Keratin degradation by dermatophytes relies on cysteine dioxygenase and a sulfite efflux pump.

Grumbt M, Monod M, Yamada T, Hertweck C, Kunert J, Staib P (2013) Keratin degradation by dermatophytes relies on cysteine dioxygenase and a sulfite efflux pump. *J Invest Dermatol* 133(6), 1550-1555.

Abstract

Millions of people suffer from superficial infections caused by dermatophytes. Intriguingly, these filamentous fungi exclusively infect keratin-rich host structures such as hair, nails, and skin. Keratin is a hard, compact protein, and its utilization by dermatophytes for growth has long been discussed as a major virulence attribute. Here, we provide strong support for the hypothesis that keratin degradation is facilitated by the secretion of the reducing agent sulfite, which can cleave keratin-stabilizing cystine bonds. We discovered that sulfite is produced by dermatophytes from environmental cysteine, which at elevated concentrations is toxic for microbes and humans. We found that sulfite formation from cysteine relies on the key enzyme cysteine dioxygenase Cdo1. Sulfite secretion is supported by the sulfite efflux pump Ssu1. Targeted mutagenesis proved that dermatophyte mutants in either Cdo1 or Ssu1 were highly growth-sensitive to cysteine, and mutants in Ssu1 were specifically sensitive to sulfite. Most notably, dermatophyte mutants in Cdo1 and Ssu1 were specifically growth-defective on hair and nails. As keratin is rich in cysteine, our identified mechanism of cysteine conversion and sulfite efflux supports both cysteine and sulfite

tolerance per se and progression of keratin degradation. These in vitro findings have implications for dermatophyte infection pathogenesis.

Beteiligte Forschungseinheiten

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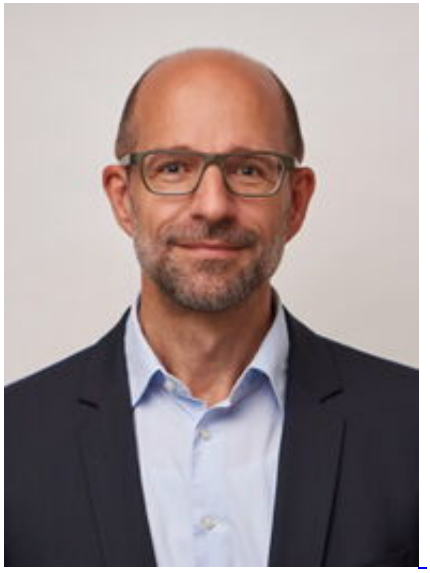

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Details

Identifier

doi: 10.1038/jid.2013.41

PMID: 23353986