**Context and objectives**

Peptidoglycan, a specific bacterial cell-wall polymer that is essential for maintaining the cell integrity, constitutes an interesting target to be exploited in a search for new antibacterial compounds. Bacteria themselves have developed systems to fight and eliminate competitors. They produce toxins allowing them to prevail within cell populations and fully express their virulence. Colicin M that is produced by Escherichia coli was the only colicin known to interfere with peptidoglycan biosynthesis. The recent elucidation of its mechanism of action (enzymatic degradation of peptidoglycan lipid intermediates) and the detection of homologous genes in the genomes of pathogenic Pseudomonas species constituted a very favourable context for the development of a detailed and multidisciplinary study of this family of enzymatic colicins targeting peptidoglycan metabolism.

**Results**

* Identification of genes and biochemical characterization of ColM homologues (PaeM, PRM and PsyM) produced by certain strains of *P. aeruginosa* and *P. syringae*.* Site-directed mutagenesis of ColM identified five residues (D 226, D229, Y228, H235 and Y238) that is 50 fold more active than the full-length protein.

* Dissection of ColM protein translocation (T), reception (R ) and activity (A) domains was performed. allowing us to delineate an independent activity domain (17 KDa, residues 124-271) that is 50 fold more active than the full-length protein.

* Site-directed mutagenesis of ColM identified five residues (D226, D229, Y228, H235 and Y238) that is 50 fold more active than the full-length protein.

**Conclusions and perspectives**

Detailed investigations of this newly identified and little family of peptidoglycan-targeting bacteriocins that are produced by *E. coli* and *Pseudomonas* species were developed by using various complementary approaches. A dissection of the colicin M structure and biochemical characterization of its functionally independent toxicity domain were performed. Demonstration that these enzymes (phosphotransferases) could act on lipids II of different structures, that are representative of the variability of the peptidoglycan structure in bacterial world, opens the way to a potential exploitation of these toxins as large-spectrum antibacterial agents.

**Publications**


