Structural Characterization of a Membrane-Active Region of the Hepatitis C Virus E2 Envelope Glycoprotein

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Hepatitis C (HCV) is the leading cause of liver disease, and, approximately 3% of the world's population is chronically infected. HCV entry is a slow and complex multistep process, with scarce available data. Two HCV envelope glycoproteins, E1 and E2, are supposed to play a crucial role in viral binding and fusion. Recent evidence indicates that the simple picture of a virus fusion protein interacting with cell and viral membranes by means of only the fusion peptide is oversimplified. Instead, different membranotropic segments of the fusion proteins seems to be required. In this study, the peptide corresponding to the residues 421-445 of E2 was synthesized and its interaction with lipid vesicles and different detergent micelles was characterized by biophysical methodologies. Fluorescence spectra analyses showed that Trp residues were exposed to the polar aqueous environment which was partially reverted in the presence of vesicles and micelles. The increase of spectral center of mass of Trp suggests that this peptide can interact with detergent micelles. Acrylamide quenching experiments revealed that Trp residues are more protected from the quencher when micelles were present. The peptide was also able to induce aggregation of phosphatidylglycerol vesicles in a concentration and pH dependent manner. Calorimetric analysis shows that peptide-n-octyl-ß-D-glucopyranoside micelle interaction is enthalpically driven. Circular dicroism data indicate that the peptide gain structure in the presence of TFE and SDS. Our results show that this peptide can interact with liposomes and micelles and became structured, suggesting that it may participate in the fusion process of the HCV. Further characterizations of these artificial systems may help in understanding the molecular processes that trigger the fusion process.

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