DEPARTMENT OF BIOCHEMISTRY

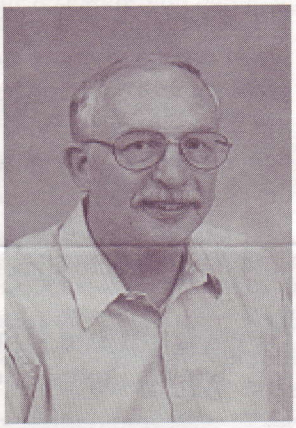
KANSAS STATE UNIVERSITY

Alumni and Friends Newsletter

Fall, 1999

Head News (Swan Song)

Tom Roche



This past academic year was my ninth and final year as Department Head. Charlie Hedgcoth has taken on this responsibility. The Department will move forward with great confidence under his leadership. Besides providing some updates, I hope you will abide some retrospective comments (including some old news). As I entered the headship, I emphasized the need to return to full staffing of faculty positions by hiring excellent researcher/teachers, the need for improving facilities, the acquisition of biophysical equipment, and the need to expand the student programs. Due to sustained efforts of the faculty, strides have been made in these areas.

A highlight of my headship was the hiring of outstanding faculty. I will not review all those changes and our rise from only 8 faculty in the Spring of 1991 to 14 faculty in the fall of 1997. To illustrate the notable advance in research strength with the hiring of six new faculty, I will comment on the programs of Mike Kanost and Xuemin (Sam) Wang, who were recruited in my first year as Head. Each has developed research programs which have received international recognition. Mike has delved deeply into the production and molecular action of defense proteins that protect insects from invading organisms (see enclosed). Not only has Mike continually been supported by major grants but, while working in Mike's laboratory, two postdoctoral researchers have obtained five year NIH grants. In a rare example of plant studies leading the way for studies on animals, Sam Wang was the first to clone (isolated the coding DNA) and recombinantly produce an enzyme, phospholipase D, that facilitates important changes in the membranes of plants. He has discovered several forms (isozymes) and has gained an advanced understanding of their very different properties. He has begun to elucidate their roles in cellular communication (signaling) that influence plant development and other transformations.

The faculty staffing situation includes some complexities. Beyond traditional interests, John Tomich serves half-time as Director of the Biotechnology Core Facility. During 1999, Jerry Reeck was again bitten by the administrative bug (a dangerous beast) and has taken on a half-time role as Associate Dean in the College. At the end of the 1999 academic year, Dr. Delbert Mueller has retired. We greatly appreciate Del's dedicated efforts in teaching, advising, and research (cf. enclosed article). In recent years, Del used solid state NMR to map distances in the activation site/active site region of Rubisco (the abundant enzyme that fixes CO2). This work, which was supported by USDA funds, has provided important insights into the function/regulation of this key enzyme.

Over the past nine years, considerable renovation occurred. Advances included the doubling of the Department's main administrative office space and

renovations to incorporate the core facilities (Biotechnology and NMR) and space for a computational biochemist (Paul Smith). I am most proud of and gave up the most hide in getting Burt Hall renovated. As I emphasized in the last Newsletter, this building now has effective fume hoods in all laboratories (at least two with tempered make-up air) and substantial renovation, most importantly all new windows. During the past year, continuous changes have been introduced into the Ackert II construction plans. This future building is scheduled to house the personnel and the functions of the Department which presently reside in Willard Hall and the Chemistry/ Biochemistry building. Planning has been constrained by budget restrictions that have compelled incorporating maximum efficiency. The plans are essentially finalized and will be put out for bid this fall. The building is then scheduled to be occupied by fall of 2001. Interactions within the Department will be facilitated since the new construction will extend to within about 140 feet of Burt Hall. Even for those moving from the upscale confines of C/B, there will be improved space for support personnel and in common instrument rooms. Yes, some investigators will have reduced laboratory space and it is not clear where some activities occurring in Willard Hall (e.g. Dr. Davis's bioremediation research or desk space for first year graduate students) will find a home. The Department will retain space for 14 faculty research suites, with five located in Burt Hall.

