

**Master 2 internship project
Year 2025-2026**

Laboratory/Institute: Institut de Biologie Structurale
Team: Pneumococcus Group

Director: W. Weissenhorn
Head of the team: Cécile Morlot

Scientist in charge of the project: André Zapun, CR CNRS

HDR: yes ☒ no ☐

Address: IBS, 71 av. des Martyrs, 38044 Grenoble

Phone: +33 4 57 42 85 43

e-mail: andre.zapun@ibs.fr

Program of the Master's degree in Biology:

- ☒ Microbiology, Infectious Diseases and Immunology ☒ Biochemistry & Structure
☐ Physiology, Epigenetics, Differentiation, Cancer ☐ Neurosciences and Neurobiology

Title of the project:

Investigation of the interaction of muropeptides with peptidoglycan transpeptidases from *Streptococcus pneumoniae*

Objectives:

The objective is to characterize the interaction of defined peptidoglycan fragments or muro-peptides-beta-lactams hybrid compounds with Penicillin-Binding Proteins from *Streptococcus pneumoniae*.

Abstract:

Beta-lactam drugs, such as penicillin, combat infections by preventing the cross-linking of peptidoglycan, the main component of the bacterial cell wall.

The pneumococcus resists beta-lactams such as penicillin by expressing variants of peptidoglycan transpeptidases (the Penicillin-Binding Proteins or PBPs) that are not inhibited by the drugs while retaining their enzymatic activity. This constitutes a paradox since beta-lactams are structural mimics of the natural substrates of PBPs.

To understand how this apparent paradox occurs, we will study the interaction of PBPs from susceptible and resistant strains with defined peptidoglycan fragments or compounds that are hybrids of peptidoglycan fragments and beta-lactams.

Methods (up to 3 lines):

Recombinant protein production and purification

In vitro enzymology

Bacterial cell culture and MIC determination

Up to 3 relevant publications of the team:

Morlot, et al. (2018) Structure of the essential peptidoglycan amidotransferase MurT/GatD complex from *Streptococcus pneumoniae*. Nature Commun. 9, 3180. [doi](#)

Calvez, et al. (2017) Substitutions in PBP2b from β -lactam resistant *Streptococcus pneumoniae* have different effects on enzymatic activity and drug reactivity. J. Biol. Chem. 292, 2854-65. [doi](#)

Zapun et al. (2008) Penicillin-binding proteins and beta-lactam resistance. FEMS Microbiol. Rev. 32, 361-85. [doi](#)

Requested domains of expertise:

Curiosity and interest in biochemistry and in vitro reconstitution of biochemical processes