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SUR programme 2025
Coralie Fumeaux lab Project description

The bacterium *Pseudomonas aeruginosa* is an opportunistic pathogen that is naturally highly resistant to many classes of antibiotics. The main mechanism responsible for beta-lactam resistance is the induction of the beta-lactamase AmpC, an enzyme able to cleave beta-lactam antibiotic molecules.
In the clinical setting, spontaneous mutations can emerge, causing AmpC induction and treatment failure. These mutations are often located in cell wall-related enzymes. For example, a strain deleted for *ampD* (a cell wall recycling enzyme) overproduces AmpC and is beta-lactam resistant. We performed a genetic screen in the *ampD* mutant to identify the genes required for AmpC production. We now have a list of new genes most likely involved in cell wall homeostasis to test.
The student will learn to create deletion mutants for the candidate genes in *Pseudomonas aeruginosa* wild-type strain and the *ampD* mutant. The mutants will then be tested for beta-lactam resistance (MIC, spot dilution), for *ampC* expression and production (nitrocefin assay, Western blot, transcriptional assay) and phenotypic characterization (morphology, growth rate). Based on our screen, we should observe a reduction in AmpC production and beta-lactam resistance in the *ampD* mutant deleted for the candidate gene(s). If the phenotype is confirmed, a complemented strain will be created.
Getting a better understanding of this resistance mechanism and cell wall biology is crucial for allowing the development of new antimicrobial compounds. The use of beta-lactams associated to beta-lactamase inhibitors is already widespread in the clinics. Preventing beta-lactamase induction could also be a good strategy. Our screen might identify potential targets for drug design or screening