The Department has added $1.5 million in biophysical equipment and is on a favorable path towards improving equipment supporting teaching laboratories. Dr. Om Prakash, director of the high field NMR facility, has provided the energy and leadership to make our 500 MHz facility regionally recognized. The Biotechnology Core Facility has a MALDI mass spectrometer and past acquisitions of the Department include a CD/MCD, titration calorimetry and scanning calorimetry equipment.

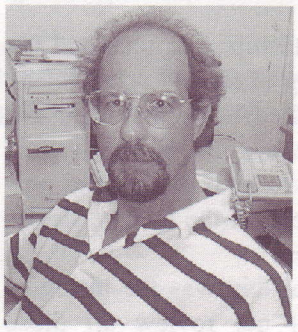
In the past year, we have replaced our old Model E's with a much more capable and much smaller analytical ultracentrifuge. (Do you remember those large gray instruments in the Dave Cox laboratory?) In part, this instrument can determine the mass of proteins and protein assemblages and characterize protein interactions. Advances in our teaching laboratory equipment have been and will continue to be made. A new student activity fee is providing funds to purchase needed teaching equipment. The upgrade started with the purchase of $60K in equipment last year. Dolores (Dee) Takemoto ably led this acquisition effort.

The Department research success rests on the high quality of the research efforts of our undergraduate, graduate and postdoctoral researchers. For the past four years, the number of individuals in each of these ranks averaged 40% higher than the pre-1990 level. In no small part due to the success of these student research efforts, each faculty research program has been supported by significant (competitively attracted) external funds in the past year. If Roche would have gotten his NIH grant renewed, the departmental extramural support would have gone well over $1.5 million for the first time in the past year (still well over $1.3 million).

With great enthusiasm, I fully turn my focus to my research program. I am on sabbatical leave this fall. A large number of manuscripts including a couple of invited review articles and a revised NIH grant proposal will keep me busy. Our research focus is on the four kinase isozymes that regulate the pyruvate dehydrogenase complex. A long-term goal is to develop inhibitors of specific kinase isoforms that are over expressed in diabetes and act to shut down glucose use by inactivating this enzyme complex.

News from the Biotech Core Facility

J.M. Tomich, Professor and Director



This past year the facility provided reagents or services to support the research of 47 faculty members at K-State, representing the Colleges of Agriculture, Veterinary Medicine and Arts and Sciences. Almost all of these researchers are members of the Kansas Agricultural Experiment Station. These services included oligonucleotide synthesis, peptide synthesis, protein sequencing, amino acid analysis, mass analysis and custom organic synthesis. For a more comprehensive guide to our services and fees, consult our website: *www.ksu.edu/bchem/biotech/corelab.html*

We accept orders from other institutions. Some of those institutions include: University of Kansas, Washington University–St. Louis, University of Southern California and the University of Pennsylvania. This past year we have also provided services to several corporations. We ran mass analyses on synthetic peptides for Santa Cruz Biotechnology Inc., performed custom organic syntheses for Hills' Pet Foods Inc. and produced chromophoric assay reagents for Sigma Chemical Co. The core facility is operated and maintained on a day-to-day basis by Dr. Takeo Iwamoto and Mr. Gary Radke. Dr. Iwamoto is the assistant director of the facility and oversees all peptide and organic syntheses and oversees the operation of the mass spectrometer. Gary handles the oligonucleotide requests, the protein sequencing and amino acid analyses. Both Gary and Dr. Iwamoto have been with the facility since its inception in 1993. If you have any questions on how we might assist your research, you can reach us at 785-532-5956 or fax 785-532-6297.

Protein NMR Facility

Om Prakash

Nuclear Magnetic Resonance (NMR) spectroscopy is the most powerful technique besides X-ray for determining three-dimensional structures of proteins and other macromolecules. However, NMR is more ideally suited for biologically important molecules in their functional state—the solution state. Another advantage of this technology over X-ray spectroscopy is the ability to study dynamic phenomena, which are responsible for understanding how proteins achieve their unique functions.

