Molecular basis for mycophenolic acid biosynthesis in *Penicillium brevicompactum*.

Regueira TB, Kildegaard KR, Hansen BG, Mortensen UH, Hertweck C, Nielsen J (2011) Molecular basis for mycophenolic acid biosynthesis in *Penicillium brevicompactum*. *Appl Environ Microbiol* 77(9), 3035-3043.

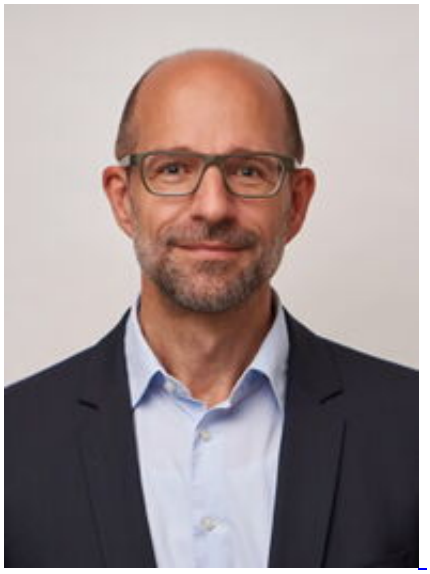
Abstract

Mycophenolic acid (MPA) is the active ingredient in the increasingly important immunosuppressive pharmaceuticals CellCept (Roche) and Myfortic (Novartis). Despite the long history of MPA, the molecular basis for its biosynthesis has remained enigmatic. Here we report the discovery of a polyketide synthase (PKS), MpaC, which we successfully characterized and identified as responsible for MPA production in Penicillium brevicompactum. mpaC resides in what most likely is a 25-kb gene cluster in the genome of Penicillium brevicompactum. The gene cluster was successfully localized by targeting putative resistance genes, in this case an additional copy of the gene encoding IMP dehydrogenase (IMPDH). We report the cloning, sequencing, and the functional characterization of the MPA biosynthesis gene cluster by deletion of the polyketide synthase gene mpaC of P. brevicompactum and bioinformatic analyses. As expected, the gene deletion completely abolished MPA production as well as production of several other metabolites derived from the MPA biosynthesis pathway of P. brevicompactum. Our work sets the stage for engineering the production of MPA and analogues through metabolic engineering.

Beteiligte Forschungseinheiten

Biomolekulare Chemie Christian Hertweck Mehr erfahren

Leibniz-HKI-Autor*innen



Christian Hertweck

Details

Identifier

doi: 10.1128/AEM.03015-10

PMID: 21398490