Design of a tilted peptide using molecular modeling techniques

C. Heinen, L. Lins, and R. Brasseur

Centre de Biophysique Moléculaire Numérique (CBMN), Faculté des Sciences Agronomiques de Gembloux (FSAGx), 5030 Gembloux, Belgium.

The purpose of this study is to create *"de novo"* tilted peptides by molecular modeling, based on the sequence of the SIV tilted peptide. Tilted peptides are short protein fragments (11 to 18 amino acids), able to destabilize an organized system presenting a pho/phi interface. They are notably characterised by a peculiar distribution of their hydrophobic residues when helical. Those new peptides are designed to match some criteria, here, for example they should have an hydrophobicity between 0.6 and 0.7 (based on the Eisenberg consensus scale), which is lower than the original peptide, an insertion angle in the membrane of about 45° and they should be able to pass through the bilayer.

ZTammo software generates mutants from the original tilted peptide. The first step of the method involves the selection of the residues that will be muted, because all mutants can't be generated in a reasonable time (theoretically, for the SIV peptide which is composed of twelve amino acids, there is 20^{12} possibilities). From the SIV wild-type peptide, we generated 1280 mutants. The same program selects some of these mutants (here, 74 peptides) according to the criteria defined initially.

Each of these 74 peptides are rebuilt and optimised using Hyperchem 6.0 and their properties of insertion into a lipid bilayer (angle, depth, etc) are calculated, using the IMPALA method. One mutant will finally be selected on the basis of its sequence. This mutant is synthesized and its ability to induce liposome fusion will be tested.

Poster n°35