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MEMBRANE INTERACTIONS OF NATURAL CYCLIC LIPODEPSIPEPTIDES OF THE VISCOSIN GROUP

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Abstract

Many *Pseudomonas* spp. produce cyclic lipodepsipeptides (CLPs), which, besides their role in biological functions such as motility, biofilm formation and interspecies interactions, are antimicrobial. It has been established that interaction with the cellular membrane is central to the mode of action of CLPs. In this work, we focus on the CLPs from the so-called viscosin group, aiming to assess the impact of the main structural variations observed within this group on both the antimicrobial activity and the interaction with model membranes. The antimicrobial activity of viscosin, viscosinamide, WLIP and pseudodesmin A were all tested on a broad panel of mainly Gram-positive bacteria. Their capacity to permeabilize or fuse PG/PE/cardiolipin model membrane vesicles is assessed using fluorescent probes. We find that the Glu2/Gln2 structural variation within the viscosin group is the main factor that influences both the membrane permeabilization properties and the minimum inhibitory concentration of bacterial growth, while the configuration of the Leu5 residue has no apparent effect. The CLP-membrane interactions were further evaluated using CD and FT-IR spectroscopy on model membranes consisting out of PG/PE/cardiolipin or POPC with or without cholesterol. In contrast to previous studies, we observe no conformational change upon membrane insertion. The CLPs interact both with the polar heads and aliphatic tails of model membrane systems, altering bilayer fluidity, while cholesterol reduces CLP insertion depth.

Keywords: viscosin group, cyclic lipodepsipeptide, model membranes, membrane permeabilization, spectroscopy, antimicrobial activity