

**Master 2 internship project  
Year 2022-2023**

**Laboratory/Institute:** IBS

**Team:** PG

**Director:** Winfried Weissenhorn

**Head of the team:** Cécile Morlot

**Name and status of the scientist in charge of the project:** André ZAPUN CR CNRS

**HDR:** yes  no

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**Program of the Master's degree in Biology:**

- Microbiology, Infectious Diseases and Immunology     Structural Biology of Pathogens  
 Physiology, Epigenetics, Differentiation, Cancer     Neurosciences and Neurobiology

**Title of the project: Penicillin-Binding Proteins interactions with peptidoglycan**

**Objectives (up to 3 lines):**

To refine our understanding of the interaction between Penicillin-Binding Proteins (PBPs) from *Streptococcus pneumoniae* and their substrates.

**Abstract (up to 10 lines):**

PBPs are the enzymes responsible for the assembly of the peptidoglycan, the main constituent of the bacterial cell wall. PBPs are the target of beta-lactams, the most widely used antibacterials. Detailed enzymological and structural studies of PBPs have been hampered by the lack of adequate substrates. We will use synthetic fragments of peptidoglycans provided by the laboratory of Sébastien Fort (CERMAV) to investigate the requirements for the transpeptidation reaction catalyzed by PBPs, such as the length of the fragments and the peptide composition. In parallel, we will set up screens of crystallogensis conditions to grow crystals of complexes between PBPs and peptidoglycan fragments for structure determination.

**Methods (up to 3 lines):**

Recombinant protein purification. In vitro spectrophotometric transpeptidase assay. Crystallogensis (hanging drops).

**Up to 3 relevant publications of the team:**

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

Calvez, P., et al. (2017) Substitutions in PBP2b from  $\beta$ -lactam resistant *Streptococcus pneumoniae* have different effects on enzymatic activity and drug reactivity. J. Biol. Chem. 292, 2854-65

Philippe, J., et al. (2015) Mechanism of  $\beta$ -lactam action in *Streptococcus pneumoniae*: the piperacillin paradox. Antimicrob. Agents Chemother. 59, 609-21

**Requested domains of expertise (up to 5 keywords):**

Strong interest for biochemistry and in vitro experiments