Engineered Biosynthesis of Plant Polyketides

Ikuro Abe
(Sch. Pharm. Sci., Univ. Shizuoka, and PRESTO, JST)

A growing number of functionally divergent type III polyketide synthases (PKSs), the chalcone synthase (CHS) superfamily enzymes, have been cloned and characterized, which include recently obtained pentaketide chromone synthase (PCS) and octaketide synthase (OKS) from aloe (*Aloe arborescens*). Recombinant PCS expressed in *Escherichia coli* catalyzed successive condensations of malonyl-CoA to produce a pentaketide, 5,7-dihydroxy-2-methylchromone, while recombinant OKS yielded octaketides, SEK4 and SEK4b, the longest polyketides produced by the structurally simple type III PKS. PCS and OKS share 92% amino acid sequence identity, and maintain the conserved Cys-His-Asn catalytic triad. The most characteristic feature is that the CHS active site residue 197 (numbering in *Medicago sativa* CHS) is uniquely replaced with Met in PCS and Gly in OKS, respectively. Site-directed mutagenesis revealed that the chemically inert single residue 197 lining the active-site cavity determines the polyketide chain length and the product specificity depending on the steric bulk of the side chain.