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The expression of the acarbose biosynthesis gene cluster in *Actinoplanes* sp. SE50/110 is dependent on the growth phase

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Abstract

Background: *Actinoplanes* sp. SE50/110 is the natural producer of the diabetes mellitus drug acarbose, which is highly produced during the growth phase and ceases during the stationary phase. In previous works, the growth-dependency of acarbose formation was assumed to be caused by a decreasing transcription of the acarbose biosynthesis genes during transition and stationary growth phase.

Results: In this study, transcriptomic data using RNA-seq and state-of-the-art proteomic data from seven time points of controlled bioreactor cultivations were used to analyze expression dynamics during growth of *Actinoplanes* sp. SE50/110. A hierarchical cluster analysis revealed co-regulated genes, which display similar transcription dynamics over the cultivation time. Aside from an expected metabolic switch from primary to secondary metabolism during transition phase, we observed a continuously decreasing transcript abundance of all acarbose biosynthetic genes from the early growth phase until stationary phase, with the strongest decrease for the monocistronically transcribed genes *acbA, acbB, acbD* and *acbE*. Our data confirm a similar trend for *acb* gene transcription and acarbose formation rate.
Surprisingly, the proteome dynamics does not follow the respective transcription for all *acb* genes. This suggests different protein stabilities or post-transcriptional regulation of the Acb proteins, which in turn could indicate bottlenecks in the acarbose biosynthesis. Furthermore, several genes are co-expressed with the *acb* gene cluster over the course of the cultivation, including eleven transcriptional regulators (e.g. ACSP50_0424), two sigma factors (ACSP50_0644, ACSP50_6006) and further genes, which have not previously been in focus of acarbose research in *Actinoplanes* sp. SE50/110.

Conclusion: In conclusion, we have demonstrated, that a genome wide transcriptome and proteome analysis in a high temporal resolution is well suited to study the acarbose biosynthesis and the transcriptional and post-transcriptional regulation thereof.

Keywords: *Actinoplanes*, Acarbose, Transcriptomic, Proteomic, Expression dynamics, Co-regulation

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