Poster Presentation

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Crystal structure analysis of dipeptidyl amino peptidase from P. mexicana WO24.

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Dipeptidyl aminopeptidase (DAP or DPP, EC 3.4.14) catalyses the removal of dipeptides from the amino termini of peptides and proteins. In microorganisms, we have reported the identification, purification, and characterization of DAP BI, DAP BII, DAP BIII, and DAP IV (bacterial DPP4), POP from *Pseudoxanthomonas mexicana* WO24, and demonstrated that DAP BI, DAP BIII, DAP IV and POP belong to the POP family and they are classified into the clan SC, family S9 in the MEROPS database. On the basis of the enzymological data we obtained, we proposed that bacterial DAPs should be classified in a manner different from that of mammalian DPPs, except for the DAP IV. The DAP IV liberates dipeptides from the free amino terminus and has a specificity for both proline and hydroxyproline residues in the penultimate position of peptides. Here, we report the first structure of the bacterial DPP IV (*P. mexicana* WO24 DAP IV) complexed with an inhibitor at 2.2 Å resolution. The subunit structure is composed of two domains, the N-terminal eight-bladed β-propeller domain and the C-terminal alpha/beta/alpha sandwich catalytic domain. These structural features are conserved with clan SC S9 family. However, the N-terminal domain contains a unique helix region that extends over the active site acting as a lid, gating substrate or product access. Based upon the structural data, as well as molecular modeling, a model suggesting that the unique helix region is conserved in some kind of bacterial DPP4s except for mammalian DPP4s and some bacterial DPP4s. Some asaccharolytic and anaerobic bacteria can be used protein or peptides as an energy source. Therefore, these bacteria secrete many types of proteases and peptidases. Especially, the elucidation of degradation mechanisms of collagen, including proline and hydroxyproline, are very important from the point of view of host tissue breakdown in pathogens. Our findings suggest that different ligand recognition mechanisms from the bacterial DPP IV to mammalian DPP4 raise the possibility of an antimicrobial development targeting DPP IV from bacteria.

Keywords: DPP4, peptidase, clan SC S9