

## Structural Requirements for Sindbis virus (SINV) and SinV Fusion Peptide Fusion with Different Lipids Bilayers

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Sindbis virus (SV) is a positive-sense, single-stranded RNA virus of the *Alphavirus* genus in the *Togaviridae* family. The mature SV particle contains an inner shell composed entirely of the capsid protein (C) associated with viral genome surrounded by a membrane bilayer that anchors other two structural proteins, the glycoproteins E1 and E2. The glycoprotein E1 is a class II fusion protein that exposes, at the acidic environment of the endosome, a hydrophobic domain directly involved on membrane fusion process, the fusion peptide. In order to better understand the mechanisms involved in SV membrane fusion process, we investigated the kinetics of the hydrophobic domain exposure by fluorescence spectroscopy techniques applied both to the whole viral particle and to synthetic E1 fusion peptides. We also evaluated the interactions of the fusion peptides with large unilamellar vesicles with different lipids compositions. Our results suggest that the hydrophobic-domain exposure is irreversible and pH dependent. In addition, our data show an essential role of W89 for membrane fusion as well as an evident requirement of sphingomyelin and cholesterol in the membranes. Taken together, these results shed light on the minimal requirements for the viral infection, allowing further understanding of this process and eventually the development of strategies for its inhibition.

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