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Sars-cov-2 Fp1 Destabilizes Lipid Membranes and Facilitates Pore Formation

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SARS-CoV-2 viral entry requires membrane fusion, which is facilitated by the fusion peptides within its spike protein. These predominantly hydrophobic peptides insert into target membranes; however, their precise mechanistic role in membrane fusion remains incompletely understood. Here, we investigate how FP1 (SFIEDLLFNKVTLADAGFIK), the N-terminal fusion peptide, modulates membrane stability and barrier function across various model membrane systems. Through a complementary suite of biophysical techniques—including electrophysiology, fluorescence spectroscopy, and atomic force microscopy—we demonstrate that FP1 significantly promotes pore formation and alters the membrane's mechanical properties. Our findings reveal that FP1 reduces the energy barrier for membrane defect formation and stimulates the appearance of stable conducting pores, with effects modulated by membrane composition and mechanical stress. The observed membrane-destabilizing activity suggests that, beyond its anchoring function, FP1 may facilitate viral fusion by locally disrupting membrane integrity. These results provide mechanistic insights into SARS-CoV-2 membrane fusion mechanisms and highlight the complex interplay between fusion peptides and target membranes during viral entry.

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