Funding from NSF-EPSCOR and Kansas State University supported the establishment of a 500MHz NMR facility in the Department of Biochemistry to investigate the structure and dynamics of proteins and other biological macromolecules. The NMR equipment, focused on protein research, was not previously available in the state of Kansas. The primary instrument at the facility is a 500MHz Varian UNITY plus NMR spectrometer containing a Sun SPARC station, a pulsed field gradient accessory, a three channel detection system, a 5mm triple resonance and indirect detection pulse field gradient and 5mm broad band probes with high-stability temperature controller for multi-nuclear/multi-dimensional NMR experiments. A cluster of Silicon Graphic workstations is also available for off-line NMR data processing. Each remote workstation is equipped with a 7 Gbytes hard drive and a 20 Gbytes optical disk drive for data storage and 3D and 4D NMR data processing, as well as molecular calculations. This state-of-the- art facility not only provides the latest technology in the area of protein science available for faculty researching at the frontier of biochemistry, but also makes certain that our students are educated using the latest technology. Prior to establishing this facility, faculty were dependent on out-of-state facilities.

The major impact of this center to researchers at K-State and other regent's institutions in Kansas is to open the door to understanding how proteins work at a molecular level. Such understanding is important for progress in medicine, nutrition, environmental concerns and agricultural productions. More than 35 researchers from KSU, KU, WSU and other academic institutions as well as four industries use this facility in their research program. This facility has supported more than 20 grant applications for extramural funding. Several of these research projects involve investigation of proteins or protein domains that have been cloned and require knowledge of their three-dimensional structure. This is done not only for understanding their functions but also to intelligently implement site-directed mutagenesis to generate new, potentially useful products. These engineered proteins can be patented and will have major impacts on local and state economies.

Insect Immune Response

Mike Kanost

Insects can become infected with bacterial, fungal and viral pathogens or with parasitic nematodes. However, one must usually look carefully to find a sick insect, because they have efficient defenses against most microorganisms. Consider housefly or stablefly larvae (maggots) living in a moist garbage pile or in a heap of manure. They thrive in an environment rife with bacteria, in which

a wound is very likely to become infected. But maggots do very well, as proved by the number of flies that attend the Biochemistry picnic each September at Tuttle Creek Reservoir. Research in the laboratory of Mike Kanost in the Department of Biochemistry is aimed at understanding biochemical mechanisms by which insects recognize and respond to infections.

Insects (and other invertebrates) do not have B-cells or make antibodies, but they do have mechanisms very similar to those that comprise the "innate" immune system of mammals. Insects have phagocytic blood cells similar in function to neutrophils and macrophages, and they make antimicrobial proteins in a type of acute phase response. Kanost and his group are studying the functions of the blood cells (hemocytes) and plasma proteins that participate in insect immune responses. Most of their work involves a large caterpillar, Manduca sexta (the elephant of the insect world) as an experimental insect, but some work is also being done with mosquitoes and the Indian meal moth. They have made a panel of monoclonal antibodies to Manduca hemocytes, and have isolated antibodies that can be used as markers for four different populations of hemocytes, each with a separate function. These antibodies have also helped to identify cell surface proteins that appear to function as cell adhesion proteins in an encapsulation response, in which hemocytes cooperate to form a multicellular capsule around a parasite such as a nematode or the egg of a parasitic wasp (work of Elizabeth Willott, David Levin and Jeremy Gillespie). After a parasite is trapped by the hemocyte capsule, it is killed by mechanisms that may include generation of reactive oxygen intermediates and toxic effects of quinones produced by a phenoloxidase present in the blood.

How do insects know when they are infected? Kanost's group has identified several plasma proteins that bind to polysaccharides on the surface of bacteria or fungi (work of Xiao-Qiang Yu and CongCong Ma). Binding of these lectins to their targets triggers the activation of a cascade of serine proteases in plasma. The proteases then activate the phenoloxidase zymogen and cytokine precursors. Haobo Jiang and Yang Wang have isolated and cloned a cDNA for a serine protease that specifically activates the prophenoloxidase zymogen after an insect is wounded or infected. This protease exists in plasma as an inactive zymogen until it is itself activated by yet another protease. Jiang and Wang have cloned cDNAs for four other proteases expressed by hemocytes that are candidates for participants in this reaction or perhaps in other protease cascades.

