FEBS J. 2010 Nov;277(22):4662-73. doi: 10.1111/j.1742-4658.2010.07873.x. Epub 2010 Oct 4.

The Mycobacterium tuberculosis ORF Rv0654 encodes a carotenoid oxygenase mediating central and excentric cleavage of conventional and aromatic carotenoids.

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Abstract

Mycobacterium tuberculosis, the causative agent of tuberculosis, is assumed to lack carotenoids, which are widespread pigments fulfilling important functions as radical scavengers and as a source of apocarotenoids. In mammals, the synthesis of apocarotenoids, including retinoic acid, is initiated by the β-carotene cleavage oxygenases I and II catalyzing either a central or an excentric cleavage of β-carotene, respectively. The M. tuberculosis ORF Rv0654 codes for a putative carotenoid oxygenase conserved in other mycobacteria. In the present study, we investigated the corresponding enzyme, here named M. tuberculosis carotenoid cleavage oxygenase (MtCCO). Using heterologously expressed and purified protein, we show that MtCCO converts several carotenoids and apocarotenoids in vitro. Moreover, the identification of the products suggests that, in contrast to other carotenoid oxygenases, MtCCO cleaves the central C15-C15' and an excentric double bond at the C13-C14 position, leading to retinal (C(20)), β-apo-14'-carotenal (C(22)) and β-apo-13-carotenone (C(18)) from β-carotene, as well as the corresponding hydroxylated products from zeaxanthin and lutein. Moreover, the enzyme cleaves also 3,3'-dihydroxy-isorenieratene representing aromatic carotenoids synthesized by other mycobacteria. Quantification of the products from different substrates indicates that the preference for each of the cleavage positions is determined by the hydroxylation and the nature of the ionone ring. The data obtained in the present study reveal MtCCO to be a novel carotenoid oxygenase and indicate that M. tuberculosis may utilize carotenoids from host cells and interfere with their retinoid metabolism.

PMID: 20929460 [PubMed - indexed for MEDLINE]