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Regulation of tailoring biosynthetic genes of the *aur1* cluster for the Angucycline antibiotic auricin in *Streptomyces aureofaciens* CCM 3239

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Streptomyces are soil Gram-positive bacteria which are characterized by extensive production of biologically active secondary metabolites, including many antibiotics. We identified angucycline antibiotic auricin in *Streptomyces aureofaciens* CCM3239. Auricin is unique angucycline antibiotic containing deoxyaminohexose D-forosamine. Gene cluster *aur1* responsible for the biosynthesis of auricin is localized on the large linear plasmid pSA3239. Auricin is produced in a short time period and its production is tightly regulated through γ -butyrolactone system, positive regulator *aur1P* (belongs to OmpR family of response regulators), negative regulator *aur1R* (belongs to TetR family of regulators), and at least two SARP (*Streptomyces* Antibiotic Regulatory Proteins) regulators. Auricin is glycosylated with the D-forosamine. This sugar moiety is synthesized by the enzymes encoded by *aur1TQSV* genes, and other genes as *sa59* (a homologue of NDP-hexose aminotransferase) and *sa52* (homologue of NDP-aminohexose N-dimethyltransferase). Attachment of D-forosamine moiety on polyketide scaffold is catalysed by two close glycosyl transferases, encoded by genes *sa46* and *sa53*. Mutant strain in both *sa46* and *sa53* genes produced deglycosylated aglycon. Deletion analysis of genes in *aur1* cluster revealed also other genes involved in the tailoring modification of auricin molecule. Analysis of the expression of the tailoring genes revealed that they are directly regulated by both SARP family regulators, *Aur1PR3* and *Aur1PR4*. Therefore the process of auricin regulation is composed of two steps. In the first one, the gene essential for the core auricin aglycon are directly regulated by *Aur1P* and *Aur1R*. In the second step, auricin tailoring genes are regulated by two SARP regulators, *Aur1PR3* and *Aur1PR4*.

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