

## **M2 project – 2021-2022**

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Team “Immunomodulation by Mycobacterial Lipids & Glycoconjugates” (Resp: J. Nigou)

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<http://www.ipbs.fr/index.php/immunomodulation-mycobacterial-lipids-and-glycoconjugates>

### **Title: Identification of cytosolic or nuclear protein ligands of *Mycobacterium tuberculosis* lipids in macrophages**

*Mycobacterium tuberculosis* (Mtb) has evolved numerous strategies to evade clearance by the immune system and most particularly the innate immune system. Notably, Mtb has adapted to replicate within macrophages and to subvert their function. It is able to inhibit phagosome maturation, to evade autophagy, or to dampen the production of pro-inflammatory cytokines. However, the molecular mechanisms by which Mtb circumvents host defenses are not completely understood.

A hallmark of Mtb is the production of highly diverse and abundant cell envelope lipids that are potent immunomodulators playing a key role in host-pathogen interactions. Indeed, Mtb lipids modulate phagocytic cell functions, at different stages of the infection, different localizations in the cells, and beyond the infected cells. Upon infection, they first act as ligands, either agonists or antagonists, of Pattern Recognition Receptors. Then, they can be released in the phagosome and traffic in the endosomal pathway, where they manipulate the cellular machinery.

Our assumption is that Mtb lipids, as already described for Mtb proteins, can also reach the cell cytosol and the cell nucleus to act as modulins hijacking cellular processes.

The aim of the Master internship will be to evaluate whether Mtb can subvert host defences by delivering lipids to the macrophage cytosol or nucleus. More precisely, we will:

- i) search for protein ligands of Mb lipids in cytosolic or nuclear fractions of macrophages by pull-down experiments using lipid-coated beads and proteomic analysis
- ii) determine the consequences of lipid/protein ligand interaction on macrophage function by gene silencing.

#### Selected publications of the team on this topic:

- Decout A *et al.* (2017) PNAS, 114(10):2675.
- Blanc L *et al.* (2017) PNAS, 114(42):11205.
- Vergne I *et al.* (2015) Front Cell Infect Microbiol, 4:187