

Oak-associated negativicute equipped with ancestral aromatic polyketide synthase produces antimycobacterial dendrubins.

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Abstract

Anaerobic bacteria have only recently been recognized as a source of antibiotics; yet, the metabolic potential of Negativicutes (Gram-negative staining Firmicutes) such as the oak-associated *Dendrosporobacter quercicolus* has remained unknown. Genome mining of *D. quercicolus* and phylogenetic analyses revealed a gene cluster for a type II polyketide synthase (PKS) complex that belongs to the most ancestral enzyme systems of this type. Metabolic profiling, NMR analyses, and stable-isotope labeling led to the discovery of a new family of anthraquinone-type polyphenols, the dendrubins, which are diversified by acylation, methylation and dimerization. Dendrubin A and B were identified as strong antibiotics against a range of clinically relevant, human-pathogenic mycobacteria.

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