

INTERNSHIP PROPOSAL

Institute and Group: INSTITUT DE BIOLOGIE STRUCTURALE, Bacteria Pathogenesis group

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Research project title: Architecture of the bacterial cell wall formation machinery

5 Keywords to describe the project: Bacterial infection, bacterial cell wall, antibiotic, X-ray crystallography

Description of the project (aims, experimental techniques, recommended background):

The bacterial cell wall is a complex three-dimensional structure that plays a key role during the processes of cell division and bacterial cell wall elongation. Although targeting the cell wall formation pathway with beta-lactam antibiotics has been a highly successful strategy to combat bacterial infections for over eighty years, antibiotic resistant strains have been reported worldwide. In this project, we will structurally and functionally characterize macromolecular complexes involved in cell wall biosynthesis in the human pathogen *Pseudomonas aeruginosa* by employing a combination of X-ray crystallography and electron microscopy. A number of preliminary results, including purification protocols for stable protein complexes, are already available in the laboratory. This project thus aims at revealing key aspects of peptidoglycan assembly machineries that could be important for the eventual development of novel antibiotics.

Justification that the internship's subject fits with the general theme of GRAL:

This M2 project builds on results that our group recently published in Nature Commun. and involves structural biology, biochemistry, and microbiology aspects. The student will concentrate on X-ray crystallography/EM but his/her results will add onto other complementary data that are already available in the lab in structural and cellular microbiology.

Relevant publications of the team:

Contreras-Martel C, Martins A, Ecobichon C, Maragno Trindade D, Mattei PJ, Hicham S, Hardouin P, El Ghachi M, Boneca IG, Dessen A (2017) Molecular architecture of the PBP2:MreC core bacterial cell wall synthesis complex. **Nature Commun.** 8, 776.

Bisson-Filho AW, Discola KF, Castellen P, Blasios V, Martins A, Sforça M, Garcia W, Zeri AC, Erickson HP, Dessen A, and Gueiros-Filho FJ (2015) FtsZ filament capping by MciZ, a developmental regulator of bacterial division. **Proc. Natl. Acad. Sci. USA** 112, E2130-E2138.

Wong, SG and Dessen, A (2014) Structure of a bacterial α 2-macroglobulin reveals mimicry of eukaryotic innate immunity. **Nature Commun.** 5, 4917