JC580 **20120703**

Reprogramming a module of the 6-deoxyerythronolideB synthase for iterative chain elongation

Panthee Suresh

Among polyketide compounds, the biosynthesis of erythromycin has been extensively studied. Erythromycin is synthesized by a type I modular PKS and the gene clusters consists of three polyketide genes, each containing two modules. Type I modular polyketide biosynthesis involves the transfer of chain from ACP_n to KS_{n+1} and the translocation of chain to KS_n generally does not occur. Here, by engineering module 3 of DEBS PKS, authors have been able to convert modular PKS into iterative one. The results can be applied in rational engineering of polyketides.

紹介論文

Reprogramming a module of the 6-deoxyerythronolide B synthase for iterative chain elongation

Shiven Kapur, Brian Lowry, Satoshi Yuzawa, Sanketha Kenthirapalan, Alice Y. Chen, David E. Cane, and Chaitan Khosla PNAS, 2012, 11 4110-4115

要旨

Multimodular polyketide synthases (PKSs) have an assembly line architecture in which a set of protein domains, known as a module, participates in one round of polyketide chain elongation and associated chemical modifications, after which the growing chain is translocated to the next PKS module. The ability to rationally reprogram these assembly lines to enable efficient synthesis of new polyketide antibiotics has been a long-standing goal in natural products biosynthesis. We have identified a ratchet mechanism that can explain the observed unidirectional translocation of the growing polyketide chain along the 6-deoxyerythronolide B synthase. As a test of this model, module 3 of the 6-deoxyerythronolide B synthase has been reengineered to catalyze two successive rounds of chain elongation. Our results suggest that high selectivity has been evolutionarily programmed at three types of protein–protein interfaces that are present repetitively along naturally occurring PKS assembly lines.

References:

Kapur S, Chen AY, Cane DE, Khosla C (2010) Molecular recognition between ketosynthase and acyl carrier protein domains of the 6-deoxyerythronolide B synthase. Proc Natl Acad Sci USA 107:22066–22071.