

Abstract

Streptomyces bacteria are well-known producers of many bioactive metabolites. Its secondary metabolism is a source of many important groups of active compounds that are recently investigated by means of many new methods based on bioinformatic analyses of genome data, modern LC-MS techniques, and metabolic modeling methods.

This thesis originates from the genetic screening for a specific gene (*als*) for cyclizing 5-aminolevulinate synthase. Based on earlier studies, we consider this gene as a genetic tag of the producers of secondary metabolites containing the C₅N unit (2-amino-3-hydroxycyklopent-2-enon). Such metabolites include several groups with variable structures and biological activities, which include manumycins as well. Manumycins are small polyketides with a weak antibiotic activity, especially against gram-positive bacteria. However, its cancerostatic and anti-inflammatory effects are of greater importance. *Streptomyces monomycini* BCCO10 1552 and *Streptomyces capoamus* BCCO10 1636 strains were found positive for the presence of the *als* gene in the targeted genetic screening. By the *als* phylogeny, they cluster near the producers of manumycin compounds. This thesis aimed to determine whether these new natural isolates produce any compounds containing C₅N unit, and to characterize them in more detail. In both cases, *als* gene-deficient mutants and strains expressing *als* under the control of a strong constitutive promoter were created. According to previous experience, we already know that the overproduction of cyclizing aminolevulinate synthase often increases the production of substances with a C₅N unit significantly. In the BCCO10 1636 strain, we have proven the production of substances that seem to be directly linked to the presence of the gene for cALAS and which show weak antibiotic activity against the reference *B. subtilis* strain. In the case of BCCO10 1552 strain, the results are not so clear. Moreover, the analysis of its genomic data, available later, showed that the genome lacks an essential gene for the enzyme attaching the C₅N unit to the antibiotic backbone. Also, the other genes present in a given genomic locus do not suggest that a biosynthetic gene cluster encoding the production of a secondary metabolite may be present.

Key words: streptomycetes, secondary metabolism, manumycins, cyclizing 5-aminolevulinate synthase