Peptidoglycan binding by a pocket on the accessory NTF2-domain of Pgp2 directs helical cell shape of Campylobacter jejuni

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Every year, over 600 million people worldwide contract campylobacteriosis, a bacterial food-borne gastroenteritis primarily caused by Campylobacter jejuni. The helical cell shape of C. jejuni, a key colonization factor, is determined by the structure of the peptidoglycan (PG) layer. The helical structure of PG is determined by Pgp2, a LD-carboxypeptidase that cleaves the terminal D-Ala residue from both monomeric and cross-linked PG tetrapeptides. The interaction interface between Pgp2 and PG to select sites for peptide trimming is unknown. Here, we report a 1.6 Å resolution crystal structure that contains a conserved LD-carboxypeptidase domain and a previously uncharacterized domain with an NTF2-like fold (NTF2). We identified a pocket in the NTF2 domain formed by conserved residues that is located approximately 40 Å from the LD-carboxypeptidase active site. Site-directed mutagenesis combined with NMR-monitored titration studies were used to define the interaction interfaces of Pgp2 with several PG fragments, which bound to the active site within the LD-carboxypeptidase domain and the pocket of the NTF2 domain. We propose a model for Pgp2 binding to PG strands involving both the LD-carboxypeptidase and the NTF2 domains to guide catalytic activity to induce a helical cell shape.