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Biosynthesis of medicinally important plant metabolites by unusual type III polyketide synthasesc

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Abstract

Recent analysis progress on the "second generation" sort III polyketide synthases is summarized. This category of enzymes catalyzes uncommon condensation chemistries of CoA thioesters to come up with numerous core structures of medicinally vital plant secondary metabolites, as well as the R1–C–R2 scaffold of group quinolones, curcuminoids, yet because the 8-azabicyclo octane ring of tropane alkaloids. The invention of this fascinating catalyst taxonomic category provides glorious opportunities for the manipulation of the catalyst reactions to expand the availability of natural and unnatural molecules for future drug development. The type III polyketide synthase (PKS) taxonomic category enzymes generate unbelievably numerous core structures of medicinally vital plant secondary metabolites, as well as flavonoids, stilbenes, chromones, pyrones, phloroglucinols, resorcinols, xanthones, acridones, and quinolones . For instance, chalcone synthase (CHS) and stilbene synthase (STS) are plant-specific typical sort III PKSs that settle for p-coumaroyl-CoA because the starter substrate to catalyse 3 sequent condensations with malonyl-CoA to come up with naringenin chalcone and resveratrol, severally.

Keywords

Polyketide • Rutaceae plants • Phloroglucinols • Alkylquinolone • Solanaceae plants

Description

These enzymes utilize completely different (Claisen-type or decarboxylative aldol-type) cyclizations of associate enzyme-bound, common linear poly-β-keto intermediate. Recent organic chemistry and structural investigations have unconcealed that the homodimeric taxonomic category enzymes possess a extremely homologous overall structure, with a preserved Cys-His-Asn chemical change triad yet as a characteristic CoA-binding tunnel. The catalyst reactions ar initiated by loading of the starter substrate, polyketide chain elongation through decarboxylative condensation with the extender substrate, and termination by cyclization of the ensuing intermediate, among one site. The outstanding diversity of the functions of those extremely homologous enzymes is attributed to the slight variations within the volume and design of the site cavity, that verify the preference for the starter and extender substrates, the quantity of chain elongation reactions, and therefore the mode of cyclization reactions This short review focuses on the recently reportable uncommon "second generation" sort III PKS enzymes, that mediate the fascinating chemistry of condensation reactions of CoA thioesters to come up with numerous core structures of medicinally vital plant secondary metabolites. For instance, within the biogenesis of evocarpine in family Rutaceae plants, 2 functionally distinct sort III PKSs hand and glove mediate the condensation of 3 substrates (R1CO–CoA, R2CO–CoA, and malonyl-CoA) to come up with the R1–C–R2 core scaffold of the 2-alkylquinolone alkaloids. This can be additionally the case for the synthesis of the diarylheptanoid scaffold of curcumin in ginger family plants. In even additional attention-grabbing cases, one catalyst catalyzes the condensations of 3 substrates, to attain the one-pot biogenesis of the alkylquinolone or curcuminoid scaffold. Finally, a recently discovered uncommon sort III PKS is chargeable for the biogenesis of tropane alkaloids in family Solanaceae plants, and produces tropinone with the 8-azabicyclo octane scaffold from 2 molecules of malonyl-CoA and N-methyl-Δ1-pyrrolinium ion. These uncommon enzymes have considerably swollen the chemical change repertoires of the kind III PKS taxonomic category enzymes, and supply a wonderful platform for manipulation of the catalyst reactions for the additional production of medicinally vital natural and unnatural molecules.

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