Cell envelope and cell division factors as new antimicrobial targets in *Pseudomonas aeruginosa*

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Antibiotic resistance is on the rise worldwide and threatens our healthcare system. The WHO has established a list of particularly worrying bacterial species that cause most of the nosocomial infections. In the literature, these species are often referred to as the ESKAPE pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Enterobacter sp.*). Recently, some strains have presented resistance to all available antibiotics (carbapenems and polymyxins), making them extremely difficult to treat. There is a clear need for new antimicrobial molecules with novel mechanisms of action. However, to develop rationalize antibiotic design, we need to refine our knowledge of the basic processes required for the growth of these microorganisms.

Cell envelope, especially the cell wall, are appealing targets for the design of antibacterial drugs, as illustrated by the many classes of antibiotics that already inhibit cell wall synthesis (beta-lactams and glycopeptides). Indeed, these structures are essential and help to protect the bacterial cell against immune and environmental insults. However, how these structures are remodeled during cell division or a stress and how the involved enzymes are regulated remain largely unknown.

This research plan focuses on the cell envelope of the Gram-negative opportunistic pathogen, *Pseudomonas aeruginosa*. The general goals are (i) to determine how this pathogen maintain cell envelope homeostasis in various conditions and (ii) to identify the mechanisms that determine the site of division. To tackle these challenges, we rely upon molecular genetics, biochemistry and cell biology and develop new genetic screens. These complementary approaches will uncover new mechanisms involved in cell envelope remodeling, cell division and drug resistance. The results will reveal new targets and lead to a better understanding of how to disrupt these processes for the development of antibiotics effective against these problematic pathogens.

The PhD candidate will use a combination of genetic screens, biochemistry and microscopy to identify and characterize new proteins involved in *Pseudomonas* cell envelope homeostasis and cell division. The student will learn basic bacteriology and molecular biology techniques as well as powerful combinations of methods like transposon mutagenesis followed by high throughput sequencing.