# Combinatorial biosynthesis of deoxysugar and incorporation into polyketide by a novel glycosyltransferase

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## Abstract

The biological activity of polyketide antibiotics is often strongly dependent on the presence and type of deoxysugar residues attached to the aglycone core. Recent studies have shown that the glycosyltransferase, responsible for the glycosylation of the polyketide aglycone, has a degree of flexibility in the type of sugar accepted as substrate and in the range of aglycone core to which the sugar is transferred. In this study, a host-vector system was developed based on the pikromycin producing strain of *Streptomyces venezuelae* to test the flexibility of a novel glycosyltransferase, DesVII. This host strain can be utilized for the combinatorial biosynthesis of a wide range of deoxysugar moieties and attachment of the synthesized sugar to the aglycone substrate. *S. venezulae* mutant strain YJ003 was created by deletion of the *des* gene cluster, *desI-VII* and *desR*, involved in desosamine biosynthesis. *DesIII* and *IV* genes required to produce dTDP-4-keto-6-deoxy-D-glucose, a common sugar intermediate from which various different sugar derivatives can be biosynthesized, were integrated into the genomic DNA using an integrative plasmid, pSET152. The glycosyltransferase *desVII*, *desVIII*(function currently unknown) gene and genes involved in the biosynthesis of dTDP-D-olivose were cloned into a high-copy plasmid, pSE34 for expression in YJ003. This system is expected to test the flexibility of desVII to a new sugar, olivose, and currently the system is being validated for it's ability to attach the intermediate sugar, dTDP-4-keto-6-deoxy-D-glucose.