Characterization of Modular Bacteriophage Endolysins From Giant phiKZ Related Myoviridae Phages OBP, 201phi2-1 and PVP-SE1

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Peptidoglycan lytic enzymes (endolysins) of bacteriophages have a major role in bacterial lysis at the end of the phage replication cycle. These endolysins turned out to be potential antibacterial compounds to combat a broad range of Gram-positive pathogens, yet Gram-negative bacteria remain unharmed due to their impermeable outer membrane. With this background, we recently characterized three new endolysins from Gram-negative origin: OBPgp279 (Pseudomonas fluorescens phage OBP), PVP-SE1gp146 (Salmonella Enteritidis phage PVP-SE1) and 201phi2-1gp229 (Pseudomonas chlororaphis phage 201phi2-1). These endolysins share a modular structure with an N-terminal cell wall binding domain and a C-terminal catalytic domain, a unique property of endolysins belonging to giant phiKZ related phages and some other giant, non-related myoviruses. All three endolysins showed strong muralytic activity on the peptidoglycan of a broad range of Gram-negative bacteria, a feature linked with their modular composition. In case of OBPgp279, the presence of the cell wall binding domain is responsible for 38 % of the total muralytic activity. Moreover, the binding domain of PVP-SE1gp146 has a binding affinity for Salmonella peptidoglycan that falls within the range of typical cell adhesion molecules. Remarkably, PVP-SE1gp146 shows thermoresistant properties up to temperatures of 90°C, making it a potential candidate as antibacterial in hurdle technology for food preservation. OBPgp279, on the other hand, is able to pass the outer membrane of P. aeruginosa PAO1 using an unknown mechanism, thereby gaining access to its peptidoglycan and reduce the bacterium with 1 logarithmic unit. Addition of the outer membrane permeabilizer EDTA significantly increased the antibacterial activity of the three endolysins up to 2-3 logarithmic units. This research offers perspectives towards elucidation of the structural differences explaining the unique biochemical and antibacterial properties of OBPgp279, PVP-SE1gp146 and 201phi2-1gp229. Furthermore, these endolysins extensively enlarge the pool of potential antibacterial compounds used for treatment of Gram-negative bacterial infections.

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