Journal Club No.810 October 23, 2018

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「反復型ポリケタイド合成酵素の開始基質導入を担うドメイン構造の解明」

ポリケタイド合成酵素群（PKSs）は、微生物に由来する強力な生理活性を示す二次代謝産物の生合成を担う多機能型酵素の一群である。本論文では、タバコ白星病の病原菌である *Cercospora nicotianae* が生産する光毒素ポリケタイド、セルコスポリン（サーコスポリン、cercosporin）の生合成に関与する反復型ポリケタイド合成酵素である CTB1 のクライオ電子顕微鏡による構造解析を行い、これまで未解明であった開始基質導入に関わる acyltransferase domain の構造や、巨大酵素中における SAT ドメインの配置を初めて明らかにした。

紹介論文

The structural organization of substrate loading in iterative polyketide synthases

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Nat Chem Biol. 2018 May;14(5):474-479. doi: 10.1038/s41589-018-0026-3.

要旨

Polyketide synthases (PKSs) are microbial multienzymes for the biosynthesis of biologically potent secondary metabolites. Polyketide production is initiated by the loading of a starter unit onto an integral acyl carrier protein (ACP) and its subsequent transfer to the ketosynthase (KS). Initial substrate loading is achieved either by multidomain loading modules or by the integration of designated loading domains, such as starter unit acyltransferases (SAT), whose structural integration into PKS remains unresolved. A crystal structure of the loading/condensing region of the nonreducing PKS CTB1 demonstrates the ordered insertion of a pseudodimeric SAT into the condensing region, which is aided by the SAT-KS linker. Cryo-electron microscopy of the post-loading state trapped by mechanism-based crosslinking of ACP to KS reveals asymmetry across the CTB1 loading/–condensing region, in accord with preferential 1:2 binding stoichiometry. These results are critical for re-engineering the loading step in polyketide biosynthesis and support functional relevance of asymmetric conformations of PKSs.