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***In silico* immunoinformatics based prediction and designing of multi-epitope construct against human rhinovirus C**

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ABSTRACT Human rhinovirus C (HRV-C) is an RNA virus infecting human respiratory tract. It is associated with complexities like asthma, chronic obstructive pulmonary disease, and respiratory damage. HRV-C has many serotypes. Till date there is no vaccine. Despite some limitations, corticosteroids, bronchodilators, and common cold medicines are used to treat HRV-C infections. Here, we have used immunoinformatics approach to predict suitable cytotoxic T-cell, helper T-cell and linear B-cell epitopes from the most antigenic protein. VP2 protein of Rhinovirus C53 strain USA/CO/2014-20993 was found to be most antigenic. The multi-epitope construct was designed using the best CTL, HTL and linear B-cell epitopes and attaching them with adjuvant and linkers. Interferon-gamma inducing epitopes and conformational B-cell epitopes were also predicted from the construct. Physicochemical and structural properties of the construct were satisfactory. Binding pockets were identified that could be the targets for designing effective inhibitors. Molecular docking revealed strong binding affinity of the construct with human Toll-like receptors 2 and 4. Normal mode analysis divulged stability of the docked complex. Codon optimization, *in silico* cloning and immune simulation analysis demonstrated suitability of the construct. These findings are likely to aid *in vitro* studies for developing vaccine against HRV-C.

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Introduction

Human rhinoviruses (HRVs), first discovered in 1950's, are non-enveloped RNA viruses belonging to the Picornaviridae family (Glanville and Johnston 2015). It infects the upper and lower respiratory tracts in humans (Arruda et al. 1995; Jakiela et al. 2008) and is accountable for acute respiratory complexities in various ethnicities worldwide (Rotbart and Hayden 2000). HRVs are associated with common cold, wheezing, asthma, pneumonia, chronic obstructive pulmonary disease, and flu-like symptoms (Arden and Mackay 2009; Cordey et al. 2010). They have a high rate of mutation assisting adaptability and transmissibility (Cordey et al. 2010). HRVs are categorized into HRV-A, HRV-B, and HRV-C respectively (Hao et al. 2012). Multiple lines of evidence have revealed that HRV-C is more predominant and virulent compared to HRV-A and HRV-B (Hao et al. 2012). The high virulence of rhinovirus C stems from its ability to bind to host cells using cadherin-related family member 3 receptor (Scully et al. 2018). HRV-C is linked to severe symptoms. It is responsible for greater respiratory damage (Palmenberg et al. 2010). HRV-C has been linked to asthma exacerbations

worldwide in children (Bizzintino et al. 2011; Mak et al. 2011). Some workers have found a distinct correlation between maternal atopy and asthma in offspring (Miller et al. 2011). HRVs comprise many serotypes whose categorization is based on factors like receptor specificity, predisposition to antiviral responses, similarity in nucleotide sequences, etc. (Lau et al. 2010). The genome of HRVs is made up of a single gene. Nevertheless, its translated product yields structural and non-structural proteins (Jacobs et al. 2013). The capsid contains structural proteins viz. VP1, VP2, VP3, VP4, and VPg whereas non-structural proteins function in replication and assembly (Palmenberg et al. 2010).

Acute airway infections are the major cause of morbidity and mortality worldwide. Although HRV-C is more virulent and linked to the high incidence of asthma, chronic obstructive pulmonary disease in adults, and severe respiratory complexities in children (Bochkov and Gern 2012), little has been achieved in developing a vaccine in the last 70 years. However, the development of effective vaccines is time-consuming and costly. For clinicians, the antigenic diversity of HRVs, the number of serotypes along with lack of good animal models became stumbling blocks for developing vaccines (Papi and Con-