第220回 創薬科学 セミナー
GTR セミナー / CIBoG セミナー

日時：2026年9月18日（金曜日）16：00～ 17：30
場所：創薬科学研究館2階　講義室
このセミナーは創薬科学研究科・先端薬科学特論の単位認定となります

Lecture title：

Complete fermentative biosynthesis of doxorubicin and its derivatives in engineered *Escherichia coli*

Speaker：

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Winner of DaSilva Award 2026 in SBJ

Abstract：

Doxorubicin is a frontline anthracycline anticancer drug listed on the WHO Model List of Essential Medicines, yet its supply depends on fermentation of Streptomyces peucetius followed by multistep semisynthesis—a route constrained by the limited engineering toolkit and complex regulation of the native producer, and by low overall yields. Here we report the complete biosynthesis of doxorubicin and its derivatives in engineered Escherichia coli. A type II minimal polyketide synthase was first optimized for decaketide formation using resistomycin as a surrogate reporter, and DpsC was identified as a fidelity factor favoring propionyl-CoA as the starter unit. Combined with enhanced malonyl-CoA supply and chaperone engineering, this enabled production of ε-rhodomycinone and doxorubicinone. We separately reconstructed biosynthesis of the noncanonical sugar TDP-L-daunosamine and DnrQS-mediated glycosylation. To relieve metabolic burden, a strain harboring the core aglycone biosynthesis genes was cocultured with a second strain harboring the sugar biosynthesis and glycosylation genes, enabling complete biosynthesis of doxorubicin from glucose and propionate in fed-batch fermentation. Further introduction of an epimerase or an O-methyltransferase yielded epirubicin and non-natural 4′-O-methyl-doxorubicin, respectively, establishing E. coli as a modular platform for the fermentative production of medicinally important aromatic polyketides.

皆様奮ってご参加ください。

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