A new discovery is that a 23-residue peptide, which appears in the blood within minutes after an insect is wounded, acts as a cytokine to stimulate adhesion and spreading by one of the hemocyte types, the plasmatocytes. This response helps to seal the wound and prevent bleeding, somewhat like platelet aggregation in mammals. Wang and Jiang have found that the plasmatocyte spreading peptide is released by a specific proteolytic cleavage from an inactive precursor protein in the blood. The active peptide is the carboxyl terminus of the larger precursor. Efforts are now underway to identify the protease that is responsible for releasing the active peptide. The solution structure of the plasmatocyte spreading peptide has very recently been solved by Xiao-Qiang Yu, with help from Om Prakash in our NMR Facility, and found to have some similarity to the fold of epidermal growth factor.

Kanost's group is continuing to search for new proteins in insect blood. Graduate student Yifei Zhu is conducting screens by differential analysis of peptides by mass spectrometry and by subtractive hybridization of cDNA populations to find new proteins that appear in the blood after insects are infected by bacteria. She has identified a group of previously unknown inducible proteins and she has discovered a putative cytokine activity in the blood that stimulates synthesis of these proteins. This work may yield new types of peptides with antibacterial or antifungal activity.

A better understanding of insect immune responses has potential to improve efforts at microbial control of pest insects and to aid in strategies to block the transmission of human and animal diseases by blood-feeding insects such as mosquitoes. Insects may be a source of new types of antimicrobial peptides with unique mechanisms, which could serve as model structures for future development of new classes of antibiotics.

Distinguished Lectures

This year our department was honored by attracting two noted scientists as invited lecturers. The Richard H. and Elizabeth C. Hageman Distinguished Lecture in Agricultural Chemistry was delivered by Professor Maarten J. Chrispeels of the University of California–San Diego on April 15, 1999. Dr. Chrispeels spoke on "Aquaporins: Their roles in Plant Growth and Development." The next day he conducted a workshop on the timely topic of "The use of Lectins and Enzyme Inhibitors for Genetic Engineering". His wife Dr. Janet Chrispeels and the Hagemans attended the talks and the reception held in honor of Dr. Chrispeels.

Dr. Claude Klee, Senior Scientist from the National Cancer Institute, presented the Burroughs Wellcome Lecture in basic Medical Sciences to the University on March 9, 1999. The presentation was titled "Calcineurin: Coupling Between Oxidative Stress and Calcium Signaling". She also presented a research seminar to the department on March 8, titled "Role of Calcium binding to Calcineurin B in the regulation of Calcineurin Protein Phosphatase Activity". Dr. Klee also held discussion sessions with graduate and undergraduate students relating to their research projects involving calcium functions.

The annual Hageman Lectureship results from a generous endowment by the Hagemans to Kansas State University. Richard obtained a B.S. in Chemistry at K-State and a M.S. at Oklahoma State University where Elizabeth obtained B.S. and M.S. degrees. With a Ph.D. from the University of California in Berkeley, the Hagemans moved to the University of Illinois at Urbana where they had distinguished research careers. The first lecture of the series last year was delivered by Professor Eugene Nester of the University of Washington.

The Burroughs Wellcome Fund is a private foundation established to advance medical sciences by supporting research and other scientific and educational activities. It emphasizes career development of biomedical scientists and advancing underfunded areas in basic medical sciences or areas with a shortage of qualified researchers. BWF, governed by a 12-member Board of Directors of distinguished scientists and business leaders, is not affiliated with any corporation.

Del Mueller Retires

Associate Professor Delbert D. Mueller is recognized for thirty years of teaching, research and service to the College of Arts and Sciences and to Kansas State University. Previously, he held positions in industry and government as well as serving in the military.

