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Topic of Research: Expression, Purification and Characterization of Mutant G Proteins of Respiratory Syncytial Virus

PhD Findings

Respiratory syncytial virus (RSV) is the most frequent cause of bronchiolitis and pneumonia in children and elderly people. Currently, no approved vaccines or therapeutics are available against RSV infection. The heparan sulfate molecule, which is located on the surface of the host cell, helps the attachment of RSV through G protein. Previously, it was reported that the positively charged amino acid residues of the CX3C motif and heparin-binding domain (HBD) of the G protein are mainly involved in host-pathogen interactions. In this study, we determine the structure, stability, and binding interaction studies of wild-type G protein and its variants (K117A, K121A, K27A, and K130A). In this direction, we investigated the effect of amino acid substitution on the tertiary structure of the protein in a wide range of pH and also determined the stability of the protein in the presence of urea and GdmCl. Further, ITC, fluorescence quenching, absorbance spectroscopy, and molecular docking were exploited to investigate whether a mutation in the CX3C motif and HBD of G protein alters the binding with heparan sulfate. Fluorescence spectroscopy results showed no significant changes in the tertiary structure of wild-type and mutant proteins. The data of ANS fluorescence suggested that the non-native state of wild-type and all mutant proteins form a molten globule-like structure at acidic pH conditions. The chemical-induced denaturation studies showed no significant difference in the stability of wild-type and mutant proteins. Isothermal titration calorimetry, fluorescence quenching, and docking results suggested that mutant proteins showed less binding with the heparan sulfate molecule in comparison to the wild-type G protein. The obtained results suggested that positively charged amino acids in the CX3C motif and HBD of the G protein play a critical role in the binding of RSV with the host cell receptor. Hence, the mutation in the CX3C motif and HBD of the G protein might be an effective strategy to inhibit host-pathogen interaction. Taken together, the finding from this study will assist in the process of drug designing and vaccine development and thus prevention of RSV infection.