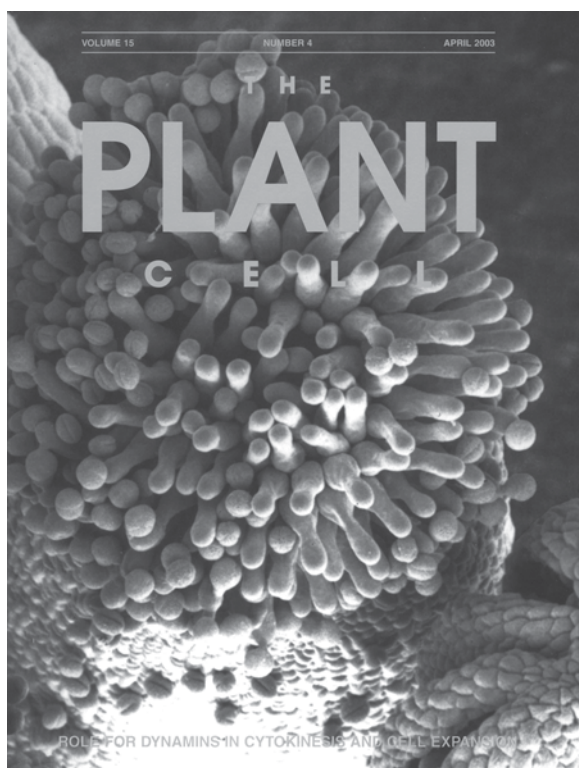
Disruption of shape-complementarity markers to create cytoxic variants of ribonuclease A (image design by H. Adam Steinberg).



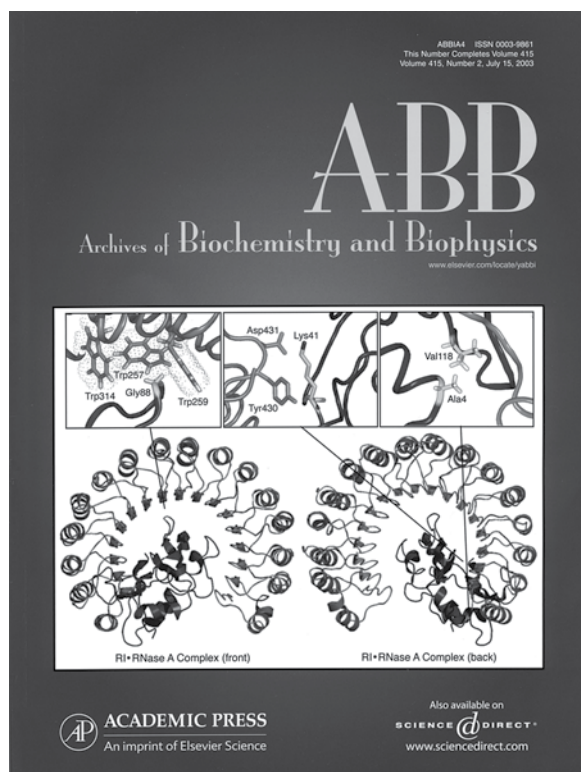
Proline residues are especially common in the triple helix of collagen, which is the most abundant protein in animals. Both predominant pyrrolidine ring puckers of proline are displayed in a 2-azabicyclo[2.1.1]hexane residue, which thus provides new insight on the effect of ring pucker on collagen stability (image design by H. Adam Steinberg).



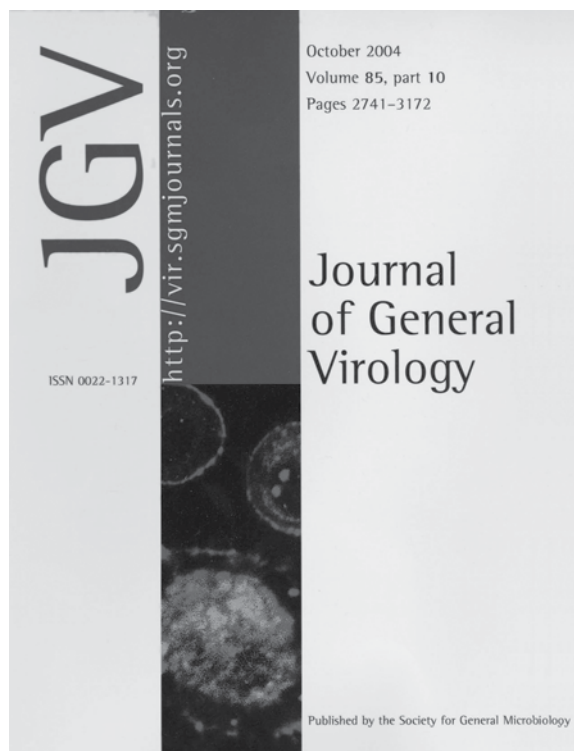
Leaf senescence is a developmental program in which nutrients are recycled. In deciduous trees, such as this maple, nutrients are moved from the leaves resulting in beautiful fall colors. The nutrients are stored in the stem and roots and, in the following spring, are used to support a new crop of leaves (photograph by Jordan Hall).



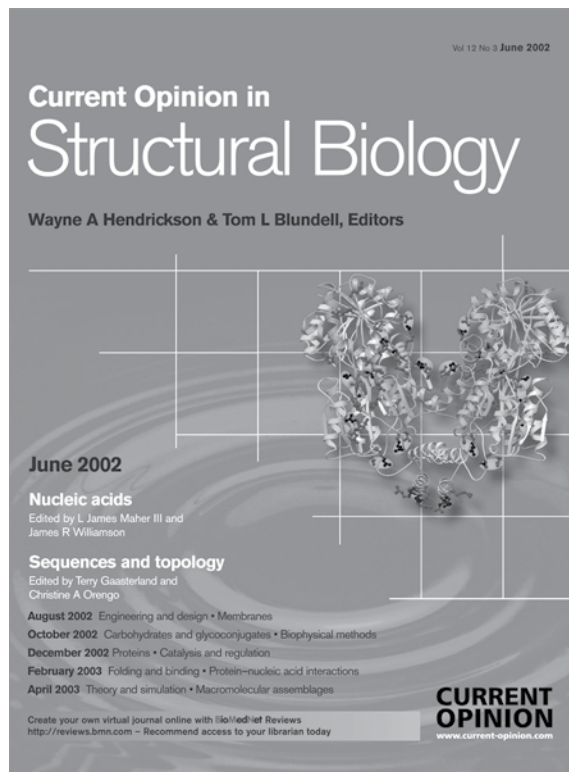
The cover image is a SEM micrograph of the stigmatic surface of a wild-type *Arabidopsis* flower (face-on view). During flower morphogenesis, the stigmatic papillae expand anisotropically to form elongated cells that serve as a receptive surface for pollen grains. Polar expansion of *adl1A* stigmatic papillae was inhibited, and the mutant cells showed defects in cell wall formation and plasma membrane recycling (photography by James Busse, image design by Robin Davies).



Interactions in the complex of ribonuclease inhibitor and ribonuclease A.



HeLa cells infected with encephalomyocarditis virus (EMCV) and harvested at 2 (top left), 4 (top right) and 6 h (bottom) post-infection. Cells were fixed, permeabilized and stained with anti-3D antibodies (visualizing EMCV 3D polymerase). Then the cells were incubated with anti-mouse FITC-conjugated antibodies and TxR-conjugated wheat germ agglutinin, localizing Golgi and nuclear membranes (by Aleksey Aminev, Institute for Molecular Virology).



The relationship between salt bridges on the surface of DNA-binding proteins and the formation of extensive (wrapped) protein-DNA interfaces. Salt bridges between cationic and anionic sidechains observed in the X-ray structure of *lac* repressor and a track of cationic sidechains wind around the protein exterior, plausibly defining the DNA wrapping interface and trajectory in the global wrapping mode. Upon binding, some or all of these salt bridges are proposed to break, profoundly affecting the observed thermodynamics of binding (image design by Ruth Spolar and H. Adam).

From the Labs



**Alan Attie
Lab**

This past year, Cupid entered our laboratory and went on a shooting spree, striking 6 members of our laboratory. **Angie, Donnie, Matt, Jessica, Oliver,** and **Phil** all got married.

Our diabetes work is progressing quite well. We got our diabetes genetics NIH grant renewed with a fantastic priority score. Our manuscript reporting our first positional cloning success, a new diabetes quantitative trait locus, was accepted in *Nature Genetics*. We also published an expression QTL study in *PLoS Genetics*, a synergistic collaboration between our group and our wonderful statistician collaborators, **Christina Kendzierski, Brian Yandell,** and Christina's student, **Meng Chen**.

Summer is in her third year of graduate study in the lab. Highlights from the past year include a visit to the Petersen Lab at the University of Aarhus, Denmark, and passing her prelim exam in late April. She continues to be an active member of the department, sitting on the student faculty liaison committee and playing on departmental kickball and dodgeball leagues. Summer looks forward to an upcoming vacation to Disney World, and the biochemistry lecture/laboratory courses for the nursing students in the spring. "I will also be participating in an interdisciplinary learning community this fall that will link students in astronomy, physics, chemistry, biology, sociology, and political science. Our theme will be sustainability."

Oliver and Summer are working closely together on angiogenesis in relation to pancreatic islets. This is an exciting and challenging new area for our lab. Oliver has done some of the work in zebrafish in collaboration with Mary Halloran's lab, and we're correlating some of the phenotypes of our congenic mouse strains with those we see in the zebrafish.

Matt graduated and is now a post-doc in James Ntambi's lab. **Jessica** will graduate this summer and then do a Nutrition clinical internship. Hong left us to take a job at Schering-Plough working on drug targets in pancreatic islets.

