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Identification of the sansalvamide non-ribosomal peptide synthetase in *Fusarium solani*

Members of the *Fusarium* genus have a huge genetic potential for production of secondary metabolites. One of the most interesting compound classes is the non-ribosomal peptides (NRPs), which are synthesized by huge multi-domain synthetases (NRPSs). In a comparative analysis of the genomes sequences from ten different *Fusarium* species we have previously identified 52 NRPS orthology groups of which only 6 produce a known compound [1]. To fill the missing pieces we set out to identify the biosynthetic pathway responsible for production of the NRP sansalvamide. This cyclic pentadepsipeptide was originally isolated from an unidentified *Fusarium* species [2] and subsequently several strains belonging to the *Fusarium solani* species complex [3]. Sansalvamide contains an A-hydroxyisocaproic acid (HICA) unit, which is also found in the cyclic hexadepsipeptide destruxin produced by *Metarhizium* species. The gene cluster responsible for destruxin biosynthesis has been identified in *M. robertsii*, which consists of non-ribosomal peptide synthetase (NRPS; DtxS1), an aldo-keto reductase (DtxS2), a cytochrome P450 monooxygenase and a decarboxylase (DtxS4) [4]. A BlastP analysis of the synthetase DtxS1 against *F. solani* sequences resulted in NRPS30 as the best hit (total score 18001; identity: 45%). An orthologue of DtxS3, which provides the HICA unit from reduction of A-ketoisocaproic acid, was furthermore identified directly downstream of NRPS30. To verify that NRPS30 is responsible for biosynthesis of sansalvamide in *F. solani* we applied an *Agrobacterium tumefaciens*-mediated transformation (ATMT) approach to generate knock-out mutants. Comparative studies of secondary metabolites in the resulting deletion mutants and wild type confirmed the absence of sansalvamide in the NRPS30 deletion mutant, implicating this synthetase in the biosynthetic pathway for sansalvamide.

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