Internship Proposal

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Project Title:
Unravel innovative antimicrobial strategies against Gram-positive pathogens

Level:

Master

Project Summary:

The massive use of antibiotics has promoted the selection of resistant pathogens. It is estimated that many antibiotics will be ineffective by 2025-30, causing 10 million deaths annually worldwide by 2050. Antibiotic resistance is thus recognized as one of the great challenges of the 21st century. Gram-positive (G+) bacteria are considered a major health care problem. Therefore, the development of novel therapeutic approaches against G+ pathogens is fundamental. Molecular Microbiology Group is using Listeria monocytogenes as a model organism of intracellular parasitism to design new therapeutic strategies against G+ pathogens. We work on the identification and characterization of new bacterial mechanisms of infection as target for alternative therapeutics to fight G+ pathogens. Rather than kill bacteria, we aim to “disarm” and “sensitize” the pathogen in order to render it more vulnerable to the host’s defences and/or to classical clinical therapies.

Work to be developed by the student:

The student will have the opportunity to develop a project aiming at identifying and characterizing new L. monocytogenes virulence mechanisms involved in modification of the bacterial surface or in the spatiotemporal expression dynamics of virulence genes at the single-bacterium level. Students working at the Molecular Microbiology group will work in a multidisciplinary environment within the microbiology scope. They will have their own research project and will engage different technical competences and laboratory methodologies along their work. We routinely work with different techniques of cellular biology (cell transfection and transduction, CRISPR, flow cytometry, immunofluorescence, microscopy, immunohistochemistry), molecular biology (cloning and mutagenesis, protein-RNA-DNA extraction, qRT-PCR, ChIP), protein biochemistry (western blot, immunoprecipitation, biotinylation, protein purification, chromatography and protein

crystallization) and animal infection (mice, zebrafish).

References:

Pombinho, R., et al. (2020). Virulence gene repression promotes Listeria monocytogenes systemic infection. Gut Microbes, 11(4), 868–881.

Pinheiro, J., et al. (2018). MouR controls the expression of the Listeria monocytogenes Agr system and mediates virulence. Nucleic Acids Research.

Carvalho, F., et al. (2015). L-Rhamnosylation of Listeria monocytogenes Wall Teichoic Acids Promotes Resistance to Antimicrobial Peptides by Delaying Interaction with the Membrane. PLOS Pathogens, 11(5), e1004919.

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