Institut Européen de Chimie et Biologie

I E C B

SEVENTH FRAMEWORK PROGRAMME

Structural biology of Helicobacter pylori infection.

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Helicobacter pylori is one of the most successful bacterial pathogen, infecting the stomach of about half of the world population and causing peptic ulcer or gastric cancer. Our laboratory is interested in two main aspects of H. pylori infection: i) the structural basis of host-cell interaction and ii) the molecular mechanisms of DNA replication initiation. To study these systems we have developed different strategies based on protein purification, Biochemistry and hybrid methods in Structural Biology (MALS, X-ray crystallography, SAXS and Electron Microscopy).

Not all H. pylori strains are detrimental to human. The most severe strains produce a sophisticated molecular syringe named cag type IV secretion system (cagT4SS) that attaches host cell integrin $\alpha5\beta1$ to deliver the oncoprotein CagA (1). The structure of the machinery and the way it delivers the toxin are a still a mystery. The basis for the function of the cagT4SS relies on a complicated and dynamic set of interactions between bacterial proteins (including CagA) and $\alpha5\beta1$ integrin. We have solved the structure of a large CagA fragment and identified its integrin-binding domain (2). I will summarize here the current knowledge and also present unpublished results on this interaction.

Our group has also studied the structural biology of replication initiation proteins from H. pylori. If the hallmarks of DNA replication are conserved in H. pylori, this bacterium has features that deviate from the “model” systems. I will present recent discoveries on H. pylori DNA replication initiation (3, 4) machinery including unpublished structural work and show that this bacteria might represent a orginial model for DNA replication study that complement pioneer work on E. coli and B. subtilis.

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4. Natrajan G, Noirot-Gros MF, Zawilak-Pawlik A, Kapp U, Terradot L. The structure of a DnaA/HobA complex from Helicobacter pylori provides insight into regulation of DNA replication in bacteria. Proc Natl Acad Sci U S A 106, 21115-21120 (2009).

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