In news from lab alumni, **Scott Lowe**, who is now a Howard Hughes Investigator, won the very prestigious Paul Marks Prize for Cancer Research. **Jonathan Stoehr** has another year in his residency program at Yale and will be Chief Resident next year. His daughter, Maddy (3), has memorized a half-dozen bedtime stories and likes to "read" books to her little brother. Jackson (18 mo) is get-

ting into all kinds of trouble -- in a good way. Jonathan and Dani miss Madison and WI very much. They'll be in Alaska this summer for 2 months where Jonathan will be working in one of the big hospitals serving the Native American population -- "I've always wanted to see a larger population of folks enriched for the "thrifty genes" we've always talked about."

Dan Gretch is now an Associate Professor at Montana State University-Billings with tenure. "A year ago, I changed research focus from things that clog your arteries to things that put holes in your brain. I transitioned into the world of prion research and received 5 years of funding through the NIH INBRE program. My research has allowed me to cut my teaching back to 50% (mostly biochemistry for science majors and nursing students). Darla is doing well and is still working in the investment world. Brice is now in high school (which he loves), is driving a car (yikes) and won the Montana state high school wrestling championship as a freshman. Brad is now in seventh grade and is doing great in school and in basketball and football as well."

Scott Cooper and his wife Amy continue to enjoy life in western Wisconsin. The highlight of last year was attending a research symposium in Cairns, Australia. They worked in a stop in New Zealand to sea kayak, and some diving on the great barrier reef. Scott's 5th and 6th graduate students finished in June, and his first graduate student, Tim Walston, finished his Ph.D. and got a teaching job at Truman State University in Missouri.

Don Gillian-Daniel is keeping busy as the Assistant Director of the Delta Program in Research, Teaching and Learning where he coordinates their teaching internship program for graduate students and post-docs. Each spring he teaches metabolism in the Vet School, something he began doing many years ago while a post-doc with Alan. On the home front, Ben (5 this April) and the Hannah and Noah (2 in June) keep Don and **Anne Lynn**, well, very busy!

Kim Dirlam-Schatz was promoted to Associate Professor at the end of the 2003-2004 academic year, but then took the next year off to be home with her second child, born at the end of September 2004. She returned again last fall and has been teaching part-time (50%) since then. She currently teaches a laboratory course for non-majors in the fall.



**Sam Butcher
Lab**

Wedged between the Markley and Fox groups on the first floor is a shady enclave of miscreants that study RNA structure and function. Please don't be too afraid of this den of rabble-rousers. They are actually a nice group of people once you get to know them. Some of them have even started to openly admit that proteins are interesting. Altogether there are 10 of these rogues, sometimes referred to collectively as "The Butcher Lab." Individually, they have many aliases but are most commonly known as: **Nick Reiter, Dipa Sashital, David Staple, Jared Davis, Ryan Marcheschi, Sarah Pillard, Vincenzo Venditti, Trent Foster, Allyssia Borski** and **Sam Butcher**.

Rumor has it that as many as four Butcher lab members may fly the coop with Ph.D.s in the near future. Be on the lookout for Staple, Reiter, Sashital and Davis to take their turns in the hot seat as they defend themselves (they are expected to sing like birds). On exhibit will be

RNA structures recently solved by NMR, including the U6 RNA stem-loop and its RNA binding protein partner Prp24 (Reiter), the frameshift site RNA of HIV-1 (Staple), the U2-U6 spliceosomal RNA complex (Sashital), and the notoriously large tetraloop receptor complex (Davis). These talented students will confess to conspiring with **John Markley's** NMRFAM gang (**Blad, Abildgaard, Cornilescu, Westler** and **Tonelli** to name a few). If you go looking, I am sure that you can find these people lurking in the basement at odd hours.

In this past year, the ringleader of the Butcher lab was promoted to Associate Professor with tenure. Tenure is a euphemism for "keep doing science but spend more time in committees." Nevertheless, if you would like to visit the dark side of biochemistry, pay a visit to 141 Biochemistry Addition. We have a Warden (**Rita Warden**) and if you look OK, she just might let you in.



**Mo Cle-
land
Lab**

Yong Liu graduated with her Masters in December. She moved to San Francisco with her husband, **Kaisheng** (post-doc Frey lab, now has a job at Amgen), and their daughter, Miranda.

Jeremy Van Vleet, a fourth year graduate student, is getting married in March to Jennifer Headman, a graduate student in the bacteriology department.

Laurie Reinhardt, assoc. scientist, and her husband Eric Steinmetz had their second son, Tyler Hudson, on April 18th of last year.

Mark Anderson, asst. scientist, finished our joint isotope effect study of dihydroorotase with Richard Christopherson in Sydney, Australia, and a paper is now in press at Biochemistry.

John Marlier and his wife and daughter spend the summer in Madison, with John determining the isotope effects on the urease-catalyzed hydrolysis of formamide. **Jill Rawlings** was also here during the summer.

Mo now has two NIH grants, one joint with two colleagues in Australia, John Wallace in Adelaide and Paul Attwood in Perth, to study pyruvate carboxylase. Mo visited the University of Florida (and the Sarasota Opera) in March and Logan State University in August (also the Utah Summer Festival Opera). 2005 was a big year for Mo's family. His older daughter, Elsa, had a boy, Maxwell Cleland Niles, in May, and his younger daughter, Erica, was married in Whistler, British Columbia, in July.





**Mike Cox
Lab**

Current Lab News:

Vessela Petrova has joined the lab as a graduate student. Vessela got her B.A. in Biochemistry and Molecular Biology at Franklin and Marshall College. She surprised us on March 1st when she presented the lab with a red and white doll. Vessela explains that in Bulgaria, martenitsas (the red and white dolls) are exchanged on March 1st to celebrate the coming of spring. Usually they're worn until the first stork or a blossoming/leafing tree is seen, then they're tied to a tree branch. Our martenitsas is attached to the Cox lab news board instead of a tree and I think we're looking for a robin instead of a stork. The lab has over looked this celebration of spring since **Mara Robu's** tenure. Welcome to the lab Vessela!

The Cox lab also has a new postdoc. **Dmitry Baitin** joined the lab in December 2005. Many Cox lab members may remember that Dmitry has visited the lab twice before as part of the Fogarty International collaboration between Mike Cox and Vladislav Lanzov who's lab is located in St. Petersburg, Russia. Welcome back to the lab Dmitry.

Rachel Britt has her preliminary examination scheduled for April 2006.

The Cox lab has submitted its first bill to the Wisconsin State Assembly! Mike and several colleagues advised Representative Terese Berceau in crafting a bill that was introduced to the Wisconsin legislature on February 7, 2006. The aim of the Science Education Protection Act is to defend the integrity of science in the state's science classrooms. Our fingers are crossed! A more detailed description of the bill and related efforts in the department can be found elsewhere in this newsletter.

On a cold Wisconsin Saturday night, a sprinkler pipe in the 1998 Biochemistry Addition burst around 1 AM. While the grad students were at

home in their beds, an undergrad working in the lab, **Reece Goiffin**, came to the rescue. The Biochemistry building was badly damaged but thanks to Reece's efforts in alerting other lab members, no equipment in the Cox lab was damaged.

Mike is having an even busier year than usual. In addition to the never-ending book writing, he organized a UCLA (Keystone) symposium held in Taos in February, and is organizing a session at the ASBMB meeting in San Francisco in April. Architects are being chosen for the new Biochemistry building project just starting up, that he will be overseeing. He is helping to spearhead efforts to create two new courses in the department (one on Molecular Evolution for undergraduate non-majors, and a professional development course for first year graduate students). He will also be an instructor in a course this summer in Corsica, sponsored by the French Centre National de Recherche Scientifique. Somebody has to do it.

Research in the lab is going particularly well. Watch the literature over the next year for new Cox lab contributions. Our research program is evolving.

Past Lab News:

Li-chun Huang sent a note saying that she'd traveled to China for the first time in November 2005, and that they'd got around by foot, bike, train, bus, and boat. She said it was quite an adventure. She also mentioned that she'd climbed Mt. Whitney August 2005. They'd completed the 6,000 foot climb, 22 mile round trip in 12 hours. That's something!

Nami Haruta wrote to say that she was making a move from Yokohama City University to Osaka University. She said she was to continue her research of *S. pombe* Rad541 and its mediators after she's relocated.

Awards:

Julia Cox received a Peterson Fellowship for 2005-2006.

Julia Drees received a Steenbock Fellowship for 2005-2006.

Julia Drees also received a Vilas Travel Award for the Keystone meeting in Taos, New Mexico, in February 2006.

Goings:

Shelley Lusetti has accepted a position of Assistant Professor at New Mexico State University, Las Cruces. Congratulations, Shelley! We're all excited for Shelley but will certainly miss her.



Michael Hobbs will be defending his thesis spring 2006 and plans to work in the Madison area.

Julia Drees defended her thesis this May and is currently deciding on a postdoc.

Julie Eggington will defend her thesis spring 2006 and (per Julie) has plans to start her own reality TV show called "The Hot Room: P32." Should her TV pilot not be picked up by the net-

works, she has back up plans to visit her grandmother in Australia over the summer, and then to join the Brenda Bass lab at the University of Utah as a postdoc working on RNA editing enzymes.

Weddings and Babies:

Julia Drees married Erin Chalmers in August of 2005. The wedding was held in Santa Cruz, California, near where Julia is from.

Nami Haruta married Satushi Takahashi in April 2005 at the Kamigamo-Shrine. Nami sent photos of the wedding and she was beautiful in her white kimono. Congratulations Nami and Satushi. Nami and Satushi also gave us the news that they've just had a baby! Nami sent a picture of Kazume who is extremely cute. What a lot of life changes for Nami in the past year. Congratulations on your new baby too!

