Structure and alignment of the membrane-associated peptaibols ampullosporin A and alamethicin by oriented 15N and 31P solid-state NMR spectroscopy.

Salnikov ES, Friedrich H, Li X, Bertani P, Reissmann S, Hertweck C, O'Neil JD, Raap J, Bechinger B (2009) Structure and alignment of the membrane-associated peptaibols ampullosporin A and alamethicin by oriented 15N and 31P solid-state NMR spectroscopy. *Biophys J* 96(1), 86-8100.

Abstract

Ampullosporin A and alamethicin are two members of the peptaibol family of antimicrobial peptides. These compounds are produced by fungi and are characterized by a high content of hydrophobic amino acids, and in particular the alpha-tetrasubstituted amino acid residue ?-aminoisobutyric acid. Here ampullosporin A and alamethicin were uniformly labeled with (15)N, purified and reconstituted into oriented phophatidylcholine lipid bilayers and investigated by proton-decoupled (15)N and (31)P solid-state NMR spectroscopy. Whereas alamethicin (20 amino acid residues) adopts transmembrane alignments in 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC) or 1,2-dimyristoyl-sn-glycero-3-phosphocholine (DMPC) membranes the much shorter ampullosporin A (15 residues) exhibits comparable configurations only in thin membranes. In contrast the latter compound is oriented parallel to the membrane surface in 1,2-dimyristoleoyl-sn-glycero-3-phosphocholine and POPC bilayers indicating that hydrophobic mismatch has a

decisive effect on the membrane topology of these peptides. Two-dimensional (15)N chemical shift -(1)H-(15)N dipolar coupling solid-state NMR correlation spectroscopy suggests that in their transmembrane configuration both peptides adopt mixed alpha-/3(10)-helical structures which can be explained by the restraints imposed by the membranes and the bulky alpha-aminoisobutyric acid residues. The (15)N solid-state NMR spectra also provide detailed information on the helical tilt angles. The results are discussed with regard to the antimicrobial activities of the peptides.

Beteiligte Forschungseinheiten

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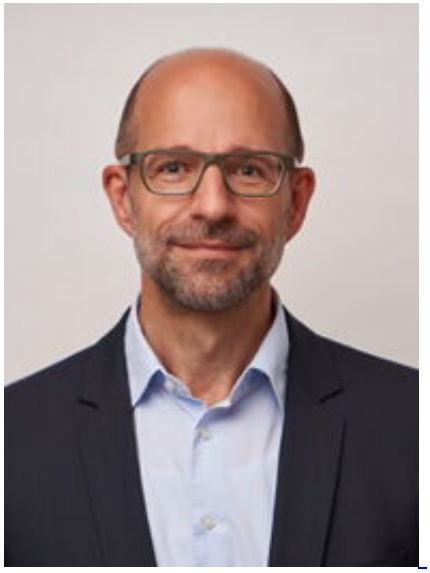

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Details

Identifier

doi: 10.1529/biophysj.108.136242

PMID: 18835909