Colicin M, a peptidoglycan lipid II-degrading enzyme: potential use for antibacterial means?

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Colicins are proteins produced by some strains of *Escherichia coli* to kill competitors belonging to the same species. Among them, colicin M (ColM) is the only one that blocks the biosynthesis of peptidoglycan, a specific bacterial cell-wall polymer essential for cell integrity. ColM acts in the periplasm by hydrolyzing the phosphoester bond of the peptidoglycan lipid intermediate (lipid II). ColM cytotoxicity is dependent upon FkpA of the targeted cell, a chaperone with cis/trans peptidyl-proline isomerase activity. Dissection of ColM was used to delineate the catalytic domain, 14 kDa in size, and to identify the active site residues. The *in vitro* activity of the isolated catalytic domain towards lipid II was 50-fold higher than that of the full-length bacteriocin. Moreover, this domain was bactericidal in the absence of FkpA under conditions that by-pass the import mechanism (FhuA-TonB machinery). Thus, ColM undergoes a maturation process driven by FkpA that is not required for the activity of the isolated catalytic domain. Genes encoding proteins with similarity to the catalytic domain of ColM were identified in pathogenic strains of *Pseudomonas* and other genera. ColM and its orthologues all act on lipids II, which display different structures representative of the diversity of peptidoglycan chemotypes. All together, these data open the way to the potential use of ColM-related bacteriocins as broad spectrum antibacterial agents.