

# Internship Proposal

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## **Project Title:**

Deciphering a novel Mycobacterium tuberculosis mechanism of interference with macrophage cytokine responses

## **Level:**

Master Student

## **Project Summary:**

Tuberculosis (TB) is one of the oldest and deadliest infectious diseases, affecting over 10 million people and causing more than 1.2 million deaths annually. TB manifests across a clinical spectrum, from latent infection to severe active disease with varying pulmonary involvement and, in some cases, dissemination and death. The TB-causing bacteria belong to the Mycobacterium tuberculosis complex (MTBC), which comprises ten human-adapted lineages of Mycobacterium tuberculosis with distinct epidemiology and pathogenesis. Lineage 6 (L6) is restricted to West Africa, progresses slowly, triggers milder immune activation, and transmits less efficiently. Understanding how M. tuberculosis L6 achieves this attenuated trajectory may reveal key pathways to prevent or control severe TB. Our published studies show that, like humans, mice infected with M. tuberculosis L6 display a slower progression of infection, with lower immune responses and less tissue pathology. Most interestingly, our preliminary studies indicate that M. tuberculosis L6 actively modulates macrophage responses by imposing a blockade of the inflammatory response and altering host-pathogen interactions. Mechanistically, we have evidence that M. tuberculosis L6 interferes with the macrophage translation process, in vitro and in vivo. These findings suggest a completely novel mechanism exploited by M. tuberculosis to evade the host immune response and persist in the organism.

## **Work to be developed by the student:**

Aim: this MSc project aims at deciphering the mechanistic details operating at the M. tuberculosis L6/macrophage interface, and use the generated knowledge to improve outcomes of TB. We expect to provide unprecedented mechanistic insights into TB pathogenesis, inform innovative strategies for diagnosis, treatment, and TB control



Main methodologies: The project combines training under biosafety level 3 containment, general microbiology techniques, animal experimentation, analyses of infection outcomes (bacterial numbers, immune response and lung pathology), generation and infection of primary macrophages, flow cytometry, mRNA and protein analysis, histology and immunofluorescence.

### References:

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