Title: Iron induction of mycma 1667 gene expression in *Mycobacterium abscessus subsp bolletii*

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Abstract:

Iron (Fe) is essential for the proper function of metabolic enzymes and consequently is crucial for the survival and replication of bacterial pathogens; nonetheless, excess of iron is toxic to cells. Studies have shown that IdeR, a repressor characterized from *Mycobacterium tuberculosis* (Mtb), binds specifically to an Iron Box, present in the genes involved with siderophores synthesis. The deletion of IdeR resulted in significant reduction of the ability of Mtb to survive in high Fe concentrations as well as in increase of the pathogen sensitivity to oxidative stress. The goal of this work was to address the importance of IdeR gene in *Mycobacterium abscessus subsp. bolletii* (GO06), a strain responsible for an outbreak in Goiania, Brazil. The mycobacterial isolates from that outbreak were shown to have unique virulence characteristics compared to other *M. abscessus* strains. The gene mycma 1667, annotated from the sequenced genome of *M. abscessus* GO06, presented 78% identity with Mtb IdeR. The expression levels of mycma 1667 gene, by RT-PCR, during *in vitro* growth of *M. abscessus* GO06 under different Fe concentrations were evaluated. The cDNA was used as template for RT-PCR with Sybr® Green and mycma 1667 specific primers. As endogenous normalizer, primers specific for 16S rDNA were used. Our results showed that mycma 1667 is differently expressed in different Fe concentrations, suggesting a possible role in the synthesis of siderophores. In vitro studies showed that the expression of mycma 1667 from GO06 was significantly increased when iron concentration was at higher levels (12.5 μM – 125 μM – 250 μM) in comparison to more physiological levels (1.25μM). Genome annotation of GO06 revealed Iron Box sequences at a region with high similarity to ESX-3 type VII secretion system of *M. tuberculosis*, which has been shown to be directly involved in the secretion of factors involved in Fe uptake by the cell. We postulate that mycma 1667 from *M. abscessus subsp. bolletii* have a similar function as IdeR from *M. tuberculosis* to allow mycobacteria to survive within the deleterious effects of excess of iron concentrations.

Keywords: Mycobcabtin, Iron, IdeR, Siderophore, Mycobacteria

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