Tanya Arenson and **Paul Marrione** sent us news that they've just had a new baby boy who they've named Jonathan. Jonathan was born on March 8, 2006. Congratulations to you both on the new addition to your family.



**Laura Kiessling
Lab**

Besides continuing to publish, review, travel, teach, and keep an eye open for WMDs, here are some of this year's activities, accomplishments, plans and quotes from the Laura Kiessling Group.

Newly crowned Lab's Most Quotable Person is grad student **Adam Courtney** with, "Why do you have to make this a house of lies?" and this unrelated declaration: "I don't conform. I defy the Microsoft Word spell checker on a regular basis." Postdoc **Coby Carlson**, who plans to land a job in industry in 2006, welcomed a baby daughter in June 2005. Maeve joined big brother Cian, age 4. Grad student **Ratmir Derda** was on TV for 5 seconds, looking in a microscope when "60 Minutes" interviewed Prof. **James Thomson**. This month Ratmir will present "High Throughput Approach to Functional Materials Supporting Human ES Cell Self-Renewal" at the American Chemical Society's spring meeting in Atlanta in an Excellence in Graduate Polymer Science Research Symposium. Laura will present similarly at the Materials Research Society's meeting. Grad student **Lingyin Li** and postdoc **Brendan Orner** also contributed to the stem cell work. Postdoc **Jessica Hollenbeck** is leaving this summer to be an assistant professor at Trinity University's Department of Chemistry in San Antonio. She will teach biochemistry and

organic chemistry. "My biggest fear is that my son [James] will grow up with a Texas accent," she says. **Elissa Hobert**, who is about to choose a graduate school, works with Jessica. Meanwhile, **Brendan Orner** plans to leave April 15 to be an assistant professor at Nanyang Technological University's Division of Chemistry and Biological Chemistry in Singapore. "I'm going to take snow tires with me because I heard you can't get them there," says Brendan.

Ashley Reinke, who works with **Eric Underbakke**, will begin the biomedical sciences program at the University of Michigan. Eric is engaged to Dipa Sashital of Biochem Associate Prof. **Sam Butcher**'s lab. He says, "Just let them know I'm still alive and kicking." **David Peal**, who plans to earn the Ph.D. soon and move to Utah for a postdoc position in Alejandro Sanchez's group. There he will chop up worms (planaria) and study regeneration. **Erik Puffer** will earn the Ph.D. soon and start a job with the Flow Cytometry core at H.L. Moffit Cancer Center in Tampa, Florida. **Katie Alfare** received a graduate research fellowship from the National Science Foundation. Katie is a member of Graduate Women in Chemistry, a relatively new group on campus formed in response to high attrition rates among female scientists. Thai scholar **Aimon Tonpenyai** is being mentored in the lab until

early June by graduate students **Emily Dykhuizen** and **Grace Jiarpinitnun**. Aimon is earning her B.Sc. in chemistry from Mahidol University. Emily was awarded a fellowship from the Division of Medicinal Chemistry of the American Chemical Society. Postdoc **Christine Brotschi** from Switzerland extended her stay in the lab, happily. She plans to seek a permanent position soon. **John May**, who is enjoying being a new dissertator, posits, "Adam tries to imitate my accent when he wants to sound intelligent."

Grad student **Jack Borrok**'s contribution to the newsletter: "If **Todd Gruber** 'borrows' my pipette one more time and doesn't return it, I'm going to go medieval on him!" Todd is safe at the moment. He is at Applied Molecular Evolution in La Jolla, California, as part of a 12-week internship under the Biotechnology Training Program. This year Todd married Corey Lastinger and adopted a beagle mix named Penny. Emily Dykhuizen did an internship last year with Abbott Laboratories as part of her BTP program. Grad student **Erin McElroy** and postdocs **Jiyoung Chang** and **Yimin Zhu** substantially round out the group's roster in the chemistry lab.

Laura hired **Sally Garbo Wedde** as an editor to assist her with new duties as editor-in-chief of the new American Chemical Society Chemical Biology Journal (<http://pubs.acs.org/journals/acbcct/currentissue.html>). The third issue is under way. The journal is accompanied by online podcasts and a Wikipedia feature that encourages the science community to discuss chemical biology and thereby help define it. Also new to the group are grad students **Rachael Carpenter**, **Richard Grant**, **Becca Splain**, **April Weir** and **Margaret Wong**. Rachael named April the group's "most fashionable." April is engaged to UW-Madison physical chemistry grad student **Jeremy Higgins**. Rachael says of Sally, "It seems that everyone is vying to be her favorite and **Joe Klim** appears to be in the lead." Sally disavows any notion of favoritism. At this writing, postdoc **Matt Allen** was debating whether to bring a watermelon to the Great Dane when he dresses as Gallagher to compete for the title of 'Stache Master of Madison. The contest is the annual finale to four weeks of mustache-growing for the fundraiser he started with 3 other Kiessling group members. Fellow lab member **Richard Grant** is participating, too. Mustaches 4 Kids Madison (<http://www.m4kmad.org>) last year raised more than \$3,000 to help the Make-A-Wish Foundation fulfill wishes for children with life-threatening medical conditions.



Alumni news: **Eva Gordon** is a science writer for the new ACS Chemical Biology Journal. **Erin Carlson** is at Scripps Research Institute in a postdoc position with Ben Cravatt. **Jason Pontrello** landed an academic position as assistant professor in chemistry at SUNY Cortland. **Andy Spencer** joined "a good group" at protein Design Labs at San Francisco after reluctantly leaving the Khosla lab in Palo Alto last summer. ChemoCentryx is the site for new work in medicinal chemistry for **Bill Thomas**. Zhi-Qiang Yang has also taken an industrial position at Merck, West Point. **Robert Owen** began work in March as a principal scientist at Pfizer in Ann Arbor, Michigan. **Yi He** took his new Ph.D. to work for 3M Biosciences. At Yi's graduation, we heard great testimony from former group member **John Phillips**. Just remember that what you say in the lab *can* come back to haunt you. Our favorite thing about Yi's new job is his title: Biochemist. **Will Sanders** recently moved to Tetrionics (in Madison), which was acquired by SAFC. Will's title is not "biochemist." **Allison Lamanna** is a postdoctoral fellow in Michigan with Rowena Matthews; **Patricia Mowery** is enjoying her time as a postdoctoral fellow in Utah with Sandy Parkinson. **John Phillips** is in the Stoltz Group at Caltech working on the total synthesis of the natural product bielschowskysin, which has been identified as a potent inhibitor of EKVX lung cancer cells. **Jason Gestwicki** is working on recruiting students to Michigan (we still like you Jason), as a member of the Department of Pathology. **Michelle Soltero-Higgin** and **Josh Higgin** (formerly of the Raines lab) welcomed a baby boy. **Ross Weatherman**, an assistant professor in the Department of Medicinal Chemistry at Purdue, is a new father. **Nikki Pohl** gave an outstanding seminar in the Department of Chemistry. Nikki has already been promoted to associate professor with tenure. A grad student in the Chem lab, **Lingyin Li**, initiated a collaboration with lab alum **Andy Hinck**, an associate professor at the University of Texas-San Antonio.

Kiessling Group members have been out on the road. Matt presented on contrast agents for MRI synthesized using ROMP at the "Imaging in 2020" conference September 25-29, 2005, in Jackson Hole, Wyoming. **Ratmir** and **Erin Carlson** attended the meeting "When Chemistry Meets Biology" on the Greek Island of Spetses. **Coby Carlson** attended the AACR-NCI-EORTC International Conference "Molecular Targets and Cancer Therapeutics" in Philadelphia in Nov. 2005. Jessica went to

the Protein Society meeting in Boston and the National Meeting of the American Chemical Society in Washington, D.C. Ron Raines and Laura also spent some time at the meeting in Greece. They can confirm that Erin and Ratmir were at the sessions and not on the beach. Their daughter, Kyra, made a very interesting poster for the meeting. Laura also visited Bordeaux, France this summer to give the Tetrahedron Young Investigator Award Lecture. After the lectures, she had a chance to sample some of the local wines. Unfortunately, the maximum number of bottles that can be transported to the U.S. was 2, so there was little benefit to the group at large. Laura, Ron and Kyra also attended Pacificchem in Hawaii, followed by a jaunt to India. ACS

and India's Council on Scientific and Industrial Research (CSIR) successfully held their first joint conference titled *Building Bridges, Forging Bonds for 21st Century Organic Chemistry and Chemical Biology*, at CSIR's National Chemical Laboratory (NCL) in Pune, India, on Jan. 7–9. A follow-on mini-symposium was held at the Indian Institute of Chemical Technology (IICT) in Hyderabad Jan. 11–12. Bob Grubbs, this year's Nobel Prize winner, enjoyed it when Kyra asked him if he was the Dumbledore of chemistry. **Laura** recently returned from a trip to England as the Rosalind Franklin lecturer. Until the missed connections at the end, the trip was delightful—the night spent in the Ramada Inn outside the Mall of America detracted a bit.



