

***Candida albicans* utilizes a modified β -oxidation pathway for the degradation of toxic propionyl-CoA.**

Otzen C, Bardl B, Jacobsen ID, Nett M, Brock M (2014) *Candida albicans* utilizes a modified β -oxidation pathway for the degradation of toxic propionyl-CoA. *J Biol Chem* 289(12), 8151-8169.

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Abstract

Propionyl-CoA arises as a metabolic intermediate from the degradation of propionate, odd-chain fatty acids, and some amino acids. Thus, pathways for catabolism of this intermediate have evolved in all kingdoms of life, preventing the accumulation of toxic propionyl-CoA concentrations. Previous studies have shown that fungi generally use the methyl citrate cycle for propionyl-CoA degradation. Here, we show that this is not the case for the pathogenic fungus *Candida albicans* despite its ability to use propionate and valerate as carbon sources. Comparative proteome analyses suggested the presence of a modified β -oxidation pathway with the key intermediate 3-hydroxypropionate. Gene deletion analyses confirmed that the enoyl-CoA hydratase/dehydrogenase Fox2p, the putative 3-hydroxypropionyl-CoA hydrolase Ehd3p, the 3-hydroxypropionate dehydrogenase Hpd1p, and the putative malonate semialdehyde dehydrogenase Ald6p essentially contribute to propionyl-CoA degradation and its conversion to acetyl-CoA. The function of Hpd1p was further supported by the detection of accumulating 3-hydroxypropionate in the hpd1 mutant on propionyl-CoA-generating nutrients. Substrate specificity of Hpd1p was determined from recombinant purified enzyme, which revealed a

preference for 3-hydroxypropionate, although serine and 3-hydroxyisobutyrate could also serve as substrates. Finally, virulence studies in a murine sepsis model revealed attenuated virulence of the hpd1 mutant, which indicates generation of propionyl-CoA from host-provided nutrients during infection.

Involved units

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