

Genetic Study on the Gene Cluster for Validamycin Biosynthesis

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The validamycins are a family of closely related pseudotrisaccharides isolated from *Streptomyces hygroscopicus* var. *limoneus*. Validamycin A, the major and most active component of the complex, is widely used in the Far East for the treatment of sheath blight disease of rice plants. The validamycin shows strong inhibition to the action of trehalase and induce a wrong hyphal growth in *Rizoctonia solani* that is the causative agent for sheath blight disease in rice plants. Validamycin A has weak inhibitory activity on α -amylase and is also the starting point for the development of a second generation α -amylase inhibitor, the semisynthetic compound voglibose, which is 20 times more potent as an enzyme inhibitor than acarbose. To study the biosynthetic pathway of the validamycin, the highly conserved gene sequences of the 2-*epi*-5-*epi*-valiolone synthase and 3-dehydroquinate synthase were used as a probe for related genes in the validamycin producer, *Streptomyces hygroscopicus* var. *limoneus*. In this way, 8,598bp DNA was isolated that contains 6 genes putatively involved in the biosynthesis of the validamycin. These 6 genes were encoding proteins with significant similarity to dehydrogenase, aminotransferase, trehalose-6-phosphate synthase, dTDP-4-keto-6-deoxyhexose reductase, 2-*epi*-5-*epi*-valiolone synthase, and glucose-1-phosphate adenylyltransferase, respectively. The putative 2-*epi*-5-*epi*-valiolone synthase was overexpressed in *E. coli* and *S. lividans*, isolated and analyzed in various chemical ways. [Supported by the 21C Frontier Microbial Genomics and Application Center Program, Ministry of Science & Technology, Republic of Korea]

저자(한글명)

1. 김정훈, 김종희, 김윤희, 양혜영, 장용근, 홍순광.