

TITLE: MYCMA 0076 PROTEIN FROM *MYCOBACTERIUM ABSCESSUS* SUBSP. *MASSILIENSE* IS INVOLVED IN IRON STORAGE

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ABSTRACT:

In recent decades the *Mycobacterium abscessus* complex has emerged as human pathogens, capable of causing several diseases. This complex drew attention to its unique characteristics, which make it difficult to diagnose and treat their infections. The success in bacterial infection is intrinsically related to their ability to regulate intracellular iron levels, mainly by iron storage proteins. The objective of this study was to characterize a protein involved in the storage of iron in *M. abscessus* subsp. *massiliense* (Mycma). For this, annotation of the Mycma genome was carried out in order to identify the gene that could encode for such a protein. Subsequently, molecular dynamics of the identified protein was carried out. In order to determine the role of the identified protein in Mycma homeostasis, studies were performed evaluating gene expression both *in vitro* and in the macrophage infection model. Finally, heterologous cloning and expression of this protein was performed in *E. coli*, and the recombinant protein structural and functional studies were done using HPLC and the ferrozine reagent, respectively. Ferritins are important proteins in the maintenance of cellular homeostasis, due to their action in reducing the toxic effects generated by excess iron. In our study we observed that the *mycma_0076* gene has 71% identity with *M. tuberculosis* Rv3841 gene (bfrB) encoding ferritin. As observed in the studies with bfrB, it was observed that *mycma_0076* is highly expressed under iron excess conditions, being also expressed during macrophages infection. In addition, we observed through protein molecular dynamics that the 0076 protein, encoded by the *mycma_0076* gene, has a ferroxidase catalytic site. Studies with the purified recombinant 0076 protein obtained revealed it has structural characteristics similar to those observed in the superfamily of ferritins that are high molecular weight complexes formed by several subunits. In addition, it was demonstrated that the protein r0076 was capable of oxidizing Fe⁺² in Fe⁺³, a function observed in ferritins. We conclude that the 0076 protein is involved in iron homeostasis in Mycma with ferritin function.

Keywords: Ferritin, Iron, *Mycobacterium abscessus* subsp. *massiliense*, Iron storage Protein.

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