
Enacyloxin polyketide synthase - NMR-led integrated structural approach to enable synthetic biology

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Résumé

Nonribosomal peptide synthetases (NRPSs) and type I modular polyketide synthases (PKSs) are comprised of specific protein domains that catalyse the biosynthesis of diverse natural products, including antibiotics, anticancer agents and anti-tumour drugs. The modular architecture of such NRPSs and PKSs make them amenable to rational manipulation to produce novel natural product derivatives. However, modular engineering often leads to reduced product yields. This is due, in part, to suboptimal interactions between protein domains for which molecular level details are often missing. In this presentation, we describe NMR-led integrated structural biology efforts to discover the molecular basis for controlling the biosynthetic process of antibiotic enacyloxin. We also discuss a number of methodological advances in solid state NMR that aim to enable better characterisation of large and dynamic protein-protein complexes complementing the information from more traditional approaches based on solution NMR and x-ray crystallography.

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