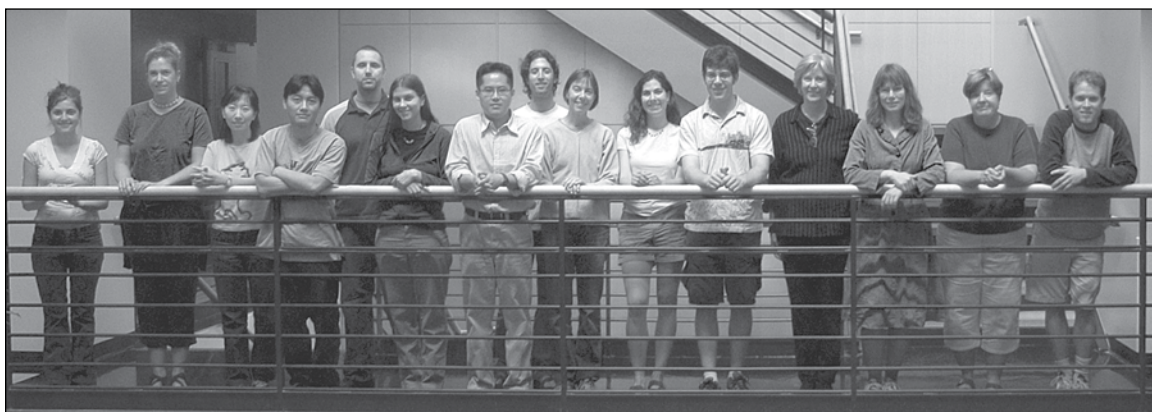
**Judith Kimble
Lab**

Over the past year, a lot has happened in the Kimble lab. On the science front, we continue to explore the regulation of germline stem cells as a model for controls of stem cells more broadly in animal development. Our most recent results are taking us in several exciting directions, including analyses of a novel β -catenin, cyclin D as a developmental coordinator and the CEH-22/Nkx2.5 homeodomain transcription as a determinant of the stem cell niche. In addition, we have uncovered a gradient of FOG-1/CPEB that controls germ line proliferation at one level and spermatogenesis at another, as well as a role for PUF-8 in control of the sperm/oocyte switch.

In 2005, **Trey Kidd** and **Jen Bachorik** both finished their Ph.D.s, and in early 2006, **Liana Lamont** and **Beth Thompson** followed suit to defend their Ph.D.s. Trey and Jen have both moved on to life as a postdoc: Trey to Duke University to work on zebrafish development in the Poss lab, and Jen to the University of Pennsylvania in the Dryefuss lab. Liana is staying in Madison, but will move to the Genetics department

as a postdoc with Xin Sun to work on vertebrate development. Beth has not yet decided where she is going, but plans to delve into the mysteries of plant development. Finally, Kit Tilmann completed his postdoc last summer, and started as an Assistant Professor at Loyola University in Baltimore, Maryland.

In addition to these big professional moves, there have been an unusual number of marriages, engagements and new babies. **Kit Tilmann** and Megan Kenney have become engaged, as have **Dan Hesselson** and Stephanie Nelson. **Liana Lamont** and Scott Meade were married last year, as were **Mike Chesney** and Tristana Von Will; **Kellee Siegfried** and Matthew Harris have become parents to Lily Anne Harris, who was born July 6, 2005. More recently, **Nayoung Suh** and Euiyoung Bae gave birth to Subin Hannah Bae on March 23 at 1:31pm, 2006. Remarkably, **Trey Kidd** and Mindy Steiger became new parents only a few hours later: their son, Henry Justus Kidd was born on March 23, 2006 at 4:11pm. All are doing well.



Despite the various departures over the last year, we also have some recent additions: several new graduate students, **John Jeong**, **Aaron Kerschner**, **Josh Snow** and **Dyan Vogel**; a post-doc, **Olivier Cinquin**; and a technician, **Maya Fuerstenau-Sharp**. Olivier is delving into the mechanism by which size of the mitotic region is controlled, and plans to model that regulatory network mathematically. The others are just getting started.

So those are the major headlines. The newsletter mafia is restricting size of the contributions this year, so I will leave it at that. But of course there is much more. So please stop in to say hello and get really caught up if you are in the neighborhood!!

Here are email addresses of the people who have left the lab over the past year. trey.kidd@cellbio.uk.edu; bachorik@mail.med.upenn.edu; cetimann@loyola.edu.



Henry Lardy
Lab

Greetings from the Lardy Lab at the Enzyme Institute! We have had some very good letters from alumni and find that more and more of you are retiring. One who is not retiring is **Shelly Schuster**. Last year I mentioned that he had become President of a new graduate school in California. It is named the Keck Graduate Institute and trains students in the combination of Biotechnology and Business. The grads have gone on to dozens of companies and universities. Contributors to his Institute have been generous—it grows!

Scientifically we have not advanced far since last year. I wrote a review on C_{19}, Δ^5 steroids for Vol. 71 of *Vitamins and Hormones*; **Padma** has synthesized about 60 compounds searching for anti-androgens that might be useful in treating prostate cancer; **Ashok** has completed analyses of blood samples for a pharmacokinetic study of ADEK, our best-so-far anti-androgen. He, together with Padma, is also continuing the characterization of steroids produced from DHEA by liver and brain tissue—some 30 compounds to go! We have been unable to get any clinicians to test ADEK on CaP patients or any pediatri-

cians to test 16α -hydroxyDHEA as a treatment for Respiratory Distress Syndrome in premature babies. The 16-hydroxyDHEA makes a 15-fold rise in the last days of normal pregnancy and preemies have very little of it. Giving the babies glucocorticoids induces the lung secretion but also retards brain development. So I think the natural lung maturing agent is the 16-hydroxy steroid and it should be tested. We have no funds for trials and the lab operates on a combination of modest royalties on 7-oxoDHEA and my savings.

We have a new post-doc in our group—**Dr. Nianjun Xu**. He brings his own salary from China! **Nancy Kneer** has Emeritus status and participates by conducting enzyme assays and literature searches. **Marion Wagner** is seriously afflicted with lung cancer. Her medications have not been effective so she has stopped taking them. Yet she is very cheerful and still enjoys activities with friends. If you wish to send cards or letters her address is: 12 Westbrook Circle, Madison, WI 53711


We look forward with eager anticipation to the first Tuesday in November 2006!



John Markley
Lab

Comings and goings. **Ed Mooberry** retired last February after 24 years of service to NMR at UW-Madison. We threw a “recognition reception” for Ed on March 3rd to send him off in style, and the Biochemistry faculty voted unanimously to grant Ed emeritus senior scientist status. **Hee-Chul Ahn**, a postdoc in NMRFAM, returned to Korea to direct the laboratory at KIST in Seoul that has a new 900 MHz NMR spectrometer. Before leaving, Hee-Chul published a paper in JACS on the structure of crambin in a mixed aqueous/organic solvent and in DPPC micelles; part of his project was in collaboration with **Slo-**

bodan Macura and Nenad Jurinac at the Mayo Clinic College of Medicine. **Craig Newman** left NMRFAM/CESG to take a position with Epic Systems, a medical informatics company that must be the fastest growing enterprise in the Madison area. **Chris Oldfield**, a Biophysics Training Grant trainee, has moved to Indiana University Purdue University at Indianapolis to work with Keith Dunker, who is a collaborator on the CESG (Center for Eukaryotic Structural Genomics) project. **Qin (Kate) Zhao** moved from CESG to Promega. **John Cao** moved from CESG (Sesame) to a position with the State of



Wisconsin Corrections Division. **Muniasamy Neerathilingam** ("Munish") joined the lab as a postdoc in NMRFAM after finishing his Ph.D. under Iain Campbell at Oxford. **András Perczel** from Eötvös University in Budapest is a visiting professor at NMRFAM on a Fulbright Grant. **Jing Li** has remained with the Sesame project but moved from support from CESG to support from our NIH-funded metabolomics project

News from former lab members:

From "**Viru**" **Virudachalam**: "Sen is a 3rd year med student at Penn State, Vanitha is a 4th year undergrad, applied math, at UC-Berkeley. Subbu continues to work in cancer research and I am quite busy and active in implementing new treatment modalities in our clinic." (Viru is Chief Physicist of Radiation Oncology at JMMD Health System in Concord, California.) **Jane Caldwell** and her husband Tim stopped by for a brief visit last summer; Jane is enjoying her work in the Dept of Biology at West Virginia University in Morgantown. **Dagmar Truckses** and her husband Nate (geologist at ExxonMobil) have a 2-year old toddler daughter, Tatjana, who "loves to imitate her mama and talks lots," Dagmar works with Ray Jacobson, Asst. Prof. at the MD Anderson Cancer Center in Houston, and was recently promoted to the position of 'Instructor.' **Bill Walkenhorst**, Chair, Chem. Dept. at Loyola Univ., New Orleans, and his family were refugees of Katrina. They got out before their house was flooded and moved in with family upriver in St. Louis. **Tim Machonkin** is moving to a faculty position at Whitman College in Walla Walla, Washington. We heard from **Chele DeRider** that she was looking for jobs in the East Coast. Where did you land, Chele? **Rob Tyler** left CESG to take a postdoc position with Brian Volkman at the Medical College of Wisconsin. **Andrei Alexandrescu** has been promoted to Assoc. Prof. at the University of Connecticut, Storrs. **Brian Volkman** has been promoted to Assoc. Prof. at the Medical College of Wisconsin. **Anne Lynn Gillian-Daniel** is doing a great job as the new administrative assistant for NMRFAM.

John's travels:

John and his son Andrew took a boundary Waters canoe trip with **George Reed** and his

son Brock last May. **Rob Tyler** and John were speakers at an NMR workshop at Montana State Univ. in Bozeman last August. **Andy Robertson**, the new Chief Scientific Officer for the Keystone Conferences, wine and dined **Eldon Ulrich** and John last January and gave them a tour of the Robertson ski chalet in the Keystone area. Sue was back in Iowa City, where the girls (Kelly and Sarah) are finishing school. The family comes together in Colorado for vacations. **Young Kee Chae** picked John up at the Seoul Airport last February and gave him a tour of Sejong University, where **Young Kee** is an Asst. Prof. **Young Kee** brought his graduate students to the meeting in Daejeon, Korea, where John gave a talk. Although **Byung Ha Oh**, professor at Pohang University in Korea, could not attend the meeting, he gave his greetings to John by telephone. One of the highlights of the Korean trip was a day of skiing at Muju--John's first experience of skiing in Asia.

