Cradle-loop barrel in Leptospira and novel GAF fusion proteins

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Abstract

Leptospirosis is an infectious disease of high incidence in tropical regions, caused by bacteria of the genus Leptospira. The second bacterial messenger, c-di-GMP, acts on different signaling pathways that result in the regulation of virulence, mobility and biofilm formation that may be related to the infectious process. The protein encoded by the LIC_11920 gene shows DUF1577 and PilZ domains(YcgR-like and PilZ), and is a recognised as a member of the cradle-loop barrel fold, which comprehends a set of protein families that act as sensor and/or flagella structure as well as type 6 secretion system proteins, such as PilZ and YcgR. PilZ is an intracellular c-di-GMP sensor whose performance has already been related to the regulation of resistance or pathogenicity in organisms such as Borrelia, but little is known about the involvement of PilZ homologues, including LIC_11920 , on the c-di-GMP-mediated signaling pathways in Leptospira interrogans serovar Copenhageni. The DUF1577 has an unusual GAF domain in fusion with a YcgR and a PilZ domains, which could be a recent autapomorphy in the leptospiral clade. Such fusions have pointed to have relationship with diversity-generating retroelements, which could have an important role in Leptospira evolution. We intend to characterize the c-di-GMP-mediated signaling pathways in L. interrogans from the structural and functional analysis of the LIC_11920 protein, as well as to clarify the classification of the fold, in order to place the DUF1577. Along with our in-silico strategies we intend to evaluate the structure of LIC_11920 in the search for a target of pharmacological intervention in the treatment of leptospirosis.

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