XVIII Simpósio Brasileiro de Química Teórica – SBQT 2015
Pirenópolis – GO, 22-25 Novembro de 2015

Dengue fusion peptide interacts with model membranes: an experimental and in silico study.

Danilo Olivier[a](PG), Neus Garcia[b](PQ), Ilja Voets[b](PQ), Amando Siuiti Ito[a] (PQ)

[a]*Faculdade de Filosofia Ciências e Letras de Ribeirão Preto, Universidade de São Paulo*
[b]*Department of Chemical Engineering and Chemistry, TU/e – The Netherlands*
doliviercg@gmail.com

Keywords: Dengue Peptide, Molecular Dynamics, Fluorescence, SAXS,

INTRODUCTION

Membrane fusion is one of the most important steps in flavivirus infection. Understanding how the fusion step occurs could help us design strategies to combat viral infection. We studied the interaction of dengue fusion peptide (DEN.II 88-123) with different membrane models. The peptide is located at the tip of the trimer and its sequence: KRFVC.KHSM.VDRGW.GNGCG.LFGKG.G IVTC.AMFTCKK. Our goal in this work is try to understand how the peptide affects the lipid vesicles and lipid membranes. To this end, we conducted a series of experiments (Fluorescence, SAXS, DLS) and molecular dynamics simulations (MDS) with different lipid composition (DMPC, DMPG) in presence and absence of DEN.II 88-123 peptide.

METHODS

All the experiments were measured at 40°C. The pepide-to-lipid ratio was 1%. For fluorescence studies the lipid concentration was 1 mM, while for DLS and SAXS it was 5 mM. For MDS the peptide was placed in water near the lipid bilayer (DMPC, DMPC:DMPG 4:1) and the simulations ran over 500 ns. The NpT ensemble were used with temperature of 313K, and 1 bar of pressure. These simulations were done with NAMD software using CHARMM 36 Force Field.

RESULTS AND DISCUSSION

Both experimental results (DLS and Fluorescence) have shown differences in the size of the vesicles, as well as in the position of the peptide after interaction. For DMPC vesicles, the size changed from 40.3 to 40.8 nm, while for DMPG vesicles it changed from 42.0 to 47.8 nm. Fluorescence of tryptophan residue (W101) had a blue-shift when interacting wing anionic vesicles (349 nm) compared with zwitterionic ones (358 nm). SAXS measurements for pure DMPC vesicles and vesicles in presence of peptides revealed that changes in structure of the bilayer was not affected. The thickness of the membrane was 4.1 nm. The the electronic density profile of MDS has shown that the peptide interacts with the membrane and the W101 residue is buried into the bilayer. It is placed near the polar head. Furthermore, the area per lipid did not change significantly over time, with a average value of 62.2 Å. The acyl chain parameter order was also not affected by the peptide, with a average value of 0.17.

CONCLUSIONS

Combining experimental and computational techniques is a powerful way to study biomolecular systems. DLS data gave information about changes in size of the vesicles, while fluorescence measurements brought some information about position of tryptophan residue. MDS and SAXS revealed that despite the interaction between the peptide and membrane model the changes in structural parameters (area per lipid, thickness) are not significant.

ACKNOWLEDGMENTS

The authors are grateful for the support given from the Capes, CNPq, INCT-Fcx, FAPESP and NAP-Fcx USP.