第39回HiHA Seminar

Hiroshima Research Center for Healthy Aging (HiHA)

主催: 広島大学健康長寿研究拠点　　HIROSHIMA UNIVERSITY

Combinatorial Synthetic Microbiology for Unnatural Natural Product Fungal Polyketides

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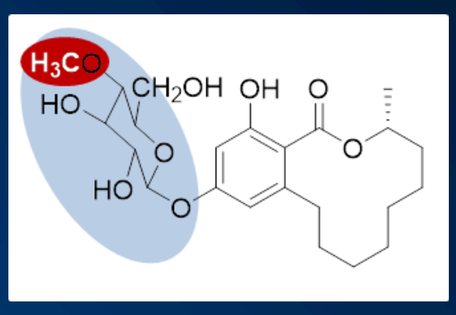
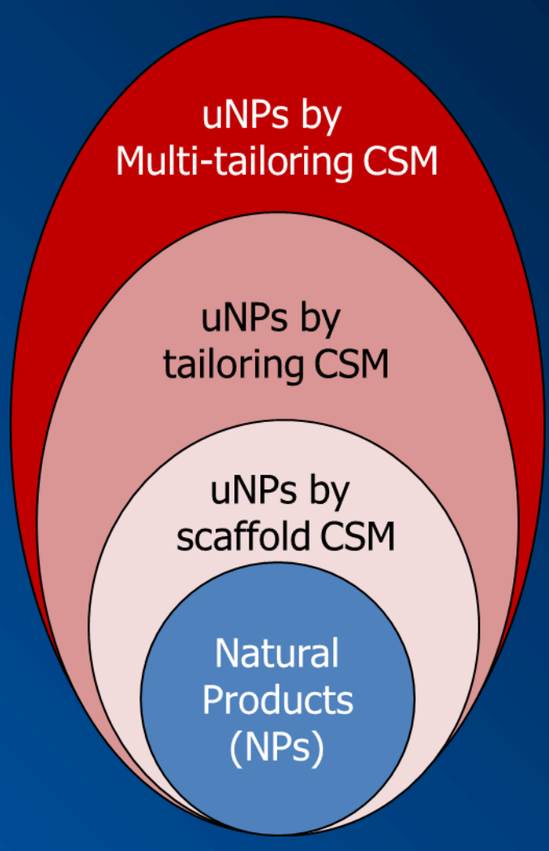
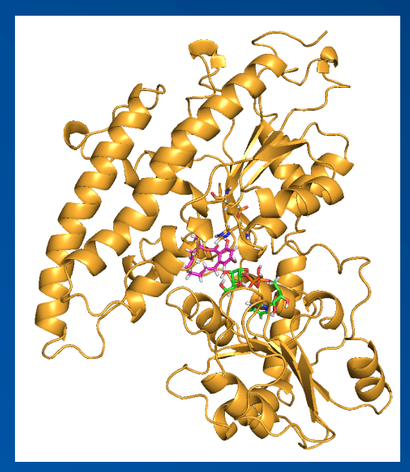
≪要旨≫

Synthetic microbiology aims to construct microbial cellular factories for the efficient, economical and scalable production of biologically active molecules, including small molecule secondary metabolite natural products (NPs). Combinatorial synthetic microbiology (CSM) ventures to create novel metabolic pathways that incorporate non-cognate combinations of biosynthetic enzymes and/or engineered enzymes with altered chemo-, regio-, or stereoselectivity, and produce unnatural NPs (uNPs). To develop CSM, my group exploits fungal polyketide biosynthetic pathways. In this presentation, I will review our recent successes in developing CSM for the biosynthetic production of uNPs based on fungal polyketides. We have recapitulated the production of model benzenediol lactone and azaphilone polyketides in the "domesticated" host *Saccharomyces cerevisiae*, and used hybrid iPKSs for the diversity-oriented biosynthesis of novel uNP scaffolds. We co-opted enzymes from fungal xenobiotic catabolism to "sugarcoat" (glycosylate) these uNPs as well as other drug-like small molecules. We engineered *O*-methyltransferase enzymes by active site remodeling to generate novel tailored uNPs, and investigated the interplay of the engineered regioselectivity of these recombinant enzymes with their substrate promiscuity. Diversity-oriented or focused CSM to produce uNPs will broaden the medicinally relevant chemical space, and provide valuable entry points for drug discovery and development.







※本セミナーは5研究科共同セミナーです

開催日時:令和 元年 6月10日(月) 13:30-14:30

会場:広島大学先端科学総合研究棟 3F 302S 会議室

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