CRYSTAL STRUCTURE OF A NOVEL PLANT TYPE III POLYKETIDE SYNTHASE THAT PRODUCES PENTaketide CHROMONE

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Pentaketide chromone synthase (PCS) from Aloe arborescens is a novel plant-specific type III polyketide synthase that catalyzes formation of 5,7-dihydroxy-2-methylchromone from five molecules of malonyl-CoA.¹) Interestingly, site-directed mutagenesis revealed that Met207 determines the polyketide chain length and the product specificity; PCS M207G mutant yielded aromatic octaketides SEK4/SEK4b, instead of the pentaketide.¹) In order to shed light on the molecular basis of the plant polyketide biosynthesis, we carried out crystallography analyses of A. arborescens PCS. Here we now present the crystal structures of both the pentaketide-producing wild-type and the octaketide-producing M207G mutant protein complexed with CoA-SH at 1.6 Å resolution. They revealed that PCS and CHS share the same three-dimensional overall fold, including the CoA binding tunnel and the geometry of the Cys-His-Asn catalytic triad. Remarkably, it was clearly demonstrated that the residue 207 lining the active-site cavity indeed occupies a crucial position for the polyketide chain elongation reactions; it is located at the entrance of a novel buried pocket that extends into the "floor" of the active site cavity. The large-to-small M207G substitution widely opens the gate to the buried pocket, thus expanding a putative polyketide chain elongation tunnel, which leads to formation of the longer octaketides SEK4/SEK4b instead of the pentaketide.