

Genes for Morphogenetic Proteins of Chaplin and Rodlin Families in Landomycin Producer *Streptomyces cyanogenus* S136

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Abstract – *Streptomyces cyanogenus* S136 attracts attention due to rich secondary metabolism and aberrant morphogenesis. LC-MS analysis of S136 showed the production of novel compounds. Sets of genes for small morphogenetic proteins, chaplins and rodlin, are reduced in S136. We revealed rather diverse pattern of their location and abundance in *Streptomyces* clade.

Keywords – *Streptomyces*, *S. cyanogenus*, antibiotics, landomycin, phylogenetics, hydrophobins, rodlin, chaplin.

Introduction

Streptomyces cyanogenus S136 produces landomycin A (LaA), an angucycline compound exhibiting strong antiproliferative properties. There is an unmet need for gram amounts of LaA for preclinical trials, fueling the S136 strain improvement attempts. We showed recently that expression of heterologous pleiotropic regulatory gene *adpA* in S136 restores aerial hyphae formation and leads to increased LaA titers [1]. This result prompted us to pursue two lines of investigations. First, we explored the metabolome of S136 in order to see what kind of compound it produces besides LaA. Second, we used genomic sequence of S136 to catalogue all genes for morphogenesis, which in its turn led to a detailed scrutiny of the genes for chaplins and rodlin, small hydrophobic proteins involved in aerial hyphae formation.

Results and Discussion

S. cyanogenus strains were grown in liquid medium GYM, and butanol extracts of the supernatant were subjected to LC-MS analysis. We revealed a number of peaks of unknown chemical nature, implying that this strain might be source of novel compounds. In *adpA*⁺ strain extracts we revealed new mass-peaks absent in the parent (Fig. 1). Apparently, *AdpA* not only enhances LaA biosynthesis, but also could activate the expression of cryptic biosynthetic gene clusters.

Chaplin (*chp*) and rodlin (*rld*) genes were collected from *S. coelicolor* M145, where they form operon *rldB-rldA-chpD-chpA*. A null hypothesis would be that each streptomycete genome carries identical operon. To verify this assumption, a large-scale phylogenetic analysis of *chp-rld* families in *Streptomyces* was undertaken using *S. coelicolor* genes as an initial query. In contrast to the initial idea, the *chp* and *rld* genes show significant diversity both in number of paralogs and their location. Genes *chpD-chpA* and *rldA* were cloned from S136 into integrative expression vectors; their genetic analysis is underway.

Conclusion

S. cyanogenus possesses rich secondary metabolism and streamlined set of chaplin-rodlin genes. Deficiency in *chp* or *rld* genes may underlie the inability of S136 to realize the transition from substrate to aerial mycelium stage of cell cycle. In the same time, importance of morphogenetic proteins for secondary metabolism remains to be studied.

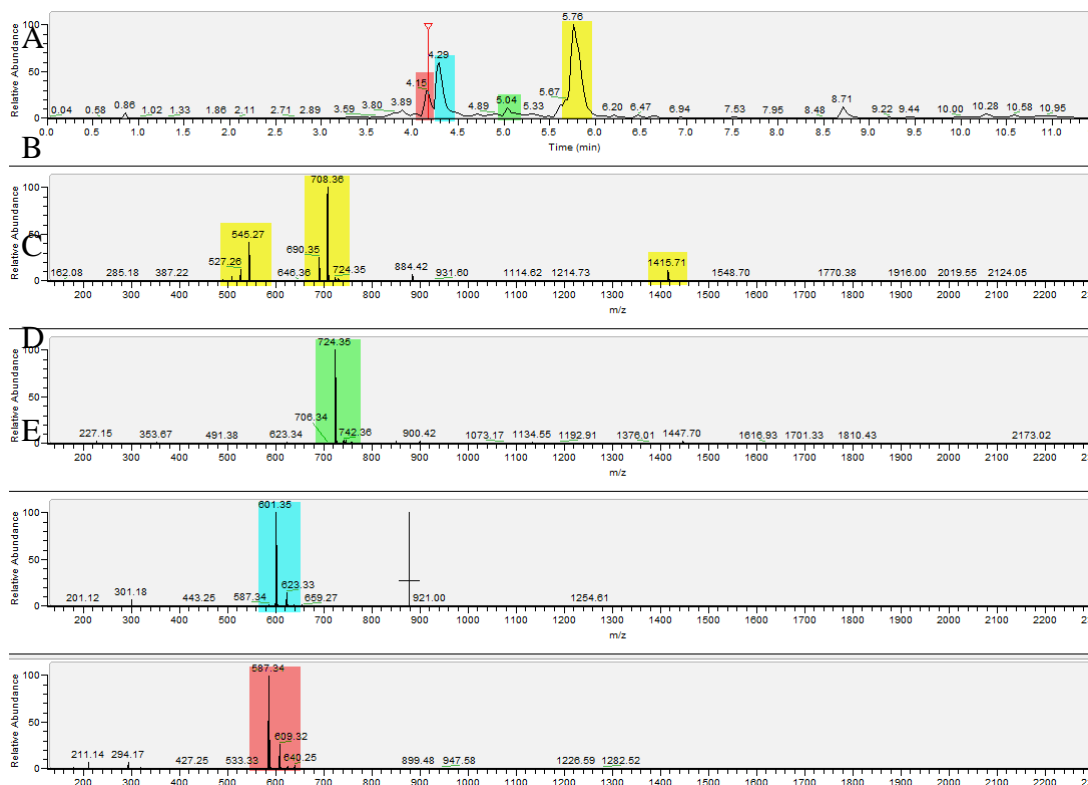


Fig. 1. Novel mass-peaks (highlighted with color) revealed in the butanol extracts of the *adpA*-expressing strain that were absent in the extracts of the parental (S136) strain. Lanes: **A**, overall trace chromatogram; **B-E**, extracted ion peaks (positive ionization). LC-MS conditions are described in [2].

References

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