Genetic and Biochemical Analysis of the Salbostatin Biosynthetic Gene Cluster

Yong-Hoon Choeng, Jong-Hee Kim, Mi-Soon Kim, Xue-Mei Jin, Yong-Keun Chang[1], Soon-Kwang Hong*

Myongji University, Yongin, Kyonggido 449-728, Korea

[1]Korea Advanced Institute of Science and Technology, Daejeon 305-701, Korea

The salbostatin is a kind of aminoglycoside antibiotics composing of two sugar moieties and has strong inhibitory effect on trehalase activity, which suggests that it might be used for the control of insects or fungi in the storage of grains or food as a nontoxic and harmless preservatory agent. The salbostatin was isolated from the fermentation culture of the polyether antibiotic salinomycin producer *Streptomyces albus*. To study the biosynthetic pathway of the salbostatin, the biosynthetic gene cluster for salbostatin was cloned and analyzed. Because the unique sugar moiety, valienamine, was one component of the salbostatin, the conserved gene sequences of the 2-*epi*-5-*epi*-valiolone synthase that catalyzes the first step in bioconversion of sedoheptulose-7-phosphate into valienamine, were used as a probe for related genes in the salbostatin producer *Streptomyces albus* KCTC 9015. In this way, a gene cluster was isolated that contains several genes putatively involved in the biosynthesis of salbostatin. Sequence analysis of a 20 Kb region revealed the presence of 19 ORFs. These 19 ORFs were encoding proteins with significant similarity to N-acetylglucosamine-6-phosphate deacetylase, sugar kinase, trehalose-phosphate synthase, transporter, trehalose-6-phosphate phosphatae, ADP-glucose synthase, regulatory enzyme, glycosyltransferase, trehalose phosphorylase, reductase, transporter, 2-epi-5-epi-valiolone 7-kinase, cyclitol dehydrogenase, cyclitol oxidoreduxtase, valiolone-7-phosphate 2-epimerase, hydrolase, 2-epi-5-epi-valiolone synthase, NTP-pyrophosphohydrolases, and quinone oxidoreductase, respectively. From the basic information, the functional confirmation of several genes through heterologous expression and biochemical analysis was performed. **[Supported by the driving force project for the next generation of Gyeonggi provincial government.]**