Biosynthesis of the Sphingolipid Inhibitors Sphingofungins in Filamentous Fungi Requires Aminomalonate as a Metabolic Precursor.

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Projects

Modular synthetic approaches towards natural sphingoid base-type signaling molecules
Details

Biosynthesis of sphingolipid inhibitors in fungi
Details

Elucidation of the translocation mechanisms of sphingolipid inhibitors in fungi
Details

Elucidation of the biosynthesis of Sphingolipid inhibitors in *Aspergillus fumigatus* and *Aspergillus niger*
Details

Abstract

Sphingofungins belong to a group of structurally related sphingolipid inhibitors produced by fungi, which specifically inhibit serine palmitoyl transferases, enzymes catalyzing the initial step during sphingolipid biosynthesis. Sphingolipids are integral parts of the eukaryotic cell membrane, and disturbances in their homeostasis have been linked to various human diseases. It has been suggested that external interventions, via sphingolipid inhibitors, may represent a promising approach for alternative therapies. Here, we identified and elucidated the biosynthetic gene cluster responsible for the biosynthesis of sphingofungins B, C, and D in *Aspergillus fumigatus*. Moreover, in vitro analyses have shown that sphingofungin biosynthesis starts with the condensation of a C18 polyketide with the uncommon substrate aminomalonate. Furthermore, the investigations on sphingofungin E and F produced by Paecilomyces variotii pointed out that different aminomalonate derivatives are used as substrates for those chemical variants. This research boosts knowledge on the general biosynthesis of sphingolipid inhibitors in fungi.

Identifier

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