Toulouse Biotechnology Institute
Bio & Chemical Engineering

MASTER 2 internship

Evaluating probiotics effects on the frequency of bacterial persister cells during antibiotics treatment

Teams : « Integrated Physiology and Fonctional Genomics of Microbial Systems » (PHYGE) in collaboration with « Bacterial Adaptation, Diversity and Engineering » (BLADE) – Toulouse Biotechnology Institute (INSA Toulouse, CNRS, INRAE)

Location: Toulouse, France

Duration: 5-6 months

Level: Master 2 (or equivalent, ex: engineering degree)

Start date: January 2026 (flexible)

Supervisor: Jean-Pascal Capp – capp@insa-toulouse.fr (PHYGE team)

Topic:

Therapeutic escape phenomena are a major problem in human and animal health. Molecular tools have made it possible to identify the genetic factors responsible for resistance phenotypes. However, research conducted over the past two decades has highlighted other types of therapeutic escape that are not associated with hereditary genetic factors, but rather with transient, non-genetic abilities to tolerate or persist in the presence of drugs. Thus, the emergence of cells that persist in the face of antibacterial therapies is primarily a phenomenon of non-genetic phenotypic heterogeneity (Figure 1a).

In this project, we propose to study the influence of probiotic bacteria and yeasts on the frequency of appearance of these persistent cells *in vitro* using models relevant to intestinal health. Thus, the main objective will be to evaluate the frequency of persistence in a target bacterial population and its possible modulation by the presence of probiotic strains, so as to determine whether the presence of probiotics has a prior effect on the appearance of persister cells, i.e., upstream of treatment (Figure 1b). This study will document the benefits of taking probiotics preventively (or even concomitantly) with antibiotic treatment in order to limit persistence.

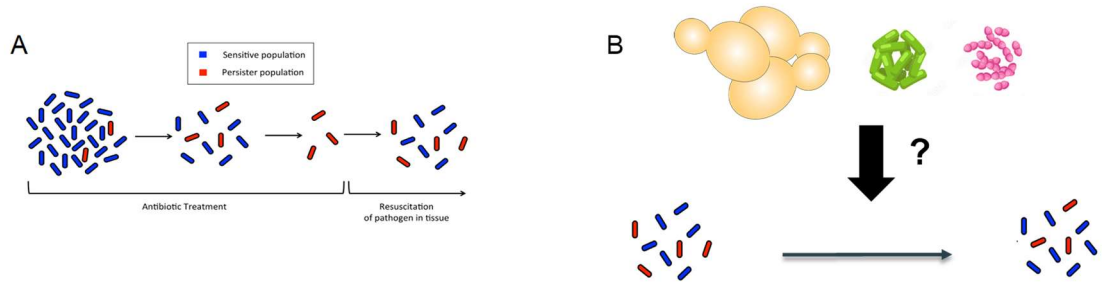

Figure 1 *: Persistence to antibiotics. (A) Persitence is a reversible non-genetic phenomenon that generates phenotypic heterogeneity in terms of survival in the presence of antibiotics. Only a subpopulation of persister bacterial cells (red) is able to survive antibiotics treatment. After antibiotics removal, growth restarts and the initial phenotypic heterogeneity is restored. (B) The hypothesis that yeast or bacterial probiotics could modulate the frequency of persister cells in the target population has never been explored. Adapted from Renbarger et al, 2017, AIMS Microbiol*

More specifically, during this internship, the student will be in charge of establishing a co-culture system with a Transwell-type culture system in which separate compartments only allow indirect metabolic interactions (Figure 2). Thus it will only be necessary to remove the insert containing the probiotic strain before proceeding with antibiotic treatment, washing the treated cells, and evaluating indirectly the persister frequency by measuring the lag time to regrow after treatment (the longer the lag time, the lower the number of persister cells) (Figure 2). We will draw on previous studies to set up the best culture medium for co-cultures, the pre-culture times for the target strain (initially the laboratory strain *Escherichia coli* K12) with or without probiotics, and the antibiotic treatment (usually between 5 and 24 hours of treatment with ofloxacin, which

will serve as the model antibiotic as in many studies on persistence). The tested probiotics include the yeast *Saccharomyces cerevisiae var. boulardii* and the bacteria *E. coli* Nissle 1917, *Lactococcus lactis*, and *Lactobacillus gasseri*.

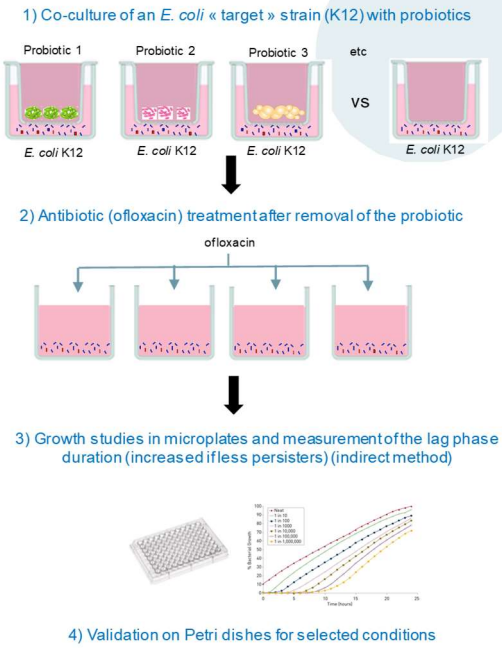

Figure 2 *: Experimental procedure. See text for details.*

Candidate profil: Master 2 student in microbiology, food sciences, bioengineering, biotechnology, or related fields ; interest in microbial physiology, functional food and health.

Environment: Please see https://www.toulouse-biotechnology-institute.fr/en/poles/equipe-phyge/
The PHYGE team's research focuses on understanding microbial physiology under environmental constraints through an integrative approach. This approach combines methods and tools from quantitative physiology—including biochemical, molecular, and biophysical techniques—with those from biochemical engineering, such as bioreactor operation and nutritional strategies. The primary objective of these research activities is to generate scientific knowledge that can be leveraged in more applied projects in industrial biotechnology and human and animal health.

Application: Please send the following documents in a single PDF file to capp@insa-toulouse.fr
- Curriculum Vitae
- Motivation letter (max. 1 page)
- Academic transcripts (Bachelor and Master 1, if available)
- Academic contacts