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POSTER SESSION ABSTRACTS
Session CS5 Applied genomics and biotechnology
CS5T72

Tuesday 5th April
14:00 - 16:00

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Heterologous production of immunosuppressant mycophenolic acid in *Aspergillus nidulans*

Filamentous fungi are well-known producers of a wide range of valuable secondary metabolites, which can be advantageously exploited *e.g.* in the pharmaceutical industry. One of the most prominent examples is mycophenolic acid (MPA). MPA inhibits inosine-5'-monophosphate dehydrogenase (IMPDH), which catalyzes the rate limiting step in the guanine nucleotide synthesis. Since B- and T-lymphocytes rely entirely on de novo purine synthesis, MPA is used as an immunosuppressant during organ transplants. We have recently identified the mpa gene cluster in *Penicillium brevicompactum* [1] and have subsequently verified several steps in the MPA biosynthetic pathway [2,3,4]. However, the role of four genes remained to be characterized. We have therefore heterologously expressed the mpa cluster in a stepwise manner in *Aspergillus nidulans* and established a cell factory for MPA production. Using this strategy, we have demonstrated that MpaA possesses prenyl transferase activity and catalyzes the conversion from 5,7-dihydroxy-4-methylphtalide to 6-farnesyl-5,7-dihydroxy-4-methylphtalide (FDHMP). We have also shown that MpaG catalyzes the last enzymatic step in the biosynthesis of MPA *in vivo*, resulting in the production of MPA. Interestingly, one of the intermediates (demethyl-MPA) can be formed from FDHMP *via* an unknown enzymatic activity present in *A. nidulans*. Lastly, we also found exciting examples of cross chemistry in *A. nidulans*, which resulted in the production of MPA variants, In conclusion, we have successfully characterized the biosynthetic pathway of the top-selling drug, MPA and we have demonstrated that *A. nidulans* is a suitable cell factory for its heterologous production.

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[2] B.G. Hansen *et al.* (2011) App. Environ. Microbiol., 77, 3044-3051.
[3] B.G. Hansen *et al.* (2012) App. Environ. Microbiol., 78, 4908-4913.
[4] B.G. Hansen *et al.* (2011) BMC Microbiol., 11, 202