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In vivo systems to study class II bacteriocins toxicity and immunity

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Class II bacteriocins are membrane-active peptides that act over a narrow spectrum of bacterial targets and have a great potential application as antibiotics in medical sciences. They act on the cytoplasmic membrane dissipating the transmembrane potential by forming pores. There is solid evidence that membrane receptor proteins are necessary for their function, however the precise role of this receptor and the nature of the pore remain elusive. The most accepted model suggest that bacteriocins bind the receptor to change its conformation, creating a channel that remains open. Nonetheless, several studies support a second model in which the bacteriocin is able to disrupt the membrane itself and the receptor might act just as an anchor allowing the subsequent bacteriocin insertion to form the pore. In order to reveal whether or not the pore structure involves the specific receptor, we designed chimeric peptides fusing the membrane protein EtpM with different class II bacteriocins. We chose E. coli as a receptor-free expression host. The fusion EtpM-bacteriocin anchors each bacteriocin to the membrane and kills the expressing host cell, even in the absence of the specific receptor. These results are in line with the second model in which the pore is formed through a receptor-independent interaction with the lipid bilayer. The effect of these interactions was also analyzed, through a fluorophore that changes its fluorescence intensity according to transmembrane potential.

On the other hand, an immunity protein protects the producer strain against its own bacteriocin. For antimicrobials under investigation for clinical applications, the potential emergence of resistant pathogens and the study of immune mechanisms are a primary concern. Though no direct in vitro interaction bacteriocin-immunity has been reported before, by using an in vivo system, we present evidence that this binding might occur, not in aqueous solution but in a membrane inserted conformation

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