Other News:

Zsolt Zolnai is continuing to develop his "Sesame" laboratory information management system. New users include one of the specialized structural genomics centers supported by the NIH Protein Structure Initiative and a structural genomics group in Australia.

Milestones:

I-jin ("Jo") Lin passed her oral prelim last December. She has taken a postdoctoral position at the Oregon Health & Science University in Portland, Oregon. **Dmitry Vinarov** and his wife Sara had their second child (a girl).

Family News:

John and Diane's son, Andrew, graduated from Carnegie Mellon University (Chemistry Major) last May and has started graduate school at the University of California San Diego in Chemistry and Biochemistry. Their daughter, Jessamyn, is a graduate student in Biology at the University of Utah in Salt Lake City.

Greetings:

Best wishes to all. Please keep in touch.



James Ntambi
Lab

Greetings from the Ntambi Lab! This year has been one of both continuity and change for the Ntambi lab as we persist in trying to understand various aspects of carbohydrate and lipid metabolism using the stearoyl CoA desaturase-1 (SCD1) deficient mouse as a model.

Over the past year, we have had to bid goodbye to two of our lab members, **Dr. Agnieszka Dobrzyn** and **Dr. Weng-Chi Man**. **Dr. Dobrzyn** returned to her hometown of Bialystok, Poland in November of 2005 and is now heading up her own lab there. **Dr. Man** was awarded her doctoral degree in December of 2005 for her thesis on "Topology of SCD1 and its co-localization with DGAT-2 in endoplasmic reticulum." She is currently in Sunny California as she starts a Post-doctoral position at Stanford.

With these two departures, we have also had the pleasure of welcoming two new members to the Ntambi Lab. **Dr. Matt Flowers**, whom many of you may have seen roaming the corridors of the 5th floor, has now decided to roam them on the 4th floor instead. Matt was awarded a Nutritional Sciences NIH-training grant and has begun work on characterizing various tissue-specific SCD1 knockouts in the Ntambi Lab.

Dr. Xueqing Liu, or simply **Liu** as we know him, has joined us from the Jefcoate lab in the Pharmacology department at UW-Madison. **Liu** obtained his doctoral degree at Ohio University and is now interested in understanding the role of inflammation in regulating hepatic function.

We are also joined by three eager undergraduate students **Andres Abreu** (Zoology), **Cora Holt** (Biochemistry) and **Amanda Doubleday**

(Biology) who are all working with various members of the lab to further their knowledge through first-hand laboratory experience. Soon, we are to be joined by the youngest member of the team, **Thezin Chonyi**. Thezin is a high-school student who will spend some of his after-school hours in the Ntambi lab.

As for the rest of us veterans of the Ntambi lab, we continue to delve into our respective projects. **Dr. Makoto Miyazaki** has been instrumental in the development of various tissue-specific SCD1 knockouts. He has also characterized the phenotype of the SCD2-deficient mouse and investigated differences in substrate specificity between various SCD isoforms.

Harini Sampath continues to make progress in her thesis project aimed at understanding how various dietary fats differentially affect lipid metabolism and risk for obesity and insulin resistance. She is also mentoring **Andres Abreu**, a senior undergraduate student who is collaborating with her on understanding differences in insulin sensitivity in various mouse models of obesity.

Kiki Chu is also continuing her thesis project in understanding the role of SCD1 in lipid metabolism, particularly looking at its effect on hypertriglyceridemia and liver steatosis and its regulation by certain nuclear receptors.

Last, but certainly not least, our fearless mentor **Dr. James Ntambi** continues to provide guidance to his protégés despite a rather hectic schedule. Dr. Ntambi continues to be invited to speak about SCD at various conferences around the world. Furthermore, the partnership that he has established between Makerere University in Uganda and the University of Wisconsin-Madison has flourished. This year alone, fifteen undergraduate students from diverse disciplines made the 3-week long, 15,000-mile trip to get a first-hand glimpse at some of the problems that face the other half of the world we live in. With this project in Uganda, Dr. Ntambi has begun to bring much-needed attention to the issue of undernutrition, which is certainly something that is often forgotten in our quest to understand the consequences of overnutrition. All the members of the Ntambi Lab hope to join him soon in this venture to bring awareness to problems that should really be obsolete by now but unfortunately are not.

We hope that you have enjoyed reading about us in this issue and wish you all the very best in your endeavors. Cheers!





**Ron Raines
Lab**

As we in the Raines lab continue to assault the interface between chemistry and biology, a multitude of changes have taken place. **Brian “gene” Miller**, our cloning expert, left to become an assistant professor at Florida State University in Tallahassee. **Kim Dickson** is now an assistant professor at Macalester College in St. Paul, MN, and already has several undergraduate students working in her laboratory. **Betsy Kersteen** works for the local biotechnology company, Eragen Biosciences. **Matt “Popo” Soellner** has migrated west to take a postdoctoral position with Jon Ellman at the University of California, Berkeley. Other lab alumni have also joined the ranks of assistant professors: **Chiwook Park** at Purdue University, and **Sang-Hyun Park** at Seoul National University. And, **Jin-Soo Kim** left ToolGen—a company that he co-founded—to become a professor at Seoul National University.

The Raines lab retirement community—the 5th floor of the 1985 wing—had its grand opening this year with three senior lab members moving to that comfortable clime. **Steve Fuchs** defended his thesis successfully, and will move south at the end of summer to take a postdoctoral position with Brian Strahl at the University of North Carolina at Chapel Hill. Steve also looks

forward to getting married this summer. **Eugene Lee** continues to resist late afternoon naps while preparing for his thesis defense and applying for postdoctorate positions. **Bryan “chummer” Smith**, who recently became a father and defended his thesis, is seeking an industrial position in Nebraska to return to his roots and teach his daughter Ava the true meaning of “country”.

After working with **Kim Dickson** for several years, undergraduate **Bernie Fula**, is now pursuing a career in medicine at the UW School of Medicine and Public Health. **Melissa Yatzeck**, a senior, is taking some time off to take care of her newborn baby girl, Mary. **Shawn Lin**, a junior, continues to work with **Jeremy Johnson** after a humanitarian trip to New Orleans. With the departure of **Julia Tretyakova** to New Mexico, former student hourly **Greg Jakubczak**, alias **LMJ**, has enthusiastically taken over as the new Raines lab manager. **Caitlin Dallich**, who makes a mean Tris buffer, is the new student hourly in the lab.

New graduate students and postdoctorates are picking up where others have left off. This year the Raines group welcomed first-year graduate students **Greg Ellis**, **Nicky McElfresh**, and **Rex Watkins**. Rex and his wife are expecting their first baby—a girl—and we wish them the best of luck. The Raines lab also welcomed two postdoctorates to the lab. **Moushumi Paul**, who considered becoming a roadie for Toad the Wet Sprocket, received her Ph.D. with Wilfred van der Donk at the University of Illinois and is working on secondary structure stabilization of ribonucleases. **Margie Borra** the co-founder of the Bay of Pigs, received her Ph.D. with John Denu in biomolecular chemistry and is working to characterize a novel human ribonuclease. Postdoctorates **Matt Allen** (Caltech) and **Thimmaiah Govindaraju** (“Govind”) (NCL, Pune) are working jointly with the Kiessling and Abbott laboratories, respectively, on projects that can only be called “interdisciplinary.”

Luke Lavis, a third-year student, passed his prelim exam and continues to develop novel fluorogenic probes to aid the group’s cell biology efforts. **Joe Binder**, an all-star cross-country runner, proudly displays lab mottos on his fume hood while applying olefin metathesis to proteins. **Matt Shoulders**, a second-year student, enjoys working with acetyl chloride, eating Indian buffet, and listening to country music. **Annie Tam**, a fourth-year student, has the most artistic fume hood in the world of chemistry,



and has developed a reagent that unites the Staudinger ligation and expressed protein ligation. Postdoctorate **Frank Kotch** recently synthesized both “human” collagen and his first baby—a boy, whose gender was revealed conclusively by ultrasound. Postdoctorate **Jason Horng** works on polyproline helices and interviews for academic positions in his native Taiwan. Third-year graduate student **Kelly Gorres** continues her research on prolyl 4-hydroxylase after a three-month internship at Beckman Coulter in Minnesota. Second-year graduate students

Cindy Chao and **Rebecca Turcotte** are working hard on their prelims. Rebecca is pursuing a joint M.D./Ph.D. degree and is in her fourth-year overall. Fourth-year grad students **Jeremy Johnson** and **Jeet Kalia** continue to pursue their next publications, while **Tom Rutkoski**, a third-year student, continues to practice his English accent and consider producing his own TV sitcom: “The Lab.”

In the meantime...**Ron** is working hard to keep all of the above functioning as smoothly as possible.



Bill Reznikoff
Lab

As many of you know, I am “retiring” from the University of Wisconsin during the summer of 2007. I am not dropping out of science (if I did so, I would drive everyone, particularly Cathy, crazy), but rather transferring my science to the Marine Biological Laboratory in Woods Hole, MA. The whole process is a bit confusing and traumatic for me and the other REZ Lab members, but nonetheless, we seem to be having a good time.