Dr. Mueller's research in physical biochemistry emphasized protein structure/function studies, especially those of a plant enzyme whose activity is uniquely responsible for incorporation of atmospheric carbon dioxide into organic biomass. In addition to directing M.S. and Ph.D. degree theses, he encouraged undergraduate student participation in research. During his tenure he was mentor to nearly thirty undergraduates who worked in his laboratory for anywhere from one to four years. Through a sabbatical leave to the Los Alamos Scientific Laboratory in 1974/1975, Dr. Mueller helped introduce at K-State the methods of nuclear magnetic resonance spectroscopy (NMR) and stable isotope labeling for structure studies of biological molecules.

A second sabbatical to Washington University in St. Louis in 1993 extended those methods to include solid-state NMR for proteins. Besides research, Dr. Mueller strongly supported the biochemistry undergraduate degree programs by helping the curricula and by serving as undergraduate advisor and lead undergraduate advisor for many years. Dr. Mueller was always generous with his time in patiently training and advising students. His teaching involved senior/graduate level courses, two of which he largely designed himself and taught for nearly his whole career. In the last 15 years, he has also been very active in teaching introductory and service courses. Dr. Mueller generously contributed in many service roles. He oversaw library acquisitions for the Department for many years and in recent years was active on the Pre-Med, Pre-Dental, Pre-Optometry Evaluation committee and the College of Arts and Sciences Life Science Committee.

Dr. Mueller is a member of several professional and honorary organizations: American Society of Biochemistry and Molecular Biology, American

Chemical Society, Sigma Xi, Phi Lambda Upsilon, and Gamma Sigma Delta. He has held numerous positions within those organizations, twice serving as President of the KSU Chapter of the American Chemical Society.

Other News & Notes

Qiang Xiao (M.S. 1998, Davis) moved to Columbus, OH after completing her M.S. She is doing research on neural tube defect genes in the Department of Pediatrics at Children's Hospital in Columbus.

Xiaowei Wu (M.S. 1998, Davis) undertook some "practical training" with a large company in Atchison, Ks. This fall she moved to Texas A&M where she is getting a graduate degree in Management and Information Systems in the College of Business.

Karen Gonzalez (Ph.D. 1995, D. Takemoto) finished a postdoc with Rob Dennell in Biology at K-State and obtained a position as an Assistant Professor at Systema University in San Juan, Puerto Rico. She continues her work on lens epithelial cell differentiation using her new confocal microscope. She is currently collaborating with Dr. Takemoto on this project.

Yong Yu (Ph.D. 1998, Davis) completed his Ph.D. and moved to Boston University. He is at the Center for Advanced Biotechnology where he is developing immunological detection methods for weapons of mass destruction, under the supervision of Charles Cantor.

Xiaolu "Lucy" Guo (Ph.D. 1996, Davis) has moved to Los Angeles where she is working at City of Hope.

Binghui Shen (Ph.D. 1990, Davis) continues as an assistant professor at the City of Hope Medical Center in Duarte, California.

Dimitri Tamalis (Ph.D. 1997, Hedgcoth), after brief stops in New York and Greece, is doing postdoctoral work with John Iandolo at the University of Oklahoma in Oklahoma City.

Wenyan Zhan (M.S. 1997, Hedgcoth) is now a Software Engineer with Hale Library at K-State.

Grace (Chan-Lan) Sun Lin (Ph.D. 1992, Krishnamoorthi) is presently a research associate at Washington University in St. Louis.

Dr. Mengli Cai (Post-Doc. 1993–1995, Krishnamoorthi) is currently a research scientist at the Abbott Research Laboratories in Chicago.

Dr. Jianhu Liu (Post-Doc. 1993–1996, Krishnamoorthi) is the director of the NMR Facility at Ohio University, in Athens.

James Dyer (Ph.D. 1996, Wang) is currently at Montclair State University, New Jersey, where he is an Assistant Professor in Chemistry.

Daqing Yang (Ph.D. 1996, Roche) is doing postdoctral work at St. Jude Children's Research Hospital.

