Soutenance

THESE

Vendredi 22 Décembre 2017 à 10h

Salle des séminaires

Institut de biologie structurale - 71 avenue des Martyrs CS 10090 38044 Grenoble Cedex 9 - T.+33 (0)4 57 42 85 00

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Structure and assembly of Mur enzyme complexes, essential for bacterial cell wall biosynthesis

Thèse de Doctorat de l'Université de Grenoble

Enzymes of the Mur family (MurA-MurG) are essential for bacteria, since they catalyse the cytoplasmic steps of peptidoglycan biosynthesis, the major component of bacterial cell wall; they metabolize molecules that do not exist in eukaryotes, and are structurally and biochemically tractable. However, despite the fact that many anti-Mur inhibitors have been developed, few of these molecules have shown promising antibacterial activity, which has prompted the hypothesis that within the bacterial cytoplasm Mur enzymes may exist in a complex where the active sites are in closed proximity, blocking small molecule access from the outside. We have obtained the first structural and functional information on the MurE-MurF fused form, present in the human pathogen Bordetella pertussis, and shown that it interacts with the peripheral glycosyltransferase MurG. These exciting results will open the path towards the understanding of how Mur enzymes interact within the bacterial cytoplasm, and could permit the eventual employment of Mur enzymes as de facto targets for novel antibiotic development.