Immunoinformatics Mediated Screening of Rotavirus A epitopes for Potential Peptide Vaccine Development

Pooja Rani Kuri[1] and Pranab Goswami[1*]
[1]Department of Biosciences and Bioengineering, Indian Institute of Technology Guwahati, Assam, India.
pooja176106028@iitg.ac.in
*Corresponding author, Email: pgoswami@iitg.ac.in

Rotavirus is a leading cause of severe infantile gastroenteritis worldwide, with about 199,000 childhood deaths in 2015, of which 90% cases occurred in low-income countries. India alone accounts for 22% of the global rotavirus gastroenteritis related deaths among children below 5 years of age. The World Health Organization recommends introduction of rotavirus vaccines as a priority in developing countries where high rates of rotavirus gastroenteritis are observed. There are however gaps in molecular data on rotavirus epidemiology in India. We therefore reviewed molecular data on rotavirus A (most common etiological agent of infantile gastroenteritis) isolated from India and also analyzed viral capsid protein genes (vp7, vp4 and vp6) to assess any particular trend with reference to different genotypes by phylogenetic analysis. Phylogenetic analysis revealed G1P[8] to be the most prevalently circulating strain of RVA in India. Therefore, capsid proteins VP4 P[8] and VP7 G[1] were subjected to antigenic analysis to determine epitopes for potential development of peptide vaccines. In this work, we identified highly antigenic, immunogenic, non-toxic and non-allergenic CTL and HTL epitopes of RVA G1P[8] capsid proteins VP4 and VP7. A total of 8 and 7 CTL epitopes were selected for RVA VP4 and VP7 respectively, while a total of 2 and 3 HTL epitopes were selected for RVA VP4 and VP7 respectively. The obtained epitopes were linked using suitable linkers followed by addition of a suitable adjuvant. The designed vaccine candidate was characterized using bioinformatics tools.

Results of the present work:

1. Molecular diversity of Indian Rotavirus A strains was determined by phylogenetic analysis and RVA G1P8 was found to be the most prevalently circulating strain.
2. Immunoinformatics approach was used to identify potential B and T cell epitopes using VP4 and VP7.
3. Selected epitopes were used to design a vaccine Sequence, followed by its computational physiochemical characterization.

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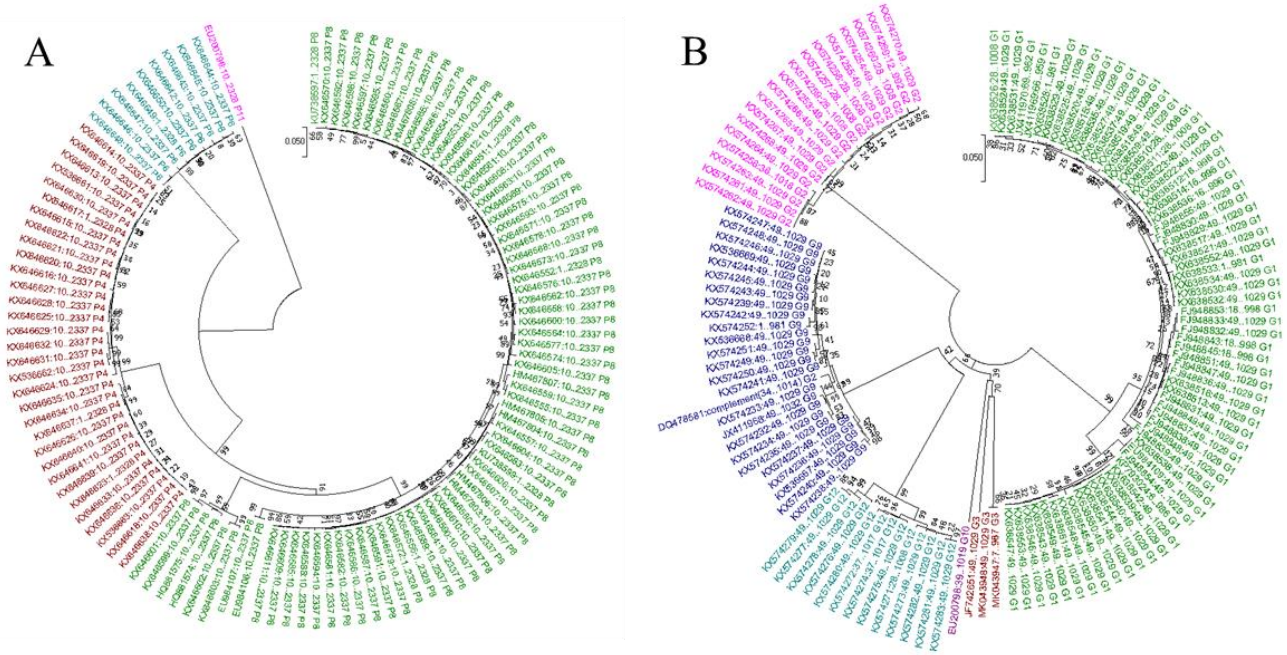

Figure 1 Molecular Diversity of Indian RVA strains. Genotypes Distribution of RVA VP4 (A) and RVA VP7 (B) determined by Phylogenetic Analysis.

A Physiochemical properties of the designed vaccine sequence (Protparam)

Number of aa	326
Molecular weight	36233.31
Theoretical pI	9.6
Estimated half-life	30 hours (mammalian reticulocytes, in vitro) >20 hours (yeast, in vivo) >10 hours (Escherichia coli, in vivo)
Instability index	36.26
Grand average of hydropathicity (GRAVY)	0.307

B

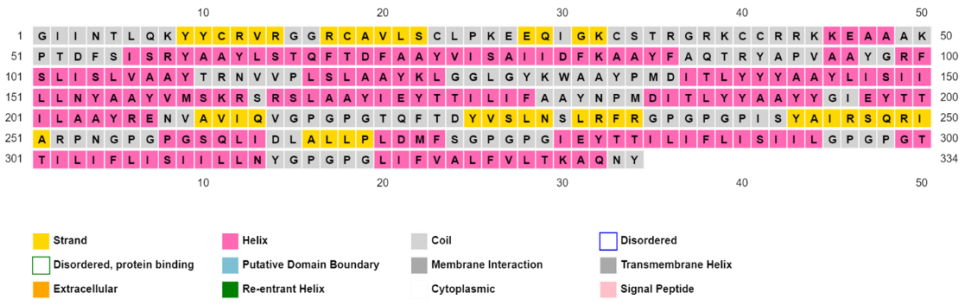

Figure 2 A. Physiochemical characterization of the designed vaccine. B.Vaccine Secondary Structure Prediction by Phyre2.