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Epitope Specificity of Antibodies from Chronic Patients and Self Resolvers of HCV Infection

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Hepatitis C virus (HCV) infections occur in approximately 170 million people, respectively in the world accounting for an immense economic burden. An effective vaccine against HCV remains to be developed. In recent years, several direct acting antiviral drugs have been approved to treat HCV infections, which can clear the virus. However, their effectiveness to lower the global disease burden is limited by their cost ineffectiveness, unavailability to low-income populations, associated side effects and emergence of drug resistant viral variants.

HCV envelope glycoprotein, E2 is the primary target for immune recognition. The recombinant E2 protein-based vaccines have not been successful possibly due to a highly glycosylated nature of E2 and the presence of highly variable regions that cover the more conserved parts of the protein. The E2 protein also incorporates few highly sequentially conserved regions that constitute receptor-binding site of the virus as this protein mediates binding of the virus to its receptors. In chronically infected patients, antibodies targeting some of these conserved epitopes are produced that can neutralize a broad range of viral variants. Some of these antibodies recognize linear amino acid sequences, called linear epitopes despite they adopt specific structural and conformational features when recognized by the antibody.

Around 25% of the HCV infected patients can clear the virus without any treatment. Chronic patients (CP) trigger a robust humoral immune response against multiple epitopes. In self-resolved (SR) individuals the immune response is mounted in a directed manner. Specific epitopes are targeted to trigger immune response. In most of the cases, this reactivity is primarily for the epitope corresponding to the E2 region spanning amino acid 434-446 (the 434 epitope). The overall ED₅₀ (effective dilution with 50% neutralization) values of the CP sera is much higher as compared to the SR sera suggesting much higher titer of total neutralizing antibodies in the CP sera. The neutralizing activity of many of the SR sera was primarily due to the presence of 434 epitope specific antibodies. Antibodies specific for the 434 epitope play a role in spontaneous viral clearance.

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