

Abstract

Investigation of Novel Cultural Properties of *Actinoplanes ramoplaninifer* ATCC 33076 in Relation to Ramoplanin Production [†]

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Ramoplanin (Rml) is a non-ribosomally produced lipoglycopeptide antibiotic from *Actinoplanes ramoplaninifer* ATCC 33076. Many biosynthetic and regulatory aspects of its production remain unclear, partially due to the challenges with cultivation and gene-engineering manipulations of the producer strain [1–3]. This work aims to address some of these issues via investigating the Rml synthesis laboratory conditions and morphological properties of the wild-type strain.

As the first step, we investigated cultural properties of ATCC 33076 while cultivated on different solid media. We have revealed that on ISP4 agar the culture exhibited heterogeneity, which led to the purification of two morphotypes, further denoted as Lt (a light orange colony color), and Bt (a bright orange colony color).

Next, during separate cultivation under the Rml production conditions [4] in liquid media Lt exhibited notably higher productivity of Rml when compared to Bt morphotype grown under the same conditions. During co-cultivation of Lt and Bt in productive liquid media, Bt gradually out-competed Lt over time, resulting in the dominance of Bt as the sole morphotype present in the culture. These results correlated with the decreased level of Rml synthesis in co-culture, corresponding to the reduced abundance of the Lt morphotype in it.

We established separate cultures for Lt and Bt morphotypes presented in wild-type strain, and conducted a thorough examination of their respective characteristics and properties. The work to correlate morphological differences with the genomic properties of both strains by sequencing and comparing the genomes of Lt and Bt is underway in our laboratories.

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2
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4
5