

Structure elucidation of the redox cofactor mycofactocin reveals oligo-glycosylation by MftF.

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Abstract

Mycofactocin (MFT) is a redox cofactor belonging to the family of ribosomally synthesized and post-translationally modified peptides (RiPPs) and is involved in alcohol metabolism of mycobacteria including *Mycobacterium tuberculosis*. A preliminary biosynthetic model had been established by bioinformatics and *in-vitro* studies, while the structure of natural MFT and key biosynthetic steps remained elusive. Here, we report the discovery of glycosylated MFT by ^{13}C -labeling metabolomics and establish a model of its biosynthesis in *Mycolicibacterium smegmatis*. Extensive structure elucidation including NMR revealed that MFT is decorated with up to nine β -1,4-linked glucose residues including 2-*O*-methylglucose. Dissection of biosynthetic genes demonstrated that the oligoglycosylation is catalyzed by the glycosyltransferase MftF. Furthermore, we confirm the redox cofactor function of glycosylated MFTs by activity-based

metabolic profiling using the carveol dehydrogenase LimC and show that the MFT pool expands during cultivation on ethanol. Our results will guide future studies into the biochemical functions and physiological roles of MFT in bacteria.

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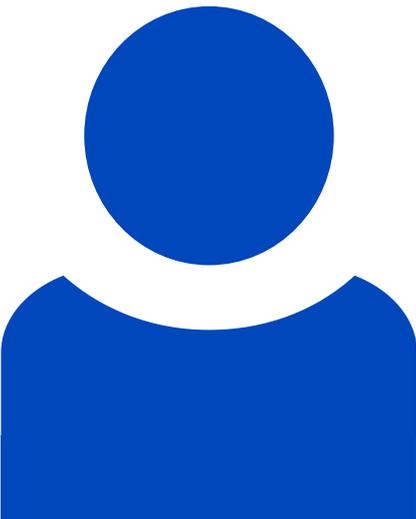
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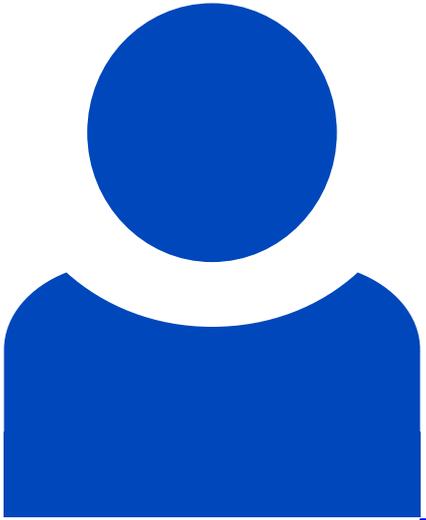
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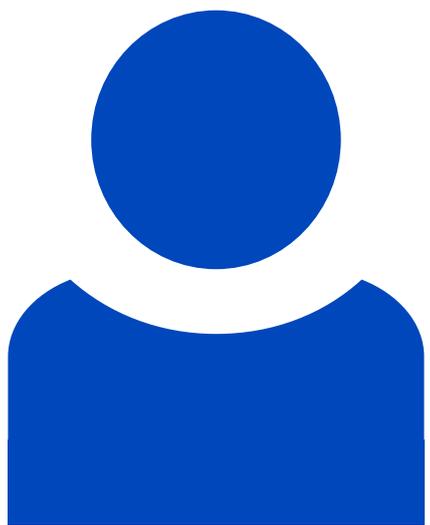
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Awards

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