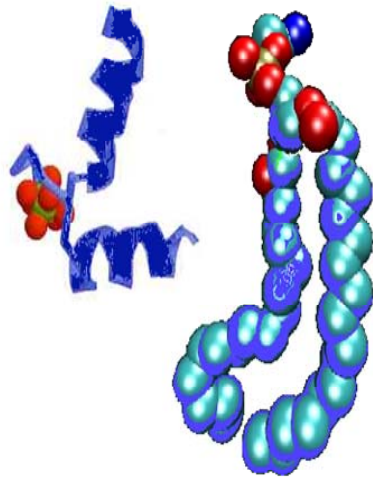


Spring Symposium

Functional Genomics Consortium



www.ksu.edu/functionalgenomics/

**APRIL 4 AND 5
BIG 12 ROOM
K-STATE
STUDENT UNION**

**An Initiative of the Targeted
Excellence Program at K-State**

Our thanks to our sponsors!

Bruker Daltonics
Jim Kalbron
719-277-0386

Applied Biosystems
Bill Seiter
913-422-8346

Functional Genomics Consortium
Nancy Huls, Program Coordinator
506 Ackert Hall, Kansas State University
Manhattan, KS 66506
Phone: 785-532-6367
E-mail: nhuls@ksu.edu

WEDNESDAY, April 4

7:30 Continental breakfast (Flint Hills Room)

Glycomics

- 8:00 Gerald Hart, Dynamic O-Glc-N-acylation of nuclear and cytoplasmic proteins: A ubiquitous nutrient/stress sensor regulating signaling and transcription in all metazoans
- 8:45 Heather Desaire, Glycoprotein analysis for HIV vaccine development
- 9:30 Yuntao Zhang, KSU, Analysis of corneal keratan sulfate oligosaccharides by tandem mass spectrometry
- 10:00 to 10:30 Break

Proteomics

- 10:30 Jay Thelen, Quantitative proteomics of seed filling in oilseeds
- 11:15 Juan Luis Jurat-Fuentes, A proteomic approach to study *Bacillus thuringiensis* toxin receptors and their alterations in resistant *Heliothis virescens* larvae
- 12:00 Yu Jiang, KSU, Application of proteomics in weight control studies
- 12:30 to 1:45 Lunch, Flint Hills Room (Reservation needed)

NMR

- 2:00 Jacob Schaefer, REDOR NMR for the structural biologist
- 2:45 Robert Powers, Functional and therapeutic analysis of novel proteins by NMR
- 3:30 James Bann, Peeling away at anthrax toxin action by NMR

THURSDAY, April 5

7:30 Continental breakfast (Flint Hills Room)

Metabolomics/Lipidomics

- 8:30 Eve Wurtele, Metabolic pathway analysis
- 9:15 Jyoti Shah, KSU, Lipids in plant defense against pathogens
- 10:00 to 10:30 Break
- 10:30 Michael Fitzgerald, ABCA transporters: Critical regulators of lipid homeostasis and human physiology
- 11:15 Richard Jeannotte, KSU, An overview of the lipidomics projects in the Functional Genomics Consortium

2:00 to 4:00 **MetNet Workshop: Ackert 232**
Eve Wurtele: The MetNet Platform: Elucidation of metabolic and regulatory networks

Gerald W. Hart, John Hopkins University

In 1983, the Hart laboratory made the surprising discovery that many nuclear and cytoplasmic regulatory proteins are dynamically modified by O-linked N-acetylglucosamine, O-GlcNAc. The O-GlcNAc modifications of Ser(Thr) residues of nucleocytoplasmic proteins is both as abundant and as dynamic as protein phosphorylation, often occurring in a reciprocal manner at the same or nearby amino acids. In recent years, O-GlcNAc has been shown to be required for life at the single cell level, to regulate both transcription and translation, and to regulate signal transduction cascades in response to the nutrient status of the cell. As a result of this research, the Hart laboratory has also become a leader in the development of methods to study difficult post-translational modifications, including state-of-the-art mass spectrometric methods.

Heather Desaire, University of Kansas

A major research focus of Dr. Desaire's group is the structural analysis of the glycoprotein that covers the surface of the HIV virus, gp120. This protein has 26 different glycosylation sites, and it is currently the leading candidate for HIV vaccine development. One chief roadblock to identifying a better mimic of viral gp120 is that the carbohydrate structures on this glycoprotein have not been characterized. (They comprise 50% of the mass of the protein.) The Desaire lab's current research focus is to fully characterize the carbohydrates on both the recombinant and viral forms of this glycoprotein, in a glycosylation site-specific fashion. Identifying the glycosylation present on bioactive (viral) isolates would be a monumental advance in HIV vaccine development, because once the glycoprotein on the viral surface is identified, a molecular target for the next generation of HIV vaccine would be known.

Functional Genomics Spring Symposium

April 4 and 5, 2007

Jay Thelen, University of Missouri, Columbia
With recent technological advances in the area of mass spectrometry in conjunction with maturing plant gene databases, high throughput identification of proteins from model and crop plants is technically feasible. Most of the ongoing research in Dr. Thelen's lab is centered on the development of quantitative proteomics approaches and applying these strategies towards seed filling in oilseeds, plants that accumulate oil as the primary storage reserve. Thelen's group is using quantitative proteomics data to predict metabolic flow in diverse oilseeds such as castor, canola, soybean and sunflower with particular emphasis on carbon assimilation and intermediary metabolism. They are also interested in the regulation and biochemistry of *de novo* fatty acid synthesis and triacylglycerol accumulation in oilseeds. Global protein profiling of oilseeds using two-dimensional gel electrophoresis has revealed multiple isoforms for many metabolic activities.

