Investigation of cell division in *Acinetobacter* species

Project proposed by Prof. Coralie Fumeaux

Institute of Microbiology, Lausanne University Hospital

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.*). Amongst this list, *Acinetobacter baumannii* is of particular interest since not much is known about its biology. *A. baumannii* is a Gram-negative bacterium often associated with pneumonia, bacteremia and outbreaks in healthcare environments. 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 this microorganism.

Cell division and cell wall biosynthesis are appealing targets for the design of antibacterial drugs. Indeed, these processes are essential for the expansion of the bacterial population. The proteins involved are often located in the periplasmic space or at the inner or outer membranes (so relatively accessible) and have little to no homology to human proteins. Unfortunately, most studies so far have been limited to two rod-shaped organisms, Bacillus subtilis (a Gram-positive bacterium) and Escherichia coli. These studies have revealed that cell division is achieved by a multiprotein complex called the divisome. In Gram-negative bacteria, this machinery is required for the concerted constriction of all three cell envelope layers: the inner membrane (IM), the peptidoglycan (PG) cell wall and the outer membrane (OM). The main actor of bacterial division is the tubulin homolog FtsZ. FtsZ polymerizes into a dynamic ring (Z-ring) that determines the division site, recruits downstream proteins and directs peptidoglycan synthesis to drive constriction.

Despite a poor sequence conservation, homologs of most division proteins can be identified in the genomes of *Acinetobacter* species. However, a few key components like the amidases (enzymes responsible for PG cleaving) and some Z-ring regulators are missing. The goal of the proposed project is to investigate the division process in *Acinetobacter* species (the non-pathogenic strain *A. baylyi* and the pathogenic *A. baumannii*) and the impact on antibiotic resistance. The PhD candidate will use a combination of genetic screens, biochemistry and microscopy to identify and characterize new proteins involved in *Acinetobacter* cell division, chromosome segregation and cell wall homeostasis. 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.