The WE in the REZ Lab includes myself, **Igor Goryshin**, **Deb Hug**, **Agata Czyz**, **Chris Adams**, and **Rich Gradman**. We are all working on the basic molecular biology of Tn5 transposition. Igor is particularly interested in the target capture process. Agata is taking off from where **Brandon** ended by using small molecule inhibitors of transposase to define the different steps in transposition. Chris is studying non-specific and specific transposase – DNA complexes using single molecule experiments (partly in John Marko’s lab in Chicago). Rich is working in two fields – studying the conformational changes needed for synapsis and working with Igor on target capture. Starting on April 1, a new postdoc (Soheila Vaezeslami) will be joining the

lab to study the detailed biochemistry of various transposase – DNA contacts. **Soheila** is just now earning her Ph.D. from Michigan State.

Big news is that Chris is getting married in June and hopes to finish his PhD work by late summer. Also big news is that Mindy has moved on to a postdoctoral position at the University of North Carolina and she and **Trey** are proud parents of Henry (3/26)! A final bit of news, **Archna** is leaving Madison for the next step in her career. She is joining the Biology Department faculty at Valdosta State University in Georgia. Hmm – maybe we will arrange a lab trip to visit Archie next January. Congratulations to **Chris**, **Mindy** and Archie!!!

This April, the College of Agricultural and Life Sciences is awarding me the extra mile award for student advising. Of course it is a big honor for me. However, the truth is that I always thought that that was what we were supposed to be doing and, in any case, I enjoyed it.

Please stop by and visit us but don’t visit during the summer. I shall be working at the MBL during the summer - actually working at the lab bench. It is great to be at the bench again!



Two New Professorships in Biochemistry

by Jim Shurts

Laurens Anderson and Henry Lardy

This past year the Department of Biochemistry created two endowed professorships to honor two of our emeritus faculty, Laurens Anderson and Henry Lardy. We are pleased to be able to pay tribute to our two distinguished colleagues, and at the same time recognize and support two of our most innovative current faculty.

Funding for the Anderson professorship included a generous donation from **James Chieh Hsia Mao**. Dr. Mao, who recently retired after a distinguished career at Abbott Labs, earned his PhD in biochemistry under Laurens Anderson in 1963.

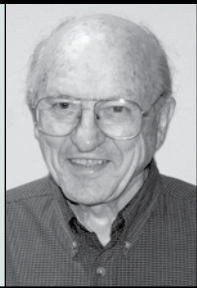
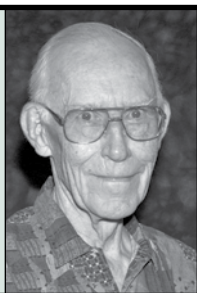
Laurens Anderson earned his BS from the University of Wyoming in 1942. He served in WWII with the Army Air Force, then went on to earn the MS and PhD in biochemistry at the University of Wisconsin. He joined Biochemistry's faculty in 1951, and served until retiring in 1986. He was Steenbock Professor of Biomolecular Structure at Wisconsin from 1981-86. Anderson's research on the chemistry, structure, and metabolism of cyclitols and sugars, and on chemical oligosaccharide synthesis, has been published in more than 90 scientific journal articles. He's been an active and respected member of the American Chemical Society's Wisconsin section and its Division of Carbohydrate Chemistry, and has received the ACS Claude S. Hudson Award in Carbohydrate Chemistry.

Henry Lardy earned his BS from the South Dakota State College in 1939, then went on to earn a MS and PhD in biochemistry at the University of Wisconsin. He joined Biochemistry's faculty in 1945, and served until retiring in 1988. He was Professor and Section Chair at

the Enzyme Institute from 1950-88. Lardy pioneered work on the preservation and storage of semen, which has made artificial insemination in livestock practical. He is an authority in biochemistry and is recognized for his research on isolation, purification and characterization of enzymes involved in carbohydrate metabolism. He has more than 370 publications in major journals and books and has received numerous awards, including the Wolf Prize.

The initial recipient of the Laurens Anderson Professorship in Biochemistry is **Laura Kiessling**. Dr. Kiessling earned her BS from the Massachusetts Institute of Technology in 1983, her PhD (1989) in organic chemistry from Yale University and did postdoctoral work in chemistry at the California Institute of Technology. In 1991, she joined the faculty at the University of Wisconsin, where she is now Professor of Chemistry and Biochemistry. Her current research emphasis is on biomolecular recognition processes and the chemistry and biology of protein-saccharide interactions.

The initial recipient of the Henry Lardy Professorship in Biochemistry is **Ron Raines**. Dr. Raines earned his BS from the Massachusetts Institute of Technology in 1980, his MA (1982) and PhD (1986) in chemistry from Harvard University and did postdoctoral work in biochemistry and biophysics at the University of California San Francisco. In 1989, he joined the faculty at the University of Wisconsin, where he is now Professor of Biochemistry and Chemistry. His current research emphasis is on chemical biology, protein design and engineering, and enzymology.



Honors & Awards:

Faculty:

Laura Kiessling – Hilldale Professorship and Harrison Howe Award

Aseem Ansari – Shaw Scientist Award and Vilas Associates Award

Bill Reznikoff – Arthur Maurer Extra Mile Award

Rick Amasino – Howard Hughes Medical Institute Teaching Professors Award; Elected member to the National Academy of Science; President-elect of the American Society of Plant Biologists

Dave Nelson – Alliant Energy Underkofler Excellence in Teaching Award

Julie Mitchell – 2006 Sloan Research Membership

Tom Record – Society Fellow, Biophysical Society

Mike Sussman – Elected Fellow of the American Association for the Advancement of Science; Appointed to WI Biofuels consortium by Gov. Doyle

Postdocs:

Paul D. Boyer Excellence Awards:



Adrian D. Hegeman

Colon cancer biomarker discovery in the Min muse through stable-isotope assisted quantitative proteomics

This award acknowledges a graduate student or postdoctoral student who is acknowledged by her/his peers and advisors as one who displays clear promise as a research scientist. Most importantly, the award is to be designated in appreciation of the student's consistent willingness to contribute to the intellectual and technical potential of his/her fellow students and colleagues through the selfless help of others.

Graduate Students:

Graduate Teaching Excellence Award

Jackie A. Fretz

This award is intended to recognize a Biochemistry graduate student who has consistently shown evidence of quality, commitment, and innovation in teaching.



Graduate Mentoring Award

Eric S. Underbakke

This award is designated to honor Biochemistry graduate students who consistently provide quality guidance and scientific training in mentoring undergraduate students in their research efforts.



Sigrid Leirmo

Memorial Award in Biochemistry

Christian D. Adams



Brad A. Hook



This award is to be given to a postdoctoral or graduate student who displays clear promise as a research scientist. The award is to be designated in appreciation of the student's consistent willingness to contribute to the intellectual and technical potential of his or her fellow students and colleagues through the selfless help of others.

Undergraduate Majors:

Mary Shine Peterson Scholarship Recipients:

Dejan Acimovic
Mia DeFino
Yejin Eun
Xinhong Lim
Rachel Teo

Kimberly Clark Scholarship Recipient:

Robert Kirchdoerfer

Sigma Aldrich Recipient (NEW):

Steven Kaul

Ezra Totten Recipient:

Nicole Jones

What should Science Education be?

by Mike Cox

What is science? To those of us trained as scientists, this is a simple question. Yet, for many, the answer is unclear. The different views in our state were made plain in late 2004, when the school district in Grantsburg, Wisconsin introduced Intelligent Design (ID) into its science curriculum as an alternative to Evolution. Dean Michael Zimmerman of UW-Oshkosh and other deans from across the UW system sent a letter to Grantsburg, asking that ID be taken out of the curriculum. Letters from scientists and educators from around the state soon reinforced the effort. Our department joined in the summer of 2005, sending a letter that urged the Grantsburg school board to reverse their action, signed by all 35 active members of the department.

Members of the Biochemistry faculty wrote Letters to the Editor on this issue. These triggered a response from a sympathetic state legislator, **Terese Berceau**. A committee consisting of **Mike Cox**, **Alan Attie** and **Rick Amasino** of the Biochemistry Department, as well as Elliott Sober, Ron Numbers, Andrew (Anj) Petto (also Professors in the UW system), and attorney Beth Cox advised Rep. Berceau and helped write a bill introduced into the legislature on Feb. 7, 2006. The bill, now called the "Science Education Protection Act", has received considerable national attention. In its entirety, it reads:

The school board shall ensure that any material presented as science within school curriculum complies with all of the following: (1) The material is testable as a scientific hypothesis and describes only natural processes. (2) The material is consistent with any description or definition of science adopted by the National Academy of Sciences.

The bill does not ban the discussion of any ideology in context. It simply states that if something

is presented as science, then it must actually be science. The wording is straightforward but potent. The bill will provide educators with legal substance to rely on when they come under pressure from groups who want to introduce pseudoscience into the curriculum. The bill will also provide parents interested in good science education with a cause of action if they need one.

The bill has received considerable national attention. It has been endorsed by the American Society for Biochemistry and Molecular Biology (ASBMB), and is under consideration for endorsement by the Federation of American Societies for Experimental Biology (FASEB) and the Association for the Advancement of Science (AAAS). Interviews with department faculty describing the bill are widely available on the internet (Alan Attie has achieved some notoriety by declaring that the bill places Wisconsin in a position to be the "un-Kansas").

On a related front, the Biochemistry department is adding a new course to its undergraduate curriculum. In fall of 2007, the department will offer its first course directed at non-majors, a course in molecular evolution. A movement has also begun to set up a one credit cross-college course, to be required for every major generating biological scientists or science teachers, that will introduce students to the definitions of science, scientists, and the scientific method(s). Farther afield, **Mike Cox** organized a session at the ASBMB meeting in San Francisco in April 2006 on "Current Topics in Molecular Evolution", which was complementary to a session on "Teaching Evolution under Threat of Alternative Views."

