Analysis of the trehalose metabolism in *Actinoplanes* sp. SE50/110 with regard to acarbose production and byproduct formation

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Background

Actinoplanes spp. are Gram-positive aerobic bacteria producing a variety of pharmaceutically relevant substances. Since 1990 the α-glucosidase-inhibitor acarbose is produced and marketed for the treatment of type-2 diabetes mellitus. *Actinoplanes sp.* SE50/110 produces different acarviostatins depending on the C-source (Wendler et al. 2014) and various acarbose-like byproducts during fermentation. Wehmeier & Piepersberg described 2004 in particular the byproduct component C (acarviosine-trehalose) which is hard to separate from acarbose during downstream processing. It is therefore worthwhile to study the biosynthesis of trehalose in *Actinoplanes sp.* SE50/110 and to clarify its role in the production of component C.

Aims of the project:

In 2008 Lee et al. postulated three putative trehalose synthetic pathways in *Actinoplanes* and suggested that one of these proteins, the maltooligosyltrehalose synthase TreY of the *treXYZ* gene cluster plays a role in the formation of component C. The goal of this Ph.D. project is now to elucidate in *Actinoplanes* sp. SE50/110 the complete machinery for trehalose biosynthesis. This can be achieved by a mutational analysis of trehalose biosynthesis genes. In addition, the transcriptional regulation of the trehalose biosynthesis genes should be analyzed. Furtheron, the influence of a mutated *treXYZ* gene cluster on the production of acarbose and the formation of component C shall be analyzed by applying metabolomics techniques.

Requirements:

Applicants should have excellent academic results and a M.Sc. or equivalent degree with a background in molecular biological sciences. Experience in molecular biology and preferably in genetics and metabolomics of microorganisms is required.

References:

Lee et al. Appl. Microbiol. Biotechnol. 2008, **80**:767-778

Wehmeier & Piepersberg *Appl. Microbiol. Biotechnol.* 2004, **63:**613-625

Wendler et al. *J. Biotechnol.* 2014, **191:**113-120