Atomic force microscopy imaging of the interaction between tilted peptides and supported lipid bilayers

K. El Kirat-Chatel[1], L. Lins[2], R. Brasseur[2], Y. F. Dufrêne[1]

[1]Unite de Chimie des Interfaces, Universite catholique de Louvain and
[2]Centre de Biophysique Moléculaire Numérique, Faculté Universitaire des Sciences Agronomiques de Gembloux, Belgium

Membrane fusion is a key process for cell life and development. Many fusion events are known to involve the active participation o hydrophobic peptides, which help destabilizing the membrane lipid bilayer. Tilted peptides represent a special class of fusogenic peptides which have a hydrophobicity gradient that runs along the axis of the helical peptide. This gradient causes them to insert at an angle of between 30-60° at a hydrophobic-hydrophilic interface. Tilted peptides are found in many membrane-interacting proteins such as viral fusion proteins, neurotoxic proteins and proteins involved in lipoprotein metabolism. So far, high resolution visualization of the interaction of tilted peptides with lipid membranes has never been reported.

In this work, we have used atomic force microscopy (AFM) to investigate the influence of a tilted α-helix peptide, the Simian Immunodeficiency Virus (SIV) fusion peptide, on the stability and organization of supported lipid bilayers composed of an equimolar mixture of dioleoylphosphatidylcholine (DOPC) and dipalmitoylphosphatidylcholine (DPPC). The SIV peptide is composed of 12 hydrophobic aminoacids and is expected to penetrate within membranes with a tilted angle of about 55 to 60° relative to the bilayer normal.

AFM images of supported DPPC/DOPC bilayers revealed phase-separation between gel DPPC and fluid DOPC domains. Injection of the SIV peptide into the solution led to the rapid appearance of nanoscale holes within the DPPC gel phase, the hole depth corresponding to the bilayer thickness, i.e. ~6 nm. Non-tilted ApoE peptides did not present this behavior. The AFM results could be directly related to their fusogenic activity as measured on model DPPC/DOPC liposomes. We attribute the formation of holes to a local weakening and destabilization of the DPPC domains due to the insertion of the peptides.

In a complementary set of experiments, we investigated the self-associative properties of SIV peptides in mixed DPPC/SIV bilayers. Depending on the preparation method, SIV peptides were either adsorbed on the bilayer in the form of supramolecular aggregates or inserted into the bilayer. These two modes of macromolecular association may correspond to the β-sheet and α-helix forms, respectively. Hole formation was not observed in DPPC/SIV bilayers, indicating a rather stable association between peptides and lipids. This work demonstrates the power of AFM to investigate peptide-membrane interactions at high resolution.