VIRAL INACTIVATION BASED ON INHIBITION OF MEMBRANE FUSION: UNDERSTANDING THE ROLE OF HISTIDINE PROTONATION TO DEVELOP NEW VIRAL VACCINES

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Membrane fusion is an essential step in the entry of enveloped viruses into their host cells, what makes it a potentially attractive target for viral inactivation approaches. Fusion is mediated by viral surface glycoproteins that undergo conformational changes triggered by interaction with specific cellular receptors or by the exposition to low pH of endossomal medium. In the last years, we developed several studies on the structural rearrangements of vesicular stomatitis virus (VSV) glycoprotein G during cellular recognition and fusion, what led us to propose a crucial role of the protonation of histidine residues for G protein activity. Moreover, we demonstrated that using diethylpyrocarbonate (DEPC), a histidine-modifying compound, it was possible to abolish viral infectivity and pathogenicity in mice, and to elicit neutralizing antibodies that confer protection in these animals against challenge using lethal doses of the virus. The presence of conserved histidine residues in a wide range of viral fusion proteins suggests that the use of DEPC might be a more general means for vaccine development.