Project Title: "*Mycobacterium tuberculosis* Drug Resistance and Antibiotic Susceptibility Testing"

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Context / Background:

Tuberculosis (TB), a disease cause by the bacterium *Mycobacterium tuberculosis* (MTB) remains a significant global public health concern, leading to millions of new infections and deaths each year. The emergence of drug-resistant tuberculosis (DR-TB) further complicates the situation, necessitating a better understanding of drug efficacy and rapid and reliable Antibiotic Susceptibility Testing (AST) to identify effective anti-TB treatments (1). DR-TB resulted in approximately 85,000 deaths in 2019, accounting for about 7% of antibiotic-resistant bacteria-related fatalities. The current TB treatment involves drug combinations, which are vital in preventing the development of DR-TB and ensuring successful cure, but pose challenges in terms of treatment duration, patient compliance, and potential toxic effects.

Aim of the Project:

The project will focus on studying anti-TB mode of action, drug activities and drug resistance mechanisms to create new rapid AST methods for MTB and new approach to address more rapidly and more accurately the efficacy of drugs and drug regimens. The project aims to explore and decipher drug activities/synergism/antagonism/metabolism, investigate existing drugs and new drugs used in clinic and next-generation anti-TB drugs.

Methods and study presentation:

The project will employ a combination of molecular, genomics, and phenotypic methods (2,3,4). Phenotypic methods will include traditional culture-based techniques, but the primary focus will be on exploring breakthrough, fast AST approaches capable of providing results within a few hours. These innovative approaches include the use of nanomotion-AST, a method recently developed, which utilizes nanomechanical sensors to assess drug efficacy against MTB in a short timeframe (5,6), as well as MALDI-TOF MS or LC MS/MS.

This project will permit a better understanding of drug activity, AB synergism/antagonism. MTB clinical and laboratory strains of our biobank will be exposed to a panel of anti-TB drugs, and the activity of these drugs will be evaluated using a combination of established antibiotic susceptibility tests and new molecular and phenotypic biomarkers.

Significance and expected results:

By leveraging these techniques, the project aims to advance drug resistance and AST knowledge, ultimately contributing to improved TB management and patient outcomes by enabling the adaptation and optimization of anti-TB treatments, ensuring patient safety, promoting compliance, and minimizing the development of antibiotic resistance.

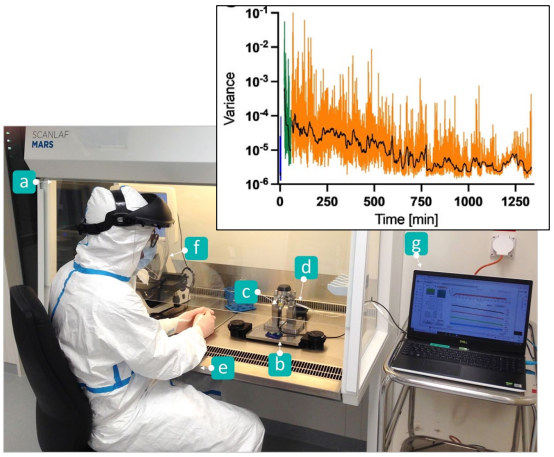

Figure adapted from Vocat et al. 2023

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