Antimicrobial Peptides as Cell-Penetrating Peptides

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A large number of cationic antimicrobial peptides composed of 15–40 amino acids have been discovered in various organisms including mammals, constituting host defense systems against invading pathogenic microorganisms [1]. These peptides are considered to be promising candidates as novel antibiotics of clinical usefulness. A major mode of action of these peptides is the permeabilization of cell membranes. We discovered that several peptides, including magainin 2 from the *Xenopus* skin, form transient toroidal pores that induce not only ion permeation but also flip-flop of membrane lipids [2]. Furthermore, these peptides translocate across lipid bilayers [2] as well as cell membranes [3] upon the disintegration of pores. Although the membrane permeabilization leads to cytotoxicity, careful design of peptide sequences may destabilize pores, therefore minimize cytotoxicity.

Recently, we found using living cells that magainin forms a toroidal pore with a diameter of ca. 3 nm in *Bacillus megaterium*, whereas it significantly perturbs CHO cell membranes by creating a huge lesion..

In this presentation, the possibility of these peptides as cell-penetrating peptides will be discussed.

[1] Zasloff, M. (2002) Nature 415, 389–395.
[2] Matsuzaki, K. (1999) Biochim. Biophys. Acta 1462, 1–10.
[3] Takeshima, K., Chikushi, A., Lee, K.-K., Yonehara, S., and Matsuzaki, K. (2003) J. Biol. Chem. 278, 1310–1315.