Internship Proposal

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Project Title:
Development of complex biofilm models for Mycobacterium abscessus

Level:

Master Student

Project Summary:

Mycobacterium abscessus (Mab) is an emerging pathogen that poses a severe health problem, especially in people with lung disorders. Patients with Mab-associated disease have poor outcomes and high treatment failure rates, recurrence, and mortality. Available drugs are largely ineffective due to an exquisitely intrinsic resistance that defeats most antibiotics. This, alongside surface adherence and biofilm formation, allows Mab to adjust and survive in hostile environments. Specifically, mycobacterial biofilms are a crucial pathogenic factor in treatment resistance and immune system evasion, which helps to explain why Mab infections are chronic and extremely difficult to treat. A significant drawback in drug development against Mab is the lack of correlation between in vitro activity and clinical response, often due to inadequate in vitro infection models.

Our work aims to establish improved and more complex infection models for pre-clinical drug screening against Mab, in particular, biofilms.

Biofilm formation in vivo occurs mainly in patients with lung disorders and altered lung environments, such as cystic fibrosis (CF). CF patients have a unique lung environment characterized by thick mucus and chronic inflammation, resulting in increased susceptibility to infections, primarily through biofilm formation. Combinatory therapies with biofilm-disrupting drugs are promising and could be a more efficient alternative to conventional antibiotic treatment.

Work to be developed by the student:

Thus, the aim of this thesis is to develop a model using a synthetic cystic fibrosis medium that results in thick, viscous mucus. Then, this model will be used to screen the activity of new molecules. Importantly, we will take advantage of our recently generated Mab double-reporter strains (that emit luminescence and fluorescence) [1,2], allowing us to follow the

infection live in all experimental setups in a non-invasive and non-terminal way.

References:

1.Bento CM, Gomes MS, Silva T (2025) The use of double-reporter Mycobacterium abscessus strains to improve anti-biofilm drug screening. J Microbiol Methods, 238: 107290 https://doi.org/10.1016/j.mimet.2025.107290

2.Bento CM, van Calster K, Piller T, Oliveira GS, de Vooght L, Cappoen D, Cos P, Gomes MS, Silva T (2024) Characterization of novel double-reporter strains of Mycobacterium abscessus for drug discovery: a study in mScarlet. Microbiol Spectr 12:e0036224; https://doi.org/10.1128/spectrum.00362-24

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