Poster Presentation

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Structural studies of Legionella effectors

K. Wong[1], Y. Zhang[1], G. Kozlov[1], K. Gehring[1]
[1]*McGill University, Department of Biochemistry, Montreal, Canada*

Legionella pneumophila is a gram-negative bacterium that causes Legionnaires' disease. It uses a Dot/Icm type IV secretion system to inject effector proteins into the host cell to manipulate host processes. Currently, about 300 Icm/Dot dependent effectors of L.pneumophila have been identified. Lpg1496 is an effector protein, which contains a conserved domain from the SidE family. To date, the middle domain and the conserved SidE domain have been crystallized and the structure solved at a resolution of 1.15Å and 2.3Å, respectively. A structural homology search using the middle domain suggested a similarity to phosphoribosylaminoimidazolesuccinocarboxamide (SAICAR) synthase, an ATPase involved in purine nucleotide synthesis. We performed 1H–15N HSQC NMR titrations to show that this domain binds ATP, ADP and AMP, with the highest binding affinity for ADP. A structural homology search using the SidE domain showed a similarity to cyclic nucleotide phosphodiesterases. To further elucidate the function of lpg1496, other fragments have been cloned, expressed, and subjected to crystallization trials. Currently, we have successfully crystallized the N-terminal domain, with crystals diffracting to <2.0Å. Obtaining the crystal structure of lpg1496 and revealing its function will not only lead to a better understanding of the virulence of L. pneumophila, but also contribute to the development of novel therapeutic treatments of Legionnaires' disease.

Keywords: bacterial effector, Legionnaire's disease, Legionella pneumophila