Biophysical Characterization of the Interactions of *Flavivirus* Fusion Peptides with Micelles and Lipid Bilayer

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[1]IBqM-UFRJ; [2]IBCCF-UFRJ

Viral fusion peptides (FPs) play a key role in mediating fusion between two closely apposed membranes. In the nonfusogenic state, the FPs are buried and protected by conformation of the glycoprotein viral. After an external stimulus (e.g., low endosomal pH), the fusion proteins undergo a conformational change, expose the FP and insert it into a target membrane. This insertion of the FP induces deformations in the membrane that favor the fusion. Despite this general principle of membrane fusion and the importance of the FP in this process have been recognized, the mechanism by which FPs of *Flavivirus* execute this role remains elusive. Here, interaction properties of two FPs of *Flavivirus* were studied through biophysical methodologies, as fluorescence spectroscopy, circular dichroism, calorimetry and molecular dynamics. Fluorescence quenching experiments indicate that both peptides were able to interact with micelles of different detergents. Peptide-SDS and peptide-n-octyl-β-D-glucopyranoside micelle interactions were also studied by calorimetry and the results show that the interaction occurs in a pH independent manner, is an exothermic process, indicating that binding is largely enthalpy-driven, with predominance of non-hydrophobic interactions. However, the presence of NaCl promotes loss of enthalpic contribution. In solution, the peptides exhibit essentially random-coil conformation. When associated with micelles or liposomes, the exposure of Trp to solvent was partially reverted and the peptides showed a change, presenting more H-bonds to stabilize the structure. Moreover, the peptides could promote leakage and lipid mixing of liposomes of different compositions. Further characterization of these interactions may help in understanding the molecular processes that bring bilayer destabilizations to the fusion process, and new drugs that inhibit viral fusion could be designed.

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