Universitat Pompeu Fabra Barcelona

Master in Bioinformatics for Health Sciences

Master project 2021-2022

Personal Information

Supervisor	Salomé Llabrés
Email	salome.llabres@ub.edu
Institution	Universitat de Barcelona
Website	http://www.ub.edu/cbcg/index.php
Group	CBCG

Project

Structural bioinformatics

Project Title:

Molecular mechanisms underpinning active drug efflux in Gram-negative bacteria

Keywords:

Membrane Proteins, Molecular Dynamics Simulations, Antimicrobial Resistance

Summary:

Antimicrobial resistance (AMR) threatens to rise morbidity, mortality and treatment cost of microbial infections in the near future. The recent increase in multidrug-resistant strains compromises the current therapeutic arsenal against bacterial infections. The case of Gram-negative (GN) bacteria is especially alarming, as listed by the World's Health Organisation for R&D of new antibiotics [1]. Active drug efflux is one of the principal mechanisms driving both intrinsic and acquired multidrug resistance in GN bacteria. It relies on the expression of tripartite efflux pumps (TEPs), which are specialised protein complexes spanning both GN membranes able to expel drugs from the bacterial cytoplasm and periplasm [2]. Since the inhibition of TEPs promises to restore the efficacy of a wide range of existing drugs, there have been a lot of efforts to characterise the components and the complex assemblies of these bacterial machinery. Leveraging the available structural information obtained by X-ray crystallography and CryoEM tomography, we aim to obtain an atomistic description of the drug export processes of TEPs. Using a combination of homology modelling, unbiased molecular dynamics (MD) simulations and enhanced sampling techniques, we will identify the molecular mechanisms underpinning the substrate export from the periplasm and the cytosol via the inner membrane transporter to the outside of the bacterial cell.

References:

[1] WHO (2017) List of bacteria for which new antibiotics are urgently needed [2] Du D et al. (2018) Nat Rev Microbiol 16, 523-539

Expected skills::

Experience with physics- and structure-based methods (e.g. Molecular dynamics) and MD software packages (e.g. GROMACS) will be an advantage.

Possibility of funding::

No

Possible continuity with PhD: :

To be discussed

Comments:

We are willing to consider other projects in the field of biomolecular simulations that match your interests and skills.