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ENDOLYSINS, AUTOLYSINS AND ANTIMICROBIAL PEPTIDES: ALTERNATIVES TO CONVENTIONAL ANTIBIOTICS

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In the era of still growing number of antibiotic resistant bacteria there is an urgent need for the discovery of novel antibacterial agents. The European Medicine Agency reports that the annual impact of resistant infections is estimated to be 1.6€ billion in excess health care costs and 2.5 million additional hospital days on the territory of the European Union. Endolysins also known as peptidoglycan (PGN) hydrolases are enzymes produced by most of dsDNA bacteriophages (viruses that infect bacteria) at the end of their replication cycle to facilitate phage progeny release from the host bacteria. The successful external use of endolysins, initially against Gram-positive bacteria, and nowadays more often against Gram-negative pathogens made them potent antimicrobial agents. In the current project, we investigated the antibacterial activity of thermostable endolysin against multi-drug resistant (MDR) clinical strains of Acinetobacter *baumannii* and *Pseudomonas aeruginosa* of the order Pseudomonadales and MDR pathogens of the order Enterobacteriales. The endolysin showed structure similarity to eukaryotic peptidoglycan recognition proteins (PGRPs), of which lytic PGRPs possess strong antibacterial activity. We used this resemblance for further search of novel antibacterials that are similar to lytic PGRPs. Putative autolysin (PGN remodeling enzyme) LysC from Gram-positive anaerobic bacterium *Clostridium intestinale* URNW has been chosen for further analysis. We revealed that LysC lyses bacteria through the mechanism that is completely independent of its enzymatic activity. Instead, we found that synthetic peptide P23 derived from the N-terminal region of LysC has bactericidal activity. The peptide showed no hemolytic and no cytotoxic activity against human keratinocyte cells. Endolysins, autolysins and antimicrobial peptides form a promising group of antimicrobials directed against both Gram-negative and Gram-positive pathogens.

Biography

Magdalena Plotka is employed as an Assistant Professor at the Department of Microbiology, Laboratory of Extremophiles Biology at the University of Gdansk, Poland. In 2012-2014, she was involved in the project "Exgenomes Molecular Enzymes" founded by EU within the 7th Framework Programme. During the project six enzymes were developed into commercial products. Among them were four proteins, in characterization of which participated dr Plotka: LysT endolysin from *Thermus* phage Pro2631, Lys2119 endolysin from *Thermus* phage Ph2119, RecA recombinase from *Thermus* phage T72 and RadA recombinase from *Pyrococcus woesei*. Currently, she is involved in the multinational European research project Virus-X (http://virus-x.eu/) funded under European Union Horizon 2020 (years 2016-2020). Within the project she is responsible for functional analysis of selected thermostable proteins which then can be used for biotechnological innovation. She is especially interested in characterization of lytic enzymes/endolysins with potential application as antimicrobial agents.

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