**Swantje Behnken**

# Genome mining of Gram-positive bacteria for secondary metabolites

In the postgenomic era the number of predicted biosynthesis genes of microorganisms clearly outnumbers the known metabolites produced by these organisms. The investigation of several *Clostridium* spp. genomes revealed a widespread existence of secondary metabolite gene clusters within this largest group of anaerobic bacteria. Nonetheless no corresponding secondary metabolites have been isolated from these or any other strictly anaerobic bacteria. Since the encoded cryptic natural products have been overlooked so far it appears the biosynthesis genes remain dormant under standard laboratory conditions and are only triggered in the presence of particular stimuli. *Clostridium cellulolyticum* was therefore cultivated under several different growing conditions and the expression of PKS-NRPS gene clusters was monitored *via* gene expression analysis with realtime-RT-PCR. The clusters are silent under standard fermentation conditions. But supplementation with bacterial extracts, imitating the natural habitat of the organism, resulted in gene cluster induction. For more directed induction of gene cluster expression a predicted regulator gene located upstream of the cryptic biosynthetic gene cluster was over expressed in *Clostridium cellulolyticum*. The resulting metabolic profile showed a similar peak pattern as the via bacterial extracts induced extract. From a larger-scale fermentation of the mutant a new compound was isolated and the structure elucidation revealed a new polythioamide, which was named *closthioamide*. This compound is, to our knowledge, the first secondary metabolite from a strictly anaerobic bacterium. The biosynthesis of the thioamide and the principle of function of the bacterial extract are now subject to further investigations.

**Publications**

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**Supervisor**

Christian Hertweck

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