Robert Edward Clegg

Robert Edward Clegg, 84, noted Professor of Biochemistry at K-State, died on June 4 at St. Luke's Hospital in Kansas City, Mo. of complications from an auto accident. He was born on July 29, 1914 in Providence Rhode Island and had been a Manhattan resident since 1948.

Dr. Clegg received a B.S. degree from the University of Rhode Island in 1936, a M.S. Degree from North Carolina State University in 1939, and a Ph.D. degree from Iowa State University in 1948. Between degrees, he enlisted in the Army during World War II and served as an officer in the medical corps.

Upon completion of his Ph.D., Dr. Clegg joined K-State as an Associate Professor in the Department of Chemistry. He joined the Department of Biochemistry when it was formed with some members of the chemistry faculty. He performed research, taught undergraduate classes, and mentored many doctoral and masters students throughout his career. In 1985, Dr. Clegg retired after 37 years.

Dr. Clegg was married to Lois McDonald on November 27, 1941, she preceded him in death on February 16, 1986. Two sons, Douglas Clegg (Manhattan, Kansas) and Robert Clegg (Urbana, Illinois), and one daughter, Victoria Clegg (Manhattan, Kansas), survive him.

Recent graduates from the Biochemistry Graduate Program

Student	Degree, Year	Major Professor	Current Position
Jason Baker	Ph.D. 99	Roche	Postdoctoral Associate, University of Nebraska Medical Center
Karinne Cortes	M.S. 99	Mueller	Technician, Georgia (Fort Benning area)
Sherri Hawthorne	M.S. 98	Kanost	Research Assistant, Department of Animal Sciences, KSU
Qijaing He	M.S. 98	Reeck	Research Assistant, California Institute of Technology
Lalida Panpradit	M.S. 98	Tomich	Ph.D. Student, Department of Biochemistry, KSU
Kirk Pappan	Ph.D. 98	Wang	Postdoctoral Associate, Department of Biochemistry, KSU
Xiaowei Wu	M.S. 98	Davis	Graduate Student in MIS, Texas A&M
Yong Yu	Ph.D. 98	Davis	Postdoctoral Fellow, Center for Adv Biotech, Boston University
Maria Zavodsky	M.S. 99	Krishnamoorthi	Technician, Michigan State University
Zhihong Zeng	M.S. 99	Davis	Research Assistant, Department of Biology, KSU
Yiqing Zheng	M.S. 98	Tomich	Technician, Bio-Synthesis, Lewisville, Texas
Xiahui Zhu	M.S. 98	Muthukrishnan	Research Assistant, Boston University

Notes from the Biochemistry Undergraduate Program

We are delighted with the continuing strength of the undergraduate program. There are about 60 majors currently. Thanks to the financial support from KSU and Biochemistry alumni, a number of these students are scholarship winners. This year's awardees are:

Premier scholarships:

Kyle Brownback (So., Lyndon, KS)	Foundation
Joella Frye (Fr., Hays, KS)	Putnam
Genee Gorup (Fr., Wichita, KS)	Medallion
Erin Powell (So., Caldwell, KS)	President
Jacob Taussig (Jr., Manhattan, KS)	Foundation
Hilary Watson (Fr., Formoso, KS)	Foundation

Continuing Departmental Hughes scholarships:

Kyle Brownback (So., Lyndon, KS)
Sara Budden (Sr., Abilene, KS)
Chris Johnson. (Sr., McPherson, KS)

Departmental scholarships:

Joella Frye (Fr., Hays, KS)	Merill
Chris Schmidt (Jr., Topeka, KS)	Merill
Genee Gorup (Fr., Wichita, KS)	Merill
Julianne Jackson (Fr, Parsons, KS)	Merill

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http://www.ksu.edu/bchem/

Our home page contains information on the Department of Biochemistry, faculty, undergraduate and graduate programs, courses, seminar, and core facilities. Other K-State-related pages that might be of interest:

KSU Alumni Foundation *http://www.ksu.edu/alumni*

E-Collegian Newspaper *http://www.spub.ksu.edu*

City of Manhattan *http://www.manhattan.org*