UFR de Chimie et de Biologie
UNIVERSITÉ Grenoble Alpes

Master's degree in Biology – Chemistry-Biology Department

Master 2 internship project
Year 2020-2021

Laboratory/Institute: Structural Biology Institute
Director: Pr. W. Weissenhorn
Team: NMR group, Antibiotics bacterial Resistance
Head of the team: Dr J.-P. Simorre

Name and status of the scientist in charge of the project: C. Bougault, Associate Professor
HDR: yes ☐ no x

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Program of the Master's degree in Biology:

☐ Immunology, Microbiology, Infectious Diseases
x Integrative Structural Biology
☐ Physiology, Epigenetics, Differentiation, Cancer
☐ Neurosciences and Neurobiology
☐ Planta International

Title of the project: Structural and dynamical study by NMR of the interactions between bacterial cell-wall components and L,D-transpeptidases in mycobacteria

Objectives (up to 3 lines):

The goal of this project is to provide structural and mechanistic insight into the interaction of peptidoglycan, and its covalently bound sugars and mycolic acids, with L,D-transpeptidases in order to develop alternative strategies to classical β-lactam antibiotic therapies.

Abstract (up to 10 lines):

The mycobacterial cell wall contains many unique features when compared to other bacterial cell walls and there is an increasing amount of evidence that suggests that these modifications are involved in conferring antibiotic resistance. This is particularly concerning with the increasing multidrug resistance cases of the opportunistic human pathogen, *Mycobacterium tuberculosis*, causing around 2 million deaths each year. The aim of this study is to examine the interaction of L,D-transpeptidases, Ldt_{Mt1} and Ldt_{Mt2}, with mycobacterial cell wall in order to gain insights into the role of this enzyme in the biosynthesis and maturation of the mycobacterial cell envelope in order to offer alternative strategies to address antibiotic resistance. Cell wall being a highly heterogeneous and NMR appears as one of the only method of study and liquid-state as well as solid-state NMR approaches will be considered for this purpose.

Methods (up to 3 lines): The master student will take part in the production and purification of bacterial cell wall samples from non-pathogenic mycobacteria, the production and purification of isotopically labeled proteins, as well as liquid- and solid-state NMR data acquisition and analysis.

Up to 3 relevant publications of the team:

S. Triboulet S, C. M. Bougault, C. Laguri, J.-E. Hugonnet, M. Arthur, J.-P. Simorre, « Acyl acceptor recognition by *Enterococcus faecium* L,D-transpeptidase Ldt_{fm}. », *Mol. Microbiol.*, **2015**, 98, 90-100

C. Bougault, I. Ayala, W. Vollmer, J.-P. Simorre, P. Schanda, « Studying intact bacterial peptidoglycan by proton-detected NMR spectroscopy at 100 kHz MAS frequency » *J. Struct. Biol.* **2019**, 206, 66-72.

R. Maya-Martinez, J.A.N. Alexander, C.F. Otten, I. Ayala, D. Vollmer, J. Gray, C.M. Bougault CM, A. Burt, C. Laguri, M. Fonvielle, M. Arthur, N.C.J. Strynadka, W. Vollmer, J.-P. Simorre, « Recognition of peptidoglycan fragments by the transpeptidase PBP4 from *Staphylococcus aureus.* » *Front. Microbiol*. **2019**, 9, 3223 (doi: 10.3389/fmicb.2018.03223).

Requested domains of expertise (up to 5 keywords):

Recombinant protein expression

Biochemistry methods of purification and extraction

Basic computer skills (eventually with linux systems)

Biomolecule visualization softwares