

Internship Proposal

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Project Title:

Biochemical and structural studies of mycobacterial efflux pumps

Level:

Master Student

Project Summary:

The project aims at the systematic characterization of mycobacterial efflux pumps (membrane proteins) implicated in drug resistance, which will enable the development of novel inhibitors or to repurpose drugs already approved for therapeutic use) that can either effectively block or sufficiently decrease efflux and the concomitant gain of resistance.

Work to be developed by the student:

Protein expression and purification; Macromolecular crystallization; Biochemical (activity assays; kinetic characterization) and biophysical (measurement of binding properties; structural determination) characterization.

References:

1. Maranha, A. et al. (2023) Self-recycling and partially conservative replication of mycobacterial methylmannose polysaccharides. *Commun Biol*, in press.
2. Ripoll-Rozada, J. et al. (2019) Biosynthesis of mycobacterial methylmannose polysaccharides requires a unique 1-O-methyltransferase specific for 3-O-methylated mannosides. *Proc Natl Acad Sci USA* 116, 835-84. DOI: 10.1073/pnas.1813450116.
3. Cereija, T.B. et al. (2019) The structural characterisation of a glucosylglycerate hydrolase provides insights into the molecular mechanism of mycobacterial recovery from nitrogen starvation. *IUCrJ* 6, 572-585. DOI: 10.1107/S2052252519005372.
4. Fraga, J. et al. (2015) Structure of mycobacterial maltokinase, the missing link in the essential GlgE-pathway. *Sci Rep* 5, 8026. DOI: 10.1038/srep08026.

5. Maranha, A. et al. (2015) Octanoylation of early intermediates of mycobacterial methylglucose lipopolysaccharides. *Sci Rep* 5, 13610. DOI: 10.1038/srep13610.



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