An Iterative O-Methyltransferase Catalyzes 1,11-Dimethylation of *Aspergillus fumigatus* Fumaric Acid Amides.

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Abstract

S-adenosyl-l-methionine (SAM)-dependent methyltransfer is a common biosynthetic strategy to modify natural products. We investigated the previously uncharacterized *Aspergillus fumigatus* methyltransferase FtpM, which is encoded next to the bimodular fumaric acid amide synthetase FtpA. Structure elucidation of two new *A. fumigatus* natural products, the 1,11-dimethyl esters of fumaryl-l-tyrosine and fumaryl-l-phenylalanine, together with ftpM gene disruption suggested that FtpM catalyzes iterative methylation. Final evidence that a single enzyme repeatedly acts on fumaric acid amides came from an in vitro biochemical investigation with recombinantly produced FtpM. Size-exclusion chromatography indicated that this methyltransferase is active as a dimer. As ftpA and ftpM homologues are found clustered in other fungi, we expect our work will help to identify and annotate natural product biosynthesis genes in various species.

Beteiligte Forschungseinheiten

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