

## W0080

**Human Complement Protein C8 $\gamma$ : Crystal Binding Studies.** L. Lovelace, B. Chiswell, C. Brannen, J.M. Sodetz, L. Lebioda, Dept. of Chemistry & Biochemistry, Univ. of South Carolina, Columbia, SC 29208.

C8 $\gamma$  is a 22-kDa subunit of C8, which is one of five components of the cytolytic membrane attack complex of complement. Within the complement system, C8 $\gamma$  has the distinction of being the only lipocalin. Lipocalins are a family of proteins that bind small hydrophobic ligands, e.g. retinol, pheromones, odorants. Crystallographic analysis of C8 $\gamma$  revealed it has a typical lipocalin fold with a distinct ligand binding pocket (Ortlund *et.al.*, *Biochemistry* 41, 7030-7037 (2002)). The upper portion of the pocket contains several positively charged residues whereas the lower portion consists of a large cavity lined with hydrophobic residues. Binding of several potential C8 $\gamma$  ligands was tested in crystal soaking and co-crystallization experiments. The alkyl chain of a free fatty acid (C12:0) and the acyl chain (C16:0) of 1-palmitoyl lysophosphatidylethanolamine were found to penetrate into the lower cavity. Structures were refined to 1.8Å resolution with approximately 20% R factors. A Y83W mutation, which closes the hydrophobic part of the pocket, prevented binding with only a minor reduction in C8 $\gamma$  activity. Co-crystallization with a peptide corresponding to the C8 $\gamma$  binding site on the C8 $\alpha$  subunit yielded non-isomorphous crystals. This structure will be reported to 1.3Å resolution.