

Biosynthesis, synthesis and activities of barnesin A, a NRPS-PKS hybrid produced by an anaerobic Epsilonproteobacterium.

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Abstract

Despite the wealth of physiological knowledge and plentiful genomes available, only few natural products of anaerobic bacteria have been identified until today and even less have been linked to their biosynthetic gene cluster. Here, we analyzed a unique NRPS-PKS hybrid gene cluster from an anaerobic Epsilonproteobacterium (*Sulfurospirillum barnesii*). Phylogenetic analysis of key biosynthetic genes, gene expression studies and comparative metabolomics resulted in the identification of the first anoxically biosynthesized NRPS-PKS hybrid metabolite, a lipo-dipeptide with a vinylogous side chain, named barnesin A. The absolute structure was verified by a modular total synthesis and barnesin and derivatives were found to have antimicrobial activity as well as selective and nanomolar inhibitory activity against pharmacological important cysteine proteases, such as cathepsin B.

Involved units

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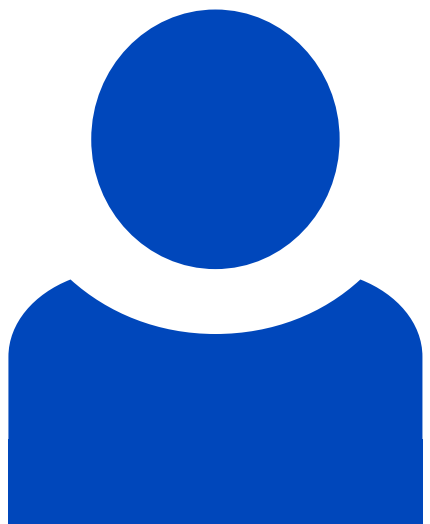
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