

Maria Stroe

Email: maria.stroe@leibniz-hki.de

Heterologous expression of silent gene clusters in fungi

Secondary metabolites (or natural products) are compounds with important biological and pharmacological activities, and are produced by a range of organisms. Their biosynthesis is encoded in genes which are usually clustered in the genome of the respective organism. Filamentous fungi have a tremendous capacity to synthesise natural products. The human pathogenic fungus *A. fumigatus* is no different, having more than 30 predicted biosynthetic gene clusters, of which many have already been linked to compound(s). However, in some instances, the genes involved are either silent or cryptic, and their products cannot be identified. Activation strategies which have been employed in the past include overexpressing associated transcription factors, altering culture conditions, manipulating global regulators and artificially remodelling the chromatin landscape. However, in cases which don't lend themselves to external manipulation, a more suitable approach to identify the new metabolite(s) is to isolate the respective gene cluster from its native organism and express it in a heterologous host. With the use of a novel methodology we developed, I am working on a cryptic gene cluster originating from *A.fumigatus* and studying it in the recipient strain *A.nidulans*.

Publications

Stroe MC, Netzker T, Scherlach K, Krüger T, Hertweck C, Valiante V, Brakhage AA (2020) Targeted induction of a silent fungal gene cluster encoding the bacteria-specific germination inhibitor fumigermin. *Elife* 9, Details PubMed

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Supervisor

Axel A. Brakhage

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