Poster Presentation

MS53.P15

Structural basis for the peptidoglycan recognition by Helicobacter pylori Csd4

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Helicobacter pylori infection causes a variety of gastrointestinal diseases including peptic ulcers and gastric cancer. The colonization of this bacterium in the gastric mucosa is required for the survival in the stomach. Its colonization of the gastric mucosa of human stomach depends on its motility, which is facilitated by the helical cell shape. In H. pylori, crosslinking relaxation or trimming of peptidoglycan muropeptide affects the helical shape. Among several cell shape-determining peptidoglycan hydrolases identified in H. pylori, Csd4 is a Zn2+-dependent D,L-carboxypeptidase that cleaves the bond between the γ-D-Glu and mDAP bond of the uncrosslinked tripeptide of peptidoglycan (L-Ala-γ-D-Glu-mDAP) to produce L-Ala-γ-D-Glu dipeptide and mDAP, promoting the helical cell shape. Inhibition of D,L-carboxypeptidase activity of Csd4 may represent a novel therapeutic approach. We report here the crystal structures of H. pylori Csd4 in three different states: the ligand-free form, the substrate-bound form, and the product-bound form. H. pylori Csd4 consists of three domains: an N-terminal D,L-carboxypeptidase domain, a novel β-barrel domain, and a C-terminal immunoglobulin-like domain. Our ligand-bound structures provide structural basis of peptidoglycan recognition by D,L-carboxypeptidase. H. pylori Csd4 recognizes primarily the terminal mDAP of the tripeptide substrate and undergoes a significant structural change upon binding either mDAP or mDAP-containing tripeptide.

Keywords: Helicobacter pylori, carboxypeptidase, Csd4