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PKS における ketosynthase‐dehydratase サブユニット間相互作用のメカニズム

ポリケチド合成酵素(PKS)はポリケチドの産出に関わる他ドメイン酵素複合体で、ポリケチドは二次代謝産物つまり天然物の主要な一群を占めている。
本論文ではその中でも type I PKS のtransAT における ketosynthase(KS)-dehydratase(DH)サブユニット間相互作用のメカニズムを解明することを目指し、KS-DH サブユニット間相互作用は特異性をもっていること明らかにした。
ドメイン間・モジュール間の相互作用は PKS ドメイン改変において重要なファクターであると考えられるため、本論文を紹介する。

紹介論文

Mechanism of intersubunit ketosynthase–dehydratase interaction in polyketide synthases

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Abstract

Modular polyketide synthases (PKSs) produce numerous structurally complex natural products that have diverse applications in medicine and agriculture. PKSs typically consist of several multienzyme subunits that utilize structurally defined docking domains (DDs) at their N and C termini to ensure correct assembly into functional multiprotein complexes. Here we report a fundamentally different mechanism for subunit assembly in *trans*-acyltransferase (*trans*-AT) modular PKSs at the junction between ketosynthase (KS) and dehydratase (DH) domains. This mechanism involves direct interaction of a largely unstructured docking domain (DD) at the C terminus of the KS with the surface of the downstream DH. Acyl transfer assays and mechanism-based crosslinking established that the DD is required for the KS to communicate with the acyl carrier protein appended to the DH. Two distinct regions for binding of the DD to the DH were identified using NMR spectroscopy, carbene footprinting, and mutagenesis, providing a foundation for future elucidation of the molecular basis for interaction specificity.