

Evolution of siderophore pathways in human pathogenic bacteria.

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Abstract

Ornibactin and malleobactin are hydroxamate siderophores employed by human pathogenic bacteria belonging to the genus *Burkholderia*. Similarities in their structures and corresponding biosynthesis gene clusters strongly suggest an evolutionary relationship. Through gene coexpression and targeted gene manipulations, the malleobactin pathway was successfully morphed into an ornibactin assembly line. Such an evolutionary-guided approach has been unprecedented for nonribosomal peptide synthetases. Furthermore, the timing of amino acid acylation before peptide assembly, the absolute configuration of the ornibactin side chain, and the function of the acyl transferase were elucidated. Beyond providing a proof of principle for the rational design of siderophore pathways, a compelling model for the evolution of virulence traits is presented.

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