

## Effects of S-adenosylmethionine on Secondary Metabolite and Morphology in *Streptomyces avermitilis* NRRL8165 and *Streptomyces peucetius* KCTC9039

Gee-Sun Yoon, Hyun-Woo Kang, Yong-Sung Kim and Yeon-Woo Ryu

Dept of Molecular Science and Technology, Ajou University, San 5, Wonchon-dong,  
Yeongtong-gu, Suwon, 443-749, Korea.

TEL: +82-31-219-2455, FAX: +82-31-216-8777

### Abstract

S-adenosylmethionine synthetase (SAM-s) catalyzes the biosynthesis of S-adenosylmethionine (SAM) from L-methionine and ATP. And SAM plays a central role as a methyl donor, donating methyl group to various proteins, nucleic acids, and polysaccharide, as well as to many metabolites associated with the primary and secondary metabolism<sup>1),2)</sup>. A putative SAM-s gene from *Streptomyces avermitilis* NRRL8165 was cloned and characterized. The gene encodes a protein of 402 amino acids with a molecular mass of about 43.5 kDa. Amino acid sequence analysis revealed high sequence identity (~84-93%) to known SAM-s proteins from *Streptomyces* species, containing the conserved sequence motifs of SAM-s proteins, such as nanopptide 276GGGAFSGKD 284 for the P-loop for ATP binding site and metal binding site (17D and 289D for Mg<sup>2+</sup> and 49G for K<sup>+</sup>). The purified protein from the transformed *Escherichia coli* synthesized SAM from ATP and L-methionine *in vitro*. This result demonstrates that the isolated gene indeed encoded the SAM-s protein. When the SAM-s was overexpressed in *S. avermitilis*, a producer of avermectin, and *S. peucetius*, a producer of doxorubicin, the production of antibiotics significantly increased by 2-fold for avermectin and 3.5-fold for doxorubicin, respectively, compared with the respective wild type strain. And overexpression of the SAM-s results in inhibition of aerial mycelium and formation of spores in *S. avermitilis* but not in *S. peucetius*.

### References

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2. Okamoto S, Lezhava A, Hosaka T, Okamoto-Hosoya Y, Ochi K. Enhanced expression of S-adenosylmethionine synthetase causes overproduction of actinorhodin in *Streptomyces coelicolor*A3(2)(2003). J Bacteriol, 185, 601-9.