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Crystal Structure of β -Hemolysin: Mechanism of Sphingomyelin Cleavage. Medora Huseby, Ke Shi, Cathleen Earhart, Douglas Ohlendorf, Dept. of Biochemistry, Molecular Biology and Biophysics, Univ. of Minnesota.

β -hemolysin is a virulence factor of *Staphylococcus aureus* that catalyzes the cleavage of sphingomyelin in biological membranes to ceramide and phosphorylcholine causing lysis of erythrocytes. β -hemolysin belongs to the neutral sphingomyelinase C family, and shares homology to mammalian neutral sphingomyelinase C enzymes which are important in sphingolipid signaling and metabolism. Crystals were found to be fully merohedrally twinned. Diffraction data were collected at the Molecular Biology Consortium facilities on beam line 4.2.2 at the Advanced Light Source. The structure was solved via molecular replacement using SmcL (sphingomyelinase C from *Listeria ivanovii*) as the search model and refined to 2.4 Å resolution. β -hemolysin belongs to α/β protein family and is arranged in a 4-layer sandwich, adopting a similar structure to that of SmcL. The structural features provide insight into the mechanism of neutral sphingomyelinases C along with the protein interaction with a sphingomyelin substrate. A C-terminal β -hairpin is thought to penetrate the lipid bilayer and aid in substrate binding and positioning. This mechanism is also assisted by a hydrophobic loop which is nearby the active site. Inactive mutants are being used to study the structure of the substrate complex.

[1] www.cdc.gov/ [2] Openshaw et al. JBC, 2005.