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The secrets and potential of a novel cyclic antimicrobial and cell penetrating peptide

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The synthetic cyclic hexapeptide cWFW (cyclo(RRRWFW)) is very stable towards proteolytic degradation, low pH and has a high activity against different Gram positive and Gram negative laboratory strains and clinical pathogens, including *S. aureus* and *L. monocytogenes*. With its amphipathic structure and high content of arginine residues, the peptide combines the prerequisites for membrane permeabilization and membrane translocation as modes of action. Using a number of techniques to study peptide interaction with bacterial and eukaryotic model membranes as well as with bacterial and eukaryotic cells, we could show that the activity of cWFW is based on a novel antimicrobial mechanism. Strong interactions with the bacterial membrane lead to reduction in membrane fluidity and disturbance of the native lipid matrix. The formation of distinct lipid domains is related to a severe disturbance in the positioning of functional proteins which finally leads to cell death. While the peptide does not enter the cytoplasm of bacteria, cWFW is rapidly internalized into human cells without decreasing cell viability. The combination of cell penetrating properties with high antimicrobial activity and the novel mechanism of action render the cyclic hexapeptide an eligible compound with regard to the treatment of intracellular bacterial infections, as e.g., in the case of tuberculosis and pneumonia.

Biography

Margitta Dathe has studied Physics at the Humboldt University of Berlin and completed her PhD in 1978 from the Academy of Sciences of the GDR. Since 1999 she has been working as the Head of the peptide-lipid interaction research group of the Leibniz Institute of Molecular Pharmacology. Her research interest is focused on targeting, cellular uptake promoting and antimicrobial peptides. She has published more than 100 papers in reputed journals.

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