

Induced biosynthesis of cryptic polyketide metabolites in a *Burkholderia thailandensis* quorum sensing mutant.

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Abstract

Genetic manipulation of the LuxR-type quorum sensing regulator system in *Burkholderia thailandensis* caused a significant change in the metabolic profile: it led to activation of the thailandamide biosynthesis gene cluster, dramatically increased thailandamide production, and induced strong pigmentation. A novel polyketide metabolite, thailandamide lactone (2), which cannot be detected in the wild type, was isolated from the mutant broth, and its structure was elucidated by high-resolution mass spectrometry and IR and NMR spectroscopy. In a biological assay using tumor cell lines, 2 showed moderate antiproliferative activities. This finding not only points to complex regulation but also serves as a proof of concept that engineering quorum sensing mutants may enable the discovery of novel bioactive natural products encoded by silent or only weakly expressed biosynthetic pathway genes.

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