Want to become involved? We have been impressed with the extraordinary impact elicited by each action we have taken. Every letter to a school board elicits grateful responses from parents. Letters sent to newspapers get published. Letters sent to legislators are read and responded to. If you are concerned about this issue, write a few letters or get involved in another small way. It need not take a lot of time.

Resources are readily available for those interested:

Websites of the National Academy of Sciences, the National Center for Science Education and the American Association for the Advancement of Science: <http://www.ncseweb.org/>, <http://www.nasonline.org/> (search for: evolution science education), <http://www.aaas.org/> (search for: evolution science education).



Representative Berceau



Faculty stand with Representative Berceau for the introduction of bill 1143 at the Wisconsin State Capitol

To learn more about the legislation: <http://www.legis.state.wi.us/assembly/asm76/news/evolution.html>

To contact representative Berceau: <http://www.legis.state.wi.us/assembly/asm76/asm76.html>

To contact the department about this issue: scienceeducation@biochem.wisc.edu

To learn what any scientist can do to help the cause of science education (an article on our experiences, published in the Journal of Clinical Investigation): <http://www.jci.org/cgi/content/full/116/5/1134>

To view interviews with members of the committee: <http://www.madison.com/archives/read.php?ref=/tct/2006/02/07/0602070356.php>,
<http://www.madison.com/archives/read.php?ref=/tct/2006/02/16/0602160364.php>,
<http://www.wpr.org> (search for, pseudosciences)

Student Faculty Liaison Committee (SFLC)

by Mark Meyer



Hello from the Student Faculty Liaison Committee! This year has been an excellent time for advancement of science as the winds of change blow into biochemistry. We saw the changing of the Biochem Chairperson, survived a flood, and began the graduate departmental merger of Biochemistry with Biomolecular Chemistry. Here are the highlights from the past year.

I would like to congratulate our 2005/2006 graduate student awards recipients: **Christian Adams** and **Brad Hook** (Sigrid Leirimo Memorial award), **Eric Underbakke** (Graduate Mentoring award), and **Jackie Fretz** (Graduate Teaching Excellence award). These awards are designed to recognize graduate students that make a significant contribution to research, teaching, and the department as a whole. Thanks to all students, especially Christian, Brad, Eric and Jackie, in their hard work that continues to make our department great.

As the fresh lot of students arrived in August, our social chairpersons, **Allyson Anding** and **Mark Marzinke**, made them all feel very comfortable and welcome with a great picnic on the Westside of Madison. Marshall Park was an excellent location, with a large pavilion, sand volleyball courts, and wonderful views of Downtown Madison over Lake Mendota. This social dynamic duo also planned a very festive Holiday Party, in which many labs participated in an ornament contest, displaying the lab PI as well as members. This year a size and weight restriction was instituted and enforced after the "snow making North Pole monstrosity" that was entered last year by Sam Butchers lab. Thanks to all who participated.

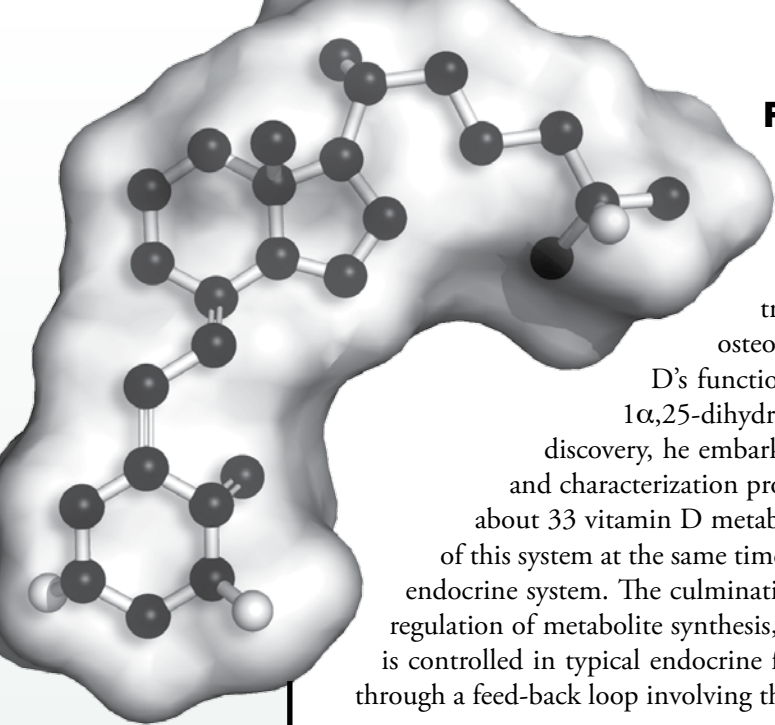
With the merging of the programs into the Integrated Program in Biochemistry, or IPiB for short, many challenges arose. These challenges were met first by our Recruiting Chairpersons, **Bryan Becklund** and **Summer Raines**. In conjunction with **Colleen Clary**, **Flavia Arana**, Ellyse Meuer (BMC), and the faculty committee, they began the trial and error of

IPiB recruiting for new students. Through their hard work, they have recruited yet another excellent class of graduate students.

Every year, the SFLC is proud to bring a student invited speaker to present a seminar and meet with graduate students. A graduate student representative tallies all nominations and votes from all Biochemistry graduate students, and then works very hard in coordinating that speaker to visit. Last year, **Christian Adams** brought Dr. Greg Verdine (Harvard University) to speak about the structure and mechanism of DNA repair proteins. This year, **Anna Fuzery** has invited Dr. Eva Harris (University of California-Berkeley) to speak in June. Her lab focuses on the Dengue virus. In 1998, Eva Harris, along with the other organizers of the Applied Molecular Biology/Appropriate Transfer Technology (AMB/ATT) Program founded the Sustainable Sciences Institute in order to promote technology transfer and capacity building in developing countries.

I wish that I could detail all the important contributions that every committee and committee member makes to the department. Special thanks are in order for our Student Seminar Series coordinator **Ryan Marcheshi** and all his hard work in organizing speakers and refreshments throughout the entire year (including the summer!), **Alison Albee's** commitment to the Departmental Retreat held in May at the Memorial Union, **Jared Davis** for his organizational efforts towards the Egg Drop which we all look forward to every year, **Todd Gruber** and **Kelly Gorres'** work on the graduate and undergraduate (respectively) curriculum for the upcoming students, **Samantha Herbst** in keeping current with the library committee, **Rachel Britt** staying in tune to "Biochem 2009" building plans, and **Steven Darnell** for the wonderful new SFLC website....come and check us out!
www.biochem.wisc.edu/SFLC

Thanks to all faculty and graduate students that have assisted the SFLC over the past year!



Faulty Research Spotlight

by Cheryl Adams Kadera

Vitamin D: The New Old Natural Wonder Drug

Although Vitamin D had long been recognized as an essential nutritional factor and key agent for curing the bone diseases rickets and osteomalacia, it was DeLuca who made the crucial discovery that vitamin D's function requires its conversion, in vivo, into 2 steps to an active hormone, $1\alpha,25$ -dihydroxyvitamin D_3 ($1,25(OH)_2D_3$, also known as calcitriol). Based on this discovery, he embarked on a comprehensive and brilliantly successful metabolite isolation and characterization program which, within roughly 15 years, resulted in the identification of about 33 vitamin D metabolites. Detailed studies of enzymology, physiology, and endocrinology of this system at the same time elucidated the calcium homeostatic system and especially the vitamin endocrine system. The culmination of the effort was DeLuca's beautifully definitive exploration of the regulation of metabolite synthesis, which established $1,25(OH)_2D_3$ as a true hormone, whose synthesis is controlled in typical endocrine fashion by the products of its action (calcium and phosphorus levels) through a feed-back loop involving the parathyroid glands and parathyroid hormone.

The isolation and characterization of the vitamin D hormone was a keenly pursued and extremely challenging problem at the time (a few micrograms of pure substance were isolated from 1500 chick intestines), and its successful solution ranks as a brilliant technical feat and a true landmark contribution to steroid chemistry and endocrinology. With his studies of the regulation of metabolite synthesis, DeLuca defined, in biochemical terms, a whole new hormonal system and added a major new subject – vitamin D endocrinology – that since has become a standard component of biochemical and medical texts and has grown into an enormously active field with numerous new investigators from diverse disciplines. With the expansion of the field has come the realization that DeLuca's vitamin D hormone is a multifunctional regulator, whose roles and sites of action include not only the maintenance of calcium homeostasis, but also the control of cellular differentiation and the modulation of immune responses. The identification of genes responsive to $1,25(OH)_2D_3$, the isolation of the vitamin D receptor protein, the cloning, characterization and regulation of expression of the receptor gene are but some of DeLuca's notable contributions. Very fruitful organic chemical syntheses are another distinguishing feature of DeLuca's vitamin D research program. DeLuca's team achieved the first chemical synthesis of calcitriol and many other natural metabolites; his group also pioneered the preparation of a variety of systematically modified analogs, thereby resolving basic questions of structure/activity relationships and contributing a number of therapeutically efficacious compounds including, for example, 1α -hydroxyvitamin D_3 , 1α -hydroxyvitamin D_2 , the "19-nor" series of analogs and the more recent 2-carbon modified analogs

that exhibit unique biologic effects. Over the years, DeLuca's group has also devoted much effort to the development and refinement of quantitative assays for the potent vitamin D metabolites used for the diagnosis of bone disorders and for the monitoring and management of therapies.

