Poster Presentation

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Crystal structure of the Csd3 protein from Helicobacter pylori

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The helical cell shape of Helicobacter pylori facilitates the penetration of thick gastric mucus and promotes virulence. The peptidoglycan plays a structural role in the bacterial cell wall and its controlled modification is essential for determining the helical shape. Several H. pylori genes were identified to contribute to its helical cell shape through alterations in peptidoglycan crosslinking and trimming of the peptide (Sycuro et al., 2010; Sycuro et al., 2012). One of them is the hp0506 gene that encodes a putative periplasmic peptidase belonging to the M23-family of zinc-metallopeptidase (Sycuro et al., 2010). The HP0506 protein carries out not only a D,D-endopeptidase activity but also a D,D-carboxypeptidase activity. Hence, it has been named Helicobacter D,D-peptidase A (HdpA) and cell shape determinant 3 (Csd3). Csd3 is the first enzyme belonging to the M23-peptidase family that can perform the D,D-carboxypeptidation to regulate the cell shape (Mathilde et al., 2010). To gain structural and functional insights at the molecular level, we have determined the crystal structure of Csd3 at 2.1 Å resolution by using the Pt SAD data. H. pylori Csd3 consists of three domains including a LytM domain, which contains the highly conserved active site motif among the M23 metallopeptidase family. An anomalous scattering experiment with Zn2+ confirmed the metal-binding site in the active site. The Zn2+ ion is tetrahedrally coordinated and a catalytic water for peptide hydrolysis is absent in the active site of Csd3. Furthermore, domain 1 blocks the active site, thus prohibiting the substrate peptide binding. Our mass analysis shows that the full-length Csd3 is inactive as the D,D-carboxypeptidase. These results suggest that proteolytic processing may be necessary for the activation of Csd3.

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