Poster Presentation

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Structure and function of the CagA oncoprotein from Helicobacter pylori

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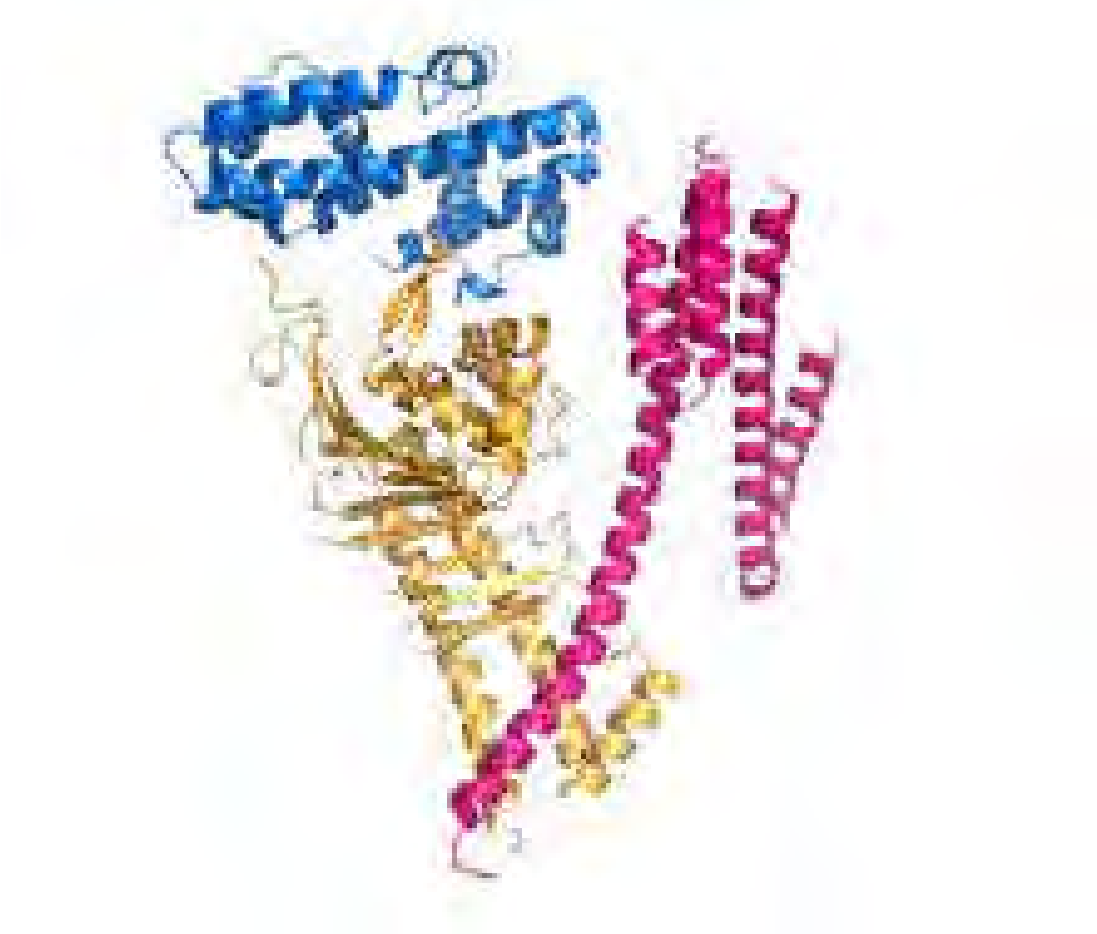
CagA is known as a major bacterial virulence determinant from Helicobacter pylori and is critical for gastric cancer. Upon delivery into the gastric epithelial cells, CagA localizes to the inner leaflet of the plasma membrane and promiscuously interacts with host proteins such as PAR1b and SHP2. The CagA-PAR1-SHP2 complex potentiates oncogenic signaling. Biochemical and physicochemical analyses revealed that CagA is comprises a structured N-terminal region (residues 1-876) and an intrinsically disordered C-terminal region (residues 877-1186). To understand the structure and function relationship of CagA, we determined the crystal structure of the N-terminal region (residues 1-876) of CagA [1]. The N-terminal CagA is rich in α-helices and composed of three domains. Domain I (residues 24-221) is linked to domain II (residues 303-644) by a disordered loop with about 80 amino acid residues. Domain II has a basic patch composed of 14 lysine and 2 arginine residues. Biological experiments revealed that the basic patch mediates the CagA-phosphatidylserine interaction to localize the inner face of the plasma membrane. In addition, we found that C-terminal disordered region forms a lariat-like loop by the interaction between NBS (residues 645 - 824) and CBS (residues 998 - 1038) in the disordered C-terminal region. The formation of the lariat-like loop facilitates promiscuous interaction of CagA with target protein such as SHP2.

[1] *Hayashi, T. et al. (2012). Cell Host & Microbe. 12, 20-33.*



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