## 1999 PROGRAM

**8:00 a.m.** **Registration and Coffee - Room HG-611, Hospital Auditorium, UK Medical Center**

**8:20 a.m.** **Welcome by Dr. Fitzgerald Bramwell, Vice President for Research and Graduate Studies, University of Kentucky - Room HG-611, Hospital Auditorium, UK Medical Center**

**8:25 a.m.** **Introductory Remarks - Dr. Robert B. Grossman, University of Kentucky**

**8:30 a.m.** **Dr. Chi-Huey Wong, Scripps Research Institute**
***"Chemoenzymatic Approach to Carbohydrate-Mediated Biological Recognitions"***

This lecture will present our recent work on the development of new chemoenzymatic approaches to tackle the problem of carbohydrate-mediated biological recognition processes. Studies of selectin–carbohydrate interaction associated with infectious and inflammatory diseases and development of new methods for the synthesis of carbohydrates and their conjugates, carbohydrate mimetics and mechanism-based inhibitors of glycosyltransferases will be discussed.

**9:20 a.m.** **Discussion**

**9:30 a.m.** **Dr. Laura L. Kiessling, University of Wisconsin**
***"Probing Saccharide Recognition with Synthetic, Multidentate Ligands"***

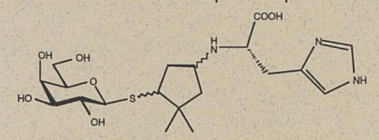
Saccharides employ unique mechanisms to mediate biologically and medically important recognition events. One key feature that distinguishes protein–carbohydrate interactions from traditional receptor-ligand binding events is that the former often requires a multivalent display of saccharide ligands. We have developed the ring-opening metathesis polymerization (ROMP) as a new method to synthesize multivalent arrays. Using this approach, we have been systematically exploring multivalent protein–saccharide binding to illuminate features that give rise to high functional affinities. In addition, we have found new functions for multidentate saccharide ligands, suggesting the *in vivo* display of saccharide clusters may have functions beyond protein–carbohydrate complexation. We have used our multivalent displays to inhibit cell–cell interactions, promote proteolytic cleavage of the protein L-selectin from the cell surface, and to control signal transduction pathways in bacterial chemotaxis.

**10:20 a.m.** **Discussion**

**10:30 a.m.** **Intermission**

**10:45 a.m.** **Dr. Ole Hindsgaul, University of Alberta**
***"Solid-Phase Synthesis and Screening of 'Carbohybrid' Mixtures"***

Solid phase combinatorial chemistry has been used to add molecular diversity to minimal carbohydrate structures in an effort to produce ligands for carbohydrate-binding proteins. We term the resulting molecules "carbohybrids" since they contain a sugar, a small organic ring spacer and a derivatized amine, usually an amino acid. The solution synthesis of such compounds has already been reported [Nilsson et al, *Biorg. Med. Chem.*, **6**, 1563 (1998)], and the chemistry has now been extended to the solid phase using unprotected sugars and a trityl linker. The synthesis of a 300-member β-GlcNAc carbohybrid library illustrates the method. The compounds, produced as mixtures, are screened using Frontal Affinity Chromatography with MS detection [Schriemer et al, *Angew. Chemie*, **37**, 3383 (1998)], which can determine the binding constants for individual compounds present in a complex mixture.




**A Carbohybrid**

**11:35 a.m.** **Discussion**

**11:45 a.m.** **Dr. C. Fred Brewer, Albert Einstein College of Medicine**
***"X-Ray Crystal Structures of Lectin-Carbohydrate Cross-Linked Complexes"***

Lectin binding to the surface of cells leads to cross-linking of glycoconjugate receptors, including glycoproteins and glycolipids, which, in many cases, is related to a variety of biological signal transduction processes. We have observed that many naturally occurring cell surface oligosaccharides are multivalent and capable of binding and precipitating with specific lectins [C. F. Brewer, *Chemtracts - Biochem. & Molec. Biol.*, **6**, 165 (1996)]. These cross-linking interactions lead to a new source of binding specificity, namely, the formation of homogeneous carbohydrate–lectin cross-linked lattices, even in the presence of mixtures of the molecules. Our recent studies show that many of these lattices are highly ordered and often crystalline. For example, the soybean agglutinin, a tetrameric GalNAc/Gal-specific lectin from Glycine max, forms crystalline cross-linked lattices with four isomeric analogs of the biantennary blood group I carbohydrate antigen [Olsen et al, *Biochemistry*, **36**, 15073 (1997)]. We will describe the x-ray crystal structures of these complexes as well as more recent structural studies which provide insight into the structure–function properties of multivalent lectins and carbohydrates.

**12:35 p.m.** **Discussion**

**1:00 p.m.** **Buffet Lunch, Faculty Club (Please return registration form by April 9, 1999 for reservations. Cost $10.00 to be paid at registration.)**

**3:00 p.m.** **Discussion with Graduate Students, Room 137, Chemistry-Physics Building**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Twenty-Fifth Annual Symposium on

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Anna S. Naff

## *Carbohydrates and Cell Recognition*

SPEAKERS
Chi-Huey Wong
Laura L. Kiessling
Ole Hindsgaul
C. Fred Brewer

**Friday, April 16, 1999**


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