

W0248

Aerolysin Binding to a GPI Anchor Core Glycan: High-Resolution Structure of Proaerolysin in Complex with the Receptor Component Mannose-6-phosphate. C.L. Brooks, S.N. Borisova, J.T. Buckley, S.V. Evans, Dept. of Biochemistry and Microbiology, Univ. of Victoria, Victoria, B.C., V8P 3W6 Canada.

Aerolysin is a bacterial channel-forming toxin produced by *Aeromonas* species. The toxin and its inactive precursor proaerolysin are both known to bind with high affinity to the conserved glycan core of glycosylphosphatidylinositol (GPI) anchored proteins, although the specific nature of these interactions was unknown. Here we report to 2.49 Å resolution the first structure of proaerolysin in complex with a component of its putative GPI glycan receptor, mannose-6-phosphate. The structure unequivocally identifies the binding site on the protein as well as some of the GPI glycan residues involved in binding. The mannose-6-phosphate residue fills part of a large groove on the surface of the protein, with the sugar ring recognized via hydrophobic stacking interactions and the phosphate moiety via specific charged-residue interactions. This structure gives unique insight into the observed different receptor specificities of related toxins that also bind to GPI anchored proteins.