Membrane insertion of a Dengue virus NS2A segment. A computational study.

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Non-structural NS2A protein of Dengue virus is essential for viral replication but poorly characterized because of its high hydrophobicity. We have previously shown experimentally that NS2A possess a segment, peptide dens25, known to insert into membranes and interact specifically with negatively-charged phospholipids. In order to characterize its membrane interaction we have used two types of molecular dynamics membrane model systems, a highly mobile membrane mimetic and an endoplasmic reticulum membrane-like model. Using the membrane mimetic system, we have been able of demonstrating the spontaneous binding of dens25 to the negatively-charged phospholipid DVPA containing membrane whereas no binding was observed for the membrane containing the zwitterionic phospholipid DVPC. Using the ER-like membrane model system, we demonstrate the spontaneous insertion of dens25 into the middle of the membrane; it maintaining its three-dimensional structure and presenting a nearly parallel orientation with respect to the membrane surface. Both charged and hydrophobic amino acids, presenting an interfacial/hydrophobic pattern characteristic of a membrane-proximal segment, are responsible for membrane binding and insertion. Dens25 might control protein/membrane interaction and be involved in membrane rearrangements critical for the viral cycle. These data should help us in the development of inhibitor molecules that target NS2A segments involved in membrane reorganization.