Juan Luis Jurat-Fuentes, University of Tennessee
Insecticidal toxins from the bacterium *Bacillus thuringiensis* (Bt) are expressed in transgenic Bt crops for efficient and environmentally sound insect control. Binding of these toxins to specific midgut receptors in susceptible larvae is required for toxicity. Therefore, identification of toxin-binding molecules is an essential stage in the characterization of target susceptible larvae. Dr. Jurat-Fuentes has used a proteomic approach to identify midgut Cry1Ac toxin-binding proteins and their alterations resulting in resistance in *Heliothis virescens* larvae. Midgut brush border membrane (BBM) proteins resolved by two-dimensional (2D) electrophoresis were probed with Cry1Ac. The Jurat-Fuentes group has identified BBM proteome alterations involved in resistance to Cry1Ac toxin by comparing BBM proteomes of one susceptible and three resistant *H. virescens* strains using 2D differential in-gel electrophoresis (2D-DIGE).

Jacob Schaefer, Washington University in St. Louis
Dr. Schaefer is the co-inventor of cross-polarization magic-angle spinning (1976) and rotational-echo double resonance (1989). Both techniques have become standard solid-state NMR methods and are currently in use world wide. The areas of focus of his research program include solid-state NMR determination of the structure and dynamics of protein binding sites, the modes of action of glycoprotein antibiotics, correlation of carbon and nitrogen assimilation in plants, and chain synthetic polymer glasses.

Robert Powers, Univ. of Nebraska, Lincoln
An abundance of protein structures emerging from structural genomics are not amenable to ready functional assignment because of a lack of sequence and structural homology to proteins of known function. The Powers group has developed a high-throughput NMR methodology (FAST-NMR) to annotate the biological function of novel proteins through the structural and sequence analysis of protein-ligand interactions. These interactions are determined through a tiered NMR screen using a functional library of compounds with known biological activity. A rapid co-structure is determined by combining the NMR defined ligand-binding site from chemical shift perturbations with the protein-ligand docking program AutoDock. Their CPASS (Comparison of Protein Active Site Structures) software and database is used to compare the active site with proteins of known function. The ligand-binding profile (a list of ligands that bind the protein) is also used to assign function in a manner similar to sequence homology.

Complementary to their efforts with FAST-NMR, is the development of NMR metabolomics to monitor the *in vivo* activity of unannotated proteins by comparing the metabolome of wild-type and mutant cells. A function is inferred by identifying the metabolites and associated pathways affected by the inactivated unannotated protein.

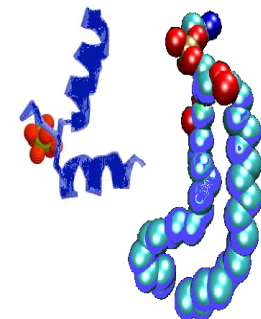
James Bann, Wichita State University
Binding of the anthrax protective antigen (PA) to the host cell receptor CMG2 triggers a complex series of events that ultimately proves fatal to the host. Part of the mechanism involves a pH-dependent conformational change in PA that leads to the formation of a membrane spanning pore. While the conformational change occurs *in vitro* in the absence of the receptor at pH 7, when PA is bound to CMG2, a pH of 6 is required to trigger the conformational change. Dr. Bann's group is utilizing NMR to examine the mechanism of the conformational change in PA, the interaction of PA with CMG2, and how these are related to the formation of a transmembrane pore.

Eve Syrkin Wurtele, Iowa State University
Plants can be considered "environmentally clean", solar-powered factories that produce a wide range of chemicals from simple precursors (carbon dioxide, nitrogen, sulfur, etc). These complex plant-derived chemicals include carbohydrates, proteins, oils, and vitamins, and have nutritional, industrial, and medicinal uses.

Wurtele's research, juxtaposed at the interface between biology and computational sciences, centers on the interplay between the metabolic and regulatory signals: the metabolic network of plants. Her foci are 1) the development of software to explore the metabolic and regulatory network in conjunction with experimental data from millions of datapoints (<http://metnet.vrac.iastate.edu/>), 2) the elucidation of metabolic networks associated with the two-carbon activated molecule, acetyl-CoA, and 3) the development of a virtual reality video game to teach cell biology to high school and undergraduate students.

Michael L. Fitzgerald, Harvard University Medical School
Dr. Fitzgerald's research group investigates a sub-family of ABC transporters that play critical roles in human cardiovascular, pulmonary and skin biology. These transporters are large polytopic membrane transporters that couple the hydrolysis of ATP to the movement of molecules across lipid bilayers. Their long-standing interest is to describe the mechanism by which ABCA1 stimulates the cellular efflux of cholesterol and phospholipids and why mutation of this gene in humans causes Tangier disease, a low HDL syndrome associated with premature cardiovascular disease and peripheral neuropathies. They have also been investigating how mutations in ABCA3 block the formation of lipid rich surfactant thus causing lung collapse and fatal neonatal respirator distress in humans. Most recently, they have become interested in the lipid transport function of ABCA12 and how mutations in this gene blocks the formation of the lipid rich stratum corneum which leads to the devastating skin disorder harlequin ichthyosis. Dr. Fitzgerald will focus on how they have applied mass spectrometry (MS) to study ABCA1 and ABCA2 function.

Functional Genomics Consortium



www.ksu.edu/functionalgenomics/