

Methylcitrate cycle activation during adaptation of *Fusarium solani* and *Fusarium verticillioides* to propionyl-CoA-generating carbon sources.

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Abstract

Propionyl-CoA is an inhibitor of both primary and secondary metabolism in *Aspergillus* species and a functional methylcitrate cycle is essential for the efficient removal of this potentially toxic metabolite. Although the genomes of most sequenced fungal species appear to contain genes coding for enzymes of the methylcitrate cycle, experimental confirmation of pathway activity in filamentous fungi has only been provided for *Aspergillus nidulans* and *Aspergillus fumigatus*. In this study we demonstrate that pathogenic *Fusarium* species also possess a functional methylcitrate cycle. *Fusarium solani* appears highly adapted to saprophytic growth as it utilized propionate with high efficiency, whereas *Fusarium verticillioides* grew poorly on this carbon source. In order to elucidate the mechanisms of propionyl-CoA detoxification, we first identified the genes coding for methylcitrate synthase from both species. Despite sharing 96 % amino acid sequence identity, analysis of the two purified enzymes demonstrated that their biochemical properties differed in several respects. Both methylcitrate synthases exhibited low K_m values for

propionyl-CoA, but that of *F. verticillioides* displayed significantly higher citrate synthase activity and greater thermal stability. Activity determinations from cell-free extracts of *F. solani* revealed a strong methylcitrate synthase activity during growth on propionate and to a lesser extent on Casamino acids, whereas activity by *F. verticillioides* was highest on Casamino acids. Further phenotypic analysis confirmed that these biochemical differences were reflected in the different growth behaviour of the two species on propionyl-CoA-generating carbon sources.

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