A systematic analysis of a broadly neutralizing antibody AR3C epitopes on Hepatitis C virus E2 envelope glycoprotein and their cross-reactivity

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Abstract

Background: Hepatitis C virus (HCV) belongs to Flaviviridae family of viruses. HCV represents a major challenge to public health since its estimated global prevalence is 2.8% of the world's human population. The design and development of HCV vaccine has been hampered by rapid evolution of viral quasispecies resulting in antibody escape variants. HCV envelope glycoprotein E1 and E2 that mediate fusion and entry of the virus into host cells are primary targets of the host immune responses. Results: Structural characterization of E2 core protein and a broadly neutralizing antibody AR3C together with E1E2 sequence information enabled the analysis of B-cell epitope variability. The E2 binding site by AR3C and its surrounding area were identified from the crystal structure of E2c-AR3C complex. We clustered HCV strains using the concept of 'discontinuous motif/peptide' and classified B-cell epitopes based on their similarity. Conclusions: The assessment of antibody neutralizing coverage provides insights into potential cross-reactivity of the AR3C neutralizing antibody across a large number of HCV variants.

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