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Bioproduction of polymyxin derivatives

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PURPOSE OF THE ABSTRACT

With the rise in bacterial resistance and overuse of antibiotics, it is necessary to find efficient treatments against human infections. One strategy is to enhance existing molecules by genetic engineering. As part of our ongoing research, we respectively isolated from the environment and a sputum of a cystic fibrosis patient two novel antibiotic producing strains of Paenibacillus, B-LR and P-32. Paenibacilli are ubiquitous bacteria that produce antibiotics such as polymyxins and fusaricidins. These molecules are obtained from specific enzymes called Non Ribosomal Peptide Synthetases (NRPS). The strains B-LR and P-32 inhibit the growth of Pseudomonas aeruginosa and Staphylococcus aureus clinical strains (including methicillin resistant strains). These peptides were purified and characterized by LC-MS. B-LR produces polymyxin E (colistin) and ten different molecules while P-32 synthesizes a new depsipeptide. Two genomic libraries were constructed and screened in order to find the gene clusters responsible for the biosynthesis of these molecules. This screening lead to the discovery of the colistin gene cluster in B-LR. This new gene cluster covers 41 kb and includes 5 ORF. Three of them encode for NRPS involved in the colistin synthesis, whereas two others are ABC transporter-like genes that may release the antibiotic. This study constitutes the first description of the biosynthesis pathway of this commercial antibiotic that could contribute to a better understanding of the biosynthesis. The biotechnological development appears to be a good way the pharmaceutical production of optimized antibacterial treatments.

FIGURES

FIGURE 1

FIGURE 2

KEYWORDS

Bioproduction | Non Ribosomal Peptide Synthetases

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