The Function of orf13 and orf16, Genes Involved in the Biosynthesis of Rifamycin B by

Amycolatopsis mediterranei S699

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Synthetically modified derivatives from rifamycin, such as rifampicin, rifabutin, and rifapentine are principal chemotherapeutic agents used for combating tuberculosis, leprosy and AIDS-related mycobacterial infections. Recently, as with many other antibiotics, the incidence of resistance of \textit{Mycobacterium tuberculosis}, the causative agent of tuberculosis, to rifamycin is continuing increase over time, due largely to mutational alterations of the target molecule. This issued the search for improved new drug candidates. Despite the preparation of a large number of rifamycin derivatives by semi-synthetic approaches, the structural modifications have been limited primarily to one of the region of the molecule, the C3- or C4- positions of the aromatic core unit. Hence there is a need for alternative, biological method of structural modifications. To this end, we investigated the reactions involved in rifamycin B biosynthesis in \textit{A. mediterranei} S699 by inactivation of orf13 or orf16, showing strong similarity to bacterial cytochrom P450, in rifamycin biosynthetic gene cluster. The conversion of rifamycin SV to rifamycin B was almost stopped by the \textit{orf16}-disrupted mutants. Rifamycin B was still produced by the \textit{orf13}-disrupted mutants with lowered productivity compared with wild-type cells.
References

