Construction of expression vectors for production of ε-rhodomycinone in *Streptomyces coelicolor* YU105

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Abstract

We have attempted production of ε-rhodomycinone, an intermediate of the anticancer agent doxorubicin, from the heterologous host, *S. coelicolor* YU105. The 80kb biosynthetic gene cluster of doxorubicin isolated from *S. peucetius caesius var.* ATCC27952 were sequenced and analyzed. The 13 genes known to be involved in the biosynthesis of ε-rhodomycinone were reorganized into two vectors, pDXR1 and pDR3, each of them containing apramycin and thiostrepton resistance marker gene respectively. The reorganized genes in each vector are all under the control of actIII-I promoter[1]. The expression vector pDXR1 contains dpsABCDGEFY genes which would produce deoxyaklanonic acid[2]. The expression vector pDXR3 contains dnrGCDEF genes which would produce ε-rhodomycinone when expressed properly together with the pDXR1 vector. The produced ε-rhodomycinone could be utilized as a substrate for glycosylation[3] of various deoxysugars. The thereafter modified anthracyclines is to be used to select the anticancer agents with improved activity.

References

1. Paloma arias, Miguel A. Fernandex-Moreno, and Francisco Malpartida (1999), Charaterization of the Pathway-Specific Positive Transcriptional Regulator for Actinorhodin Biosynthesis in Streptomyces coelicolor A3 as a DNA-Binding Protein, *J. Bacteriol.* **181**, 6958-6968.
2. Eckardt K, Tresselt D, Schumann G, Ihn W. Wagner C. (1985), Isolation ande chemical structure of aklanonic acid, an early intermediate in the biosyntehsis of anthracyclines, *J. Antibiot*(Tokyo) **38**, 1034-1039.
3. Olano C., Lomovskaya N., Fonstein L., Roll J. T, Hutchinson C. R. (1999), A two-plasmid system for the glycosylation of polyketide antibiotics: bioconversion of epsilon-rhodomycinone to rhodomycin D, *Chem Biol.* **6**, 845-855.