

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

Laboratory/Institute: IBS and CHU Grenoble

Director: W. Weissenhorn

Team: PB&RC (bacterial pathogenesis & cellular responses) **Head of the team:** I. Attrée

Name and status of the scientist in charge of the project: Yvan CASPAR and Sylvie ELSÉN

HDR: yes ☒ (S. Elsen) no ☒ (Y. Caspar)

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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: Contribution of cell surface polysaccharides to the resistance of *Klebsiella pneumoniae* to human innate immunity

Objectives:

Evaluate the contribution of the capsule, LPS and Enterobacterial Common Antigen polysaccharides to the resistance of *Klebsiella pneumoniae* to human innate immunity (impact on bacterial lysis by the complement system and on opsonophagocytosis).

Abstract:

Klebsiella pneumoniae (*Kp*) is becoming highly multi-drug resistant to several antibiotic classes and is thus considered a WHO priority pathogen. At early infection stages, primary human defense is mediated by innate immunity, mainly through the complement system in blood and opsonophagocytosis in tissues. We carried out Tn-Seq experiments on eight different clinical strains of *Kp* to decipher their mechanisms of plasma resistance and confirmed cell surface polysaccharides as main factors contributing to the susceptibility of this species to lysis by the complement system. This project will assess the individual contribution on complement resistance and opsonophagocytosis of genes of the *cps* locus (capsule), *wec* operon (ECA synthesis and first step of LPS synthesis) or LPS biosynthesis pathway in several strains of *Kp*. This work will provide key information about potential targets for monoclonal antibody therapies or vaccine development.

Methods:

Basic bacterial genetics (mating, transformation, cloning), phenotypic profiling, serum bactericidal assay, molecular biology, biochemistry (western blots, SDS-PAGE, Silver Stain PAGE, polysaccharides analysis), Flow cytometry, automated microscopy and image analysis (High Content Screening), Bioinformatics

Up to 3 relevant publications of the team:

- Pont S, et al. Bacterial behavior in human blood reveals complement evaders with some persister-like features. PLoS Pathog. 2020 Dec 16;16(12):e1008893. doi: 10.1371/journal.ppat.1008893. PMID: 33326490
- Janet-Maitre M, et al. Genome-wide screen in human plasma identifies multifaceted complement evasion of *Pseudomonas aeruginosa*. PLoS Pathog. 2023 Jan 25;19(1):e1011023. doi: 10.1371/journal.ppat.1011023. PMID: 36696456

Requested domains of expertise:

Bacteriology, molecular biology, cloning, microscopy and bioinformatics