SYNERGISTIC INSERTION OF ANTIMICROBIAL PEPTIDES INTO MEMBRANES

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The antimicrobial peptides (AMPs) PGLa and magainin 2 (MAG2) found in the skin of the African frog *Xenopus laevis* show a synergistic enhancement of their activity [1]. Both peptides form amphipathic α -helices when binding to a lipid membrane, and their orientation in membranes have been determined with high accuracy using solid state ²H-, ¹⁵N-, and ¹⁹F-NMR.

We have previously shown that PGLa inserts into DMPC/DMPG bilayers in the presence of an equimolar amount of MAG2, but not on its own, even at high concentrations [2]. This indicates formation of stable heterodimeric peptide pores, which in turn can explain the synergism between the peptides. Here, we show that MAG2, both with and without PGLa, always stays almost flat on the membrane surface; however, there is a small change in the orientation in the presence of PGLa, and dynamics is reduced, indicating that a PGLa-MAG2 complex is formed. In POPC/POPG, both peptides stay flat on the membrane surface, alone or combined. This is in agreement with our previous finding that the AMP MSI-103 always stays flat on the surface in unsaturated lipids (or more generally in lipid systems with negative spontaneous curvature), but can insert deeper into the membrane in saturated lipids (where the spontaneous curvature is positive) [3]. References: [1] E Strandberg, P Tremouilhac, P Wadhwani, AS Ulrich (2009). *Biochim Biophys Acta* **1788**, 1667–1679. [2] P Tremouilhac, E Strandberg, P Wadhwani, AS Ulrich (2006). *J Biol Chem*, **281**, 32089-32094. [3] E Strandberg, D Tiltak, S Ehni, P Wadhwani, and AS Ulrich (2011). *Biophys J* **100**, *Suppl*, 351a-351a.