Myco_Metabolism - How iron and manganese affect the central metabolism in pathogenic mycobacteria

I aim to define how Mycobacterium tuberculosis (Mtb) and Mycobacterium abscessus (Mabs) have adapted their central metabolism (CM) to variation of metals availability. Bacterial nutrition is a fundamental aspect of pathogenesis. While the host environment is in principle nutrient-rich, hosts have evolved strategies to interfere with nutrient-acquisition by pathogens. Pathogens, in turn, have developed mechanisms to circumvent these restrictions. The ability to adapt to nutrient availability drives the fitness of pathogen, influencing the outcome of infection. One of the strategies adopted by innate immune cells such as macrophages and neutrophils to limit bacterial replication is varying the availability of metals, starving or intoxicating the unwelcome guest.
The expression and the activity of some central metabolism enzymes are regulated by metal availability in pathogenic bacteria, and it is unknown how this regulation affects the assimilation of carbon sources. Preliminary data shows that Fe and Mn affect the carbon sources metabolism in these pathogens. I aim to identify potential Fe or Mn-regulated metabolic routes utilising proteomics (LC-MS/MS) and metabolomics (LC-MS). These investigations will help to elucidate a neglected aspect of mycobacterial physiology, the interaction between metal homeostasis and central metabolism, disclosing more mechanisms underlying the mycobacteria physiology.
Through this EF, I will bring the knowledge acquired during my five-year appointment at the Francis Crick Institute (UK) (mycobacterial metabolism and metabolomics) to my origin country (Italy) implementing my research line at the University of Padua. Through this EF, I will undertake training to re-enforce my independence, increase my expertise in proteomics (at the UNIPD) and metabolomics (at the secondment, Francis Crick).

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