More important than his quite astonishing output is the intellectual substance of DeLuca's work and its impact and consequences. As a result of his biochemical work, we now have a much deeper understanding of the biological mechanisms controlling normal calcium balance and a much clearer insight into the causes of several important diseases (e.g., hypo- and hyperparathyroidism, renal osteodystrophy, and various types of vitamin D-resistant rickets). Through his chemical work and his detailed studies of the biological properties and actions of metabolites and analogs, DeLuca played a decisive role in promoting the development and introduction of the natural hormone and of structural relatives as effective new drugs for the treatment of disease. Indeed, the clinical applications of vitamin D compounds are a very significant element and an important consequence of DeLuca's research. Most recently, in an outstanding chemical feat, DeLuca has synthesized a novel 2 carbon modified $1\alpha,25$ -(OH) $_2D_3$ analog termed 2-methylene-19-nor-(20S)- $1\alpha,25$ -(OH) $_2D_3$ (2MD). This compound is of particular interest as it has been shown to be efficacious in promoting new bone formation. As most current drugs utilized for the treatment of osteoporosis decrease bone mineral loss but do not stimulate new bone formation, this analog is unique, and is currently under development for the treatment of postmenopausal osteoporosis. Current or potential medical applications of vitamin D compounds,



1996



1976



1959

however, are not limited to calcium metabolism and bone disorders. The range of possible therapeutic uses expanded significantly with the demonstration that 1,25-(OH)₂D₃ promoted the differentiation and inhibited the proliferation of malignant cells, and subsequent research in many laboratories has confirmed that calcitriol, in addition to its well-established action as regulator of calcium homeostasis, also functions as a potent stimulator of cellular differentiation for a variety of cell types (e.g., osteoblasts, lymphocytes, keratinocytes, and others).

The preceding concise review illustrates the fundamental substance and numerous important practical extensions of DeLuca's research. His identification of the biologically active vitamin D metabolites transformed the long-known vitamin into a multifunctional new hormone and created vitamin D endocrinology as a new field of knowledge now productively pursued by numerous groups in medicine, physiology, biochemistry, and molecular biology. The pioneering synthetic work initiated by his team has led to a great resurgence of interest in steroid and vitamin D chemistry and that subject now engages the attention of at least a dozen academic laboratories and a roughly equal number of pharmaceutical companies. The combined efforts of these groups have yielded some elegant new synthetic routes to vitamin D compounds, and they have generated a very large collection of structural analogs exhibiting a broad range of medically useful activity patterns. Some of these compounds already have found important application for the treatment of human disease, and current intensive development efforts will undoubtedly yield further additions to the present list of therapeutically useful agents. Professor DeLuca's vitamin D research, in short, represents outstanding basic medical science with highly beneficial practical consequences.

Professor DeLuca has also been active in the creation of new commercial enterprises. He played a major role in the start-up of Tetrionics, Inc. (now Sigma Aldrich Fine Chemicals), Bone Care International (now Genzyme), QuantiGel, and most recently, his own company, Deltanoid Pharmaceuticals, Inc. For these efforts, he was recently recognized as Ernst & Young Entrepreneur of the Year (2004) for the State of Wisconsin.

In conclusion, Dr. DeLuca's entire career has been devoted to scientific discovery, invention, and developing his ideas into medications that have improved the health and wellness of people all over the world. He also demonstrated innovation and success in leading the Biochemistry Department to its current rank as one of the top biochemistry departments in the world. Added to this is the fact that he is the most prolific

1930 – Born in Pueblo, Colorado
 1951 – B.A., Chemistry (Honors), University of Colorado
 1955 – Ph.D., Biochemistry, University of Wisconsin-Madison
 1956-57 – Postdoctorate Fellow, Biochemistry,
 University of Wisconsin-Madison
 1958 – Instructor of Biochemistry,
 University of Wisconsin-Madison
 1959 – Assistant Professor, Biochemistry,
 University of Wisconsin-Madison
 1962 – Associate Professor, Biochemistry,
 University of Wisconsin-Madison
 1965-Present – Harry Steenbock Research Professor,
 Biochemistry,
 University of Wisconsin-Madison
 1970-86 – Chairman, Biochemistry,
 University of Wisconsin-Madison
 1991-05 – Chairman, Biochemistry,
 University of Wisconsin-Madison
 1968 – Meade Johnson Award
 of The American Institute of Nutrition
 1969 – Andre Lichtwitz Prize from the French Institut
 National de la Sante et de la Recherche Medicale
 1973 – Osborne and Mendel Award
 of The American Institute of Nutrition
 1974 – Honorary Degree Doctor of Science,
 University of Colorado-Boulder
 1974 – Roussel Prize of France
 1974 – Gairdner Foundation Award (Canada)
 1978 – Membership in the American Academy
 of Arts & Sciences
 1979 – Membership in the National Academy of Sciences
 1980 – Honorary Degree Doctor of Science,
 Medical College of Wisconsin, Milwaukee
 1983 – 3M Life Sciences Award of the Federation
 of American Societies for Experimental Biology
 1983 – Bristol-Myers Squibb/Meade Johnson Award
 for Distinguished Achievement in Nutrition Research
 1985 – Honorary Degree Doctor of Medicine,
 Karolinska Institute, Stockholm, Sweden
 1987 – Spencer Award, American Chemical Society,
 Kansas City Section
 2002 – Elected Fellow of the
 Wisconsin Academy of Sciences, Arts, and Letters
 Granted over 500 U.S. patents
 and 150 active foreign equivalents
 Over 1100 publications in the following fields:
 Vitamin A, Vitamin D, Parathyroid hormones and Calcitonin

inventor in the history of the Wisconsin Alumni Research Foundation (WARF), resulting in more revenues than all other inventors combined.

Following is a link to the talk given by Dr. DeLuca at the Overture Center in downtown Madison on March 7, 2006: <http://www.researchchannel.org/prog/displayevent.asp?rid=3456>

Postdoctoral Fellowships:

Name	Lab	Fellowship
Allen, Matthew J.	Raines/Kiessling	NIH - NRSA Postdoctoral Fellow
Allingham, John S.	Rayment	Canadian Postdoctoral Fellow
Byrd, Dana T.	Kimble	NIH – NRSA Postdoctoral Fellow
Clee, Susanne M.	Attie	American Heart Postdoctoral Fellow
D'Silva, Patrick R.	Craig	American Heart Postdoctoral Fellow
Higurashi, Takashi	Craig	Human Frontiers Science PD Fellow
Hollenbeck, Jessica	Kiessling	NIH – NRSA Postdoctoral Fellow
Kotch, Frank W.	Raines	NIH – NRSA Postdoctoral Fellow
Lam, Ngan	Kimble	Damon Runyon Postdoctoral Fellow
Lee, MyonHee	Kimble	Howard Hughes Postdoctoral Fellow
Nykamp, Keith R.	Kimble	Howard Hughes Postdoctoral Fellow
Phillips, Bryan T.	Kimble	NIH – NRSA Postdoctoral Fellow
Pierce, Brad S.	Fox	NIH – NRSA Postdoctoral Fellow
Sobrado, Pablo	Fox	American Heart Postdoctoral Fellow
Wang, Tao	Craig	American Heart Postdoctoral Fellow
Xia, Xiaofeng	Martin	American Heart Postdoctoral Fellow
Zhao, Enpeng	Attie	American Diabetes Postdoctoral Fellow

Graduate Student Fellowships

University:

Name	Lab	Fellowship
Nicholas Reiter	Butcher	CALS Wisconsin Distinguished Fellow
Katie Williams	DeLuca	R.H. Burris Fellow
Kara Lynch	Martin	AHA Predoctoral Fellow
Harini Sampath	Ntambi	AHA Predoctoral Fellow
Brian Thomson	Clagett-Dame	AHA Predoctoral Fellow
Melissa Davis	Holden	NSF Fellow
John May	Kiessling	NSF Fellow

Graduate Student Fellowships

Departmental:

Name	Lab	Fellowship
Sungtae Kim	Pike	Babcock Fellow
Jack Borrok	Kiessling	Biochemistry Scholar
Caroline Davis	Record	Biochemistry Scholar
Jae Eun Kwak	Wickens	Mary Shine Peterson Fellow
Julia Cox	Cox	Peterson Fellow
Karl Hauschild	Ansari	Peterson Fellow
Christopher Warren	Ansari	Peterson Fellow
Allison Albee	Wiese	Steenbock Fellow
Julia Drees	Cox	Steenbock Fellow
Dipali Sashital	Butcher	Wharton Fellow

Biochemistry Degree Listing 2005/2006

Degree Name (Major Professor) Thesis Title

PhD	Binkowski, Brock F (Belshaw)	I. Ligand Regulated Peptides: A general approach for using small molecules to regulate the interaction of intracellular peptides with target proteins II. Novel Strategies for Error Correction on Gene Synthesis Products
PhD	Flowers, Matthew, T (Attie)	The Role of ABCA1 and SCD1 in Lipoprotein and Cholesterol Metabolism
PhD	Kersteen, Elizabeth, A (Raines)	Protein Folding Enzymes: Protein Disulfide Isomerase and Prolyl 4-Hydroxylase
PhD	Hinkley Glen, T (Reed)	Ligand Effects on the Reduction Potential of the [4Fe-4S] Cluster in Lysine 2,3-Aminomutase
PhD	Levitsky, Konstantin (Belshaw)	Selective Modulation of Receptor Activity by Proximity-Accelerated Alkylation
PhD	Pottekatt, Anita (Menon)	Molecular cell biology of GlcNAc-PI de-N-acetylase (PIG-L), the second enzyme of the GPI biosynthetic pathway
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