

In-silico identification of conserved B-cell epitopes on norovirus VP1 as potential diagnostic targets

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Background and Objectives: Norovirus is a leading cause of acute gastroenteritis worldwide, and the development of broadly-reactive immunodiagnostic assays is challenged by the extensive genetic variability in the VP1 capsid protein, particularly within the P2 domain. This variability reduces the sensitivity of current diagnostic assays. This study aimed to identify conserved B-cell epitopes within the 3-D structures of norovirus VP1 across GI and GII genogroups to inform improved immunodiagnostic design.

Methods: A total of 675 VP1 full-length nucleotide sequences were retrieved from NCBI GenBank to generate genogroup-specific consensus sequences. Linear B-cell epitopes were predicted using BepiPred 2.0, followed by sequence-based filtering. Homology models were generated using SWISS-MODEL and visualised in PyMOL. Structure-based linear and conformational epitope prediction was conducted using ElliPro, prioritising solvent accessibility and structural protrusion.

Results: The VP1 S domain was highly conserved in both genogroups, whereas the P2 domain displayed substantial variability, and was excluded from further analysis. Several surface-accessible linear and conformational epitopes were identified within the S and P1 domains. In GI, four high-confidence linear epitopes were identified, including two partially cross-genotype conserved epitopes (*SQNLSI* and *TLSNRVPS*) located on exposed VP1 surfaces. In GII, three linear epitopes were identified, including one fully conserved S-domain epitope (*SPNENIVVQPQNGRC*). Conformational epitopes formed discrete surface clusters overlapping regions containing with domains containing high-confidence linear epitopes.

Conclusion: Conserved B-cell VP1 epitopes with potential to improve norovirus diagnostic assay sensitivity were identified. Integration of sequence conservation analysis with 3D structural modelling supports bioinformatics-driven target innovation. Experimental validation is recommended to confirm immunoreactivity.

