Supporting Information

Membrane interactions of novicidin, a novel antimicrobial peptide: phosphatidylglycerol promotes bilayer insertion

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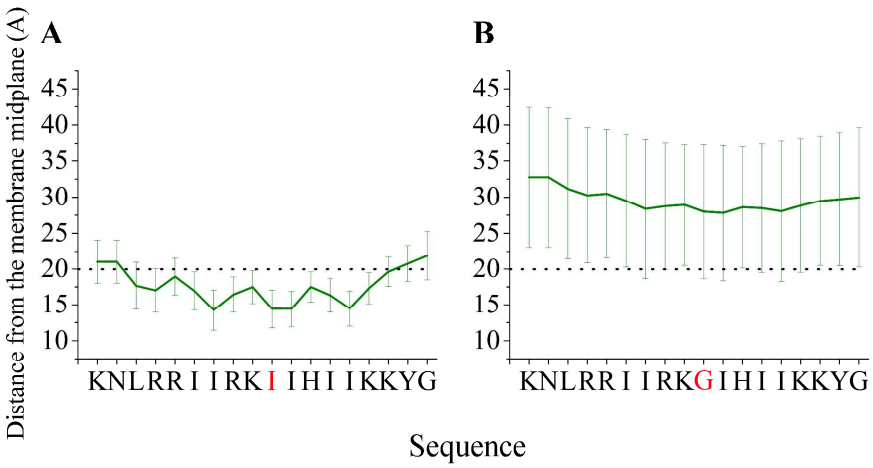

Figure S1. Location of ovispirin and novispirin in a neutral lipid bilayer based on MC simulations. The average conformations of ovispirin (**A**) and novispirin (**B**) in association with neutral (equivalent to pure PC) lipid bilayer determined as the average distance of each residue's alpha-carbon from the bilayer midplane. The error bars mark the standard deviation. The residues are indicated using a one-letter code. The horizontal dotted line marks the location of the phosphate group of the lipids polar heads. Novispirin hardly associates with the lipid bilayer but ovispirin resides in the polar headgroups region. It is remarkable that a single substitution of G to I (position 10; marked in red) is responsible for the different membrane behavior of the peptides. Apparently, novispirin is almost hydrophobic enough to partition into the membrane, and the addition of a single hydrophobic residue is enough to shift the balance.

Computational methods

The total free energy difference between a peptide in the aqueous phase and in the membrane (ΔG_{tot}) can be divided into several terms according to Eq. 1:

$$\Delta G_{tot} = \Delta G_{con} + \Delta G_{def} + \Delta G_{Coul} + \Delta G_{sol} + \Delta G_{imm} + \Delta G_{lip} \quad (1)$$

Where ΔG_{con} is the free energy change due to membrane-induced conformational changes in the peptide. ΔG_{def} is the free energy penalty associated with fluctuations of the membrane width around its resting (average) value of 30Å. ΔG_{Coul} stands for the electrostatic interactions between titratable residues of the peptide and the (negative) surface charge of the membrane. ΔG_{sol} is the free energy of transfer of the peptide from water to the membrane. It accounts for electrostatic contributions resulting from changes in the polarity of the solvent, as well as for nonpolar (hydrophobic) effects, which result from both differences in the van der Waals interactions of the peptide with the membrane and aqueous phases, and from solvent structure effects. ΔG_{imm} is the free energy penalty resulting from the confinement of the external translational and rotational motion of the peptide inside the membrane. ΔG_{lip} is the free energy penalty resulting from the interference of the peptide with the conformational freedom of the aliphatic chains of the lipids in the bilayer.