

MOLECULAR BIOTECHNOLOGY OF MYXOBACTERIA: NOVEL POTENTIAL TO PRODUCE BIOACTIVE MOLECULES

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Biologically active natural products of microbial origin are widely used by the agrochemical and pharmaceutical industries (1). Genome sequencing projects recently revealed an enormous genetic potential of microbial producers for the production of novel secondary metabolites (2). Using myxobacteria as an example, it will be demonstrated that a combination of genomics and classical natural products research can lead to the identification of novel secondary metabolites. Their biosynthesis is often accompanied by highly unusual biochemical mechanisms (3, 4), which are being studied on the molecular and enzymatic level (5, 6).

Bioactive secondary metabolites are commonly produced by extremely large multienzyme complexes (7), the genetic engineering and heterologous expression of which opens up new avenues for the production of new and altered compounds. This is especially true if the natural producers are genetically difficult to handle, slow growing, uncultivated or even unknown. We have recently developed a strategy which combines genetic engineering in *Escherichia coli* (8) with the advantages of pseudomonads as heterologous expression hosts for the analysis of known and unknown biosynthetic pathways. As pilot experiment the myxochromide biosynthesis genes from the myxobakterium *Stigmatella aurantiaca* (9) were re-engineered on one single DNA-molecule in a way introducing all necessary genetic elements for expression in pseudomonads and gene transfer from *E. coli*. The successful production after transfer of the recombinant DNA into *Pseudomonas putida* shows the possibilities of this approach for the production of novel and „unnatural secondary metabolites“ (10).

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