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## **ANTIGENIC VARIABILITY OF THE CORE PROTEIN OF THE HEPATITIS C VIRUS**

The primary structure of the Hepatitis C virus (HCV) core protein is very conserved. However, despite this conservation, there is considerable variation in the antigenic properties of this protein derived from different HCV isolates. It is known that genetic heterogeneity of the core protein affects the efficiency of antibody detection in serum from different HCV genotypes. To study how the sequence heterogeneity affects the antigenic properties of the core protein, 13 different sequences spanning the major core antigenic epitopes (2-120 aa) were selected from 266 sequences retrieved from GenBank. These sequences were selected based on (1) significant evolutionary distances between sequences and (2) representation by all 6 HCV genotypes. The amino acid sequences were converted into nucleotide sequences and the corresponding genes were assembled from synthetic oligonucleotides to synthetic genes which were cloned and expressed in *E.coli* as hybrid proteins with Glutathione S-transferase. All 13 purified HCV fusion proteins were tested against a panel of anti-HCV positive sera (n=98) obtained from patients infected with HCV genotypes 1 through 6. Each purified protein demonstrated strong immunoreactivity. Although a variable degree of genotype-specific antigenic reactivity was observed for all proteins, only two in proteins demonstrated a significant preference for immunoreacting with the homologous HCV genotype; whereas, some closely related proteins derived from the same subtype or genotype immunoreacted with variable efficiencies when tested using sera from patients infected with different HCV genotypes. These findings demonstrate that variation in the primary structure has a significant effect on the antigenic properties of the HCV core protein. This observation should be taken into a consideration when selecting diagnostic targets for the development of highly specific and sensitive diagnostic assays for the detection of anti-HCV activity in serum specimens.

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