19ème Congrès du Groupe Français des Peptides et des Protéines
17-22 mai 2015
Portbail, Normandie, France

Modeling of Antimicrobial Lipopeptides in interaction with lipidic membranes

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The resistance of bacteria and fungi to available antibiotics is a major concern worldwide, leading to enormous effort to develop innovative drugs with new modes of actions. Two families of natural peptides are in this respect promising : host-defense cationic antimicrobial peptides, and lipopeptides. Iturinic lipopeptides, in particular Mycosubtilin, shows interesting biocide activity against fungi. Its interactions with the lipidic membranes of the pathogens seem to be at the origin of the biological activities. Cholesterol or ergosterol have been shown to play a role in Mycosubtilin activities, but the precise molecular mechanisms of the interactions need to be further elucidated. In our theoretical approach, using molecular dynamics simulations, we investigated the interaction between iturinic lipopeptides and various interfaces. We have performed molecular dynamics simulation of the peptide in water, at the air/water interface, and in interaction with phospholipids or sterols monolayers. Conformations of the lipopeptide were generated using replica-exchange molecular dynamics (REMD) [1,2]. Using metadynamics simulations, the free energy of adsorption and insertion of the lipopeptide in lipid membranes was estimated. Specific interactions of the lipopeptide with sterols are observed, they may be decisive in the selectivity of its antimicrobial activity. These results are discussed along with experimental data describing physico-chemical properties of lipopeptides at various interfaces [2,3,4].

1. C. Loison et al., *Phys. Chem. Chem. Phys.* (2014) Vol. 16 (5), p. 2136.
2. M. N. Nasir et al., *Phys. Chem. Chem. Phys.* (2014) Vol. 15 (45), p. 19919.
3. M. N. Nasir and F. Besson, *Langmuir* (2011) Vol. 27 (17), p.10785.
4. M. N. Nasir et al., *Phys. Chem. Chem. Phys.* (2013) Vol. 15, p. 19919.