



Pasteur-Lille University International Doctoral Program 2023

Project

Acronym: FlagBody

Title: Flagellin-Antibody conjugate, an innovative targeted therapy for antibiotic-resistant bacterial pneumonia

Laboratory /Thesis Director

Unit /Team: Center for Infection and Immunity of Lille / Team Bacteria, antibiotics and Immunity

Thesis supervisor: Laurye Van Maele

Tel.: +33 3 20 87 11 94

E-mail : laurye.van-maele@pasteur-lille.fr

Website : <https://www.ciil.fr/teams/bacteria-antibiotics-and-immunity>

Summary of the proposed project

Infections caused by antibiotic-resistant bacteria are a major threat to human health, and innovative interventions are urgently needed to combat these infections. Stimulating the immune system offers a promising therapy to treat antibiotic-resistant bacterial infections. Interleukin-17 (IL-17) and IL-22 are known to protect mucosa against extracellular bacteria such as *Klebsiella pneumoniae*, a leading pathogen of antibiotic-resistant pneumonia. The bacterial compound: flagellin, the structural protein of flagella, is a potent activator of these key effectors via Toll-Like Receptor 5 signaling. The project aims to generate an innovative targeted flagellin-based immunotherapy that induces IL-17/IL-22-mediated antibacterial defenses immediately after administration. However, the immune response induced by administration of flagellin is not restricted to IL-17/IL-22 or to the lung environment, and thus could lead to side-effects. To develop the targeted immunotherapy, the activity of flagellin must only be directed to the cells that regulate IL-17/IL-22 immune defenses. Although the mechanism of IL-17/IL-22 activation remains unclear, there is compelling evidence that dendritic cells are key activating drivers through the production of IL-23. The project therefore will (i) produce flagellin-antibody conjugates, by site-directed bioconjugation, that target pulmonary dendritic cells to induce IL-17/IL-22-mediated defenses, (ii) identify markers specific to IL-23 producing cells to develop conjugates generated as precision medicine, (iii) address the efficacy of the conjugates to improve the treatment of bacterial pneumonia. These flagellin-antibody conjugates, when provided in combination to antibiotics, will improve the treatment of bacterial pneumonia and will offer a new therapeutic alternative against multidrug-resistant infections.