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ANTIGENIC PROPERTY OF DIFFERENT SEQUENCE VARIANTS OF THE HEPATITIS C VIRUS NS3 PROTEINS

The effect of sequence variation on the antigenic properties of the c33 antigen derived from the Hepatitis C virus (HCV) NS3 protein was studied by using recombinant proteins derived from different HCV genotypes. Six c33 protein sequence (1192-1457 aa) were selected by first testing 12 recombinant proteins containing the c33 immunodominant region derived from all 6 HCV genotypes against a panel of serum specimens obtained from patients infected with different HCV genotypes. The corresponding genes were assembled by PCR from synthetic oligonucleotides and expressed in *E.coli*. Each recombinant protein was purified and tested against a panel of 158 serum samples obtained from patients infected with different HCV genotypes. The most immunoreactive protein detecting 91.1% of anti-HCV positive sera was derived from HCV subtype 6a. This protein was 88.1% homologous to another subtype 6a protein, which interestingly only immunoreacted with 50% of the anti-HCV positive sera. The other highly immunoreactive c33 antigen variant, which detected 85% of the anti-HCV positive sera, was protein derived from HCV subtype 2c. These 2 most immunoreactive c33 variants share only 84% similarity. This variation, however, appears not to impose any strong genotype-specific immunoreactivity since none of the c33 recombinant proteins in this study demonstrated immunoreactivity solely with serum specimens obtained from infected with the homologous HCV genotype. In conclusion, these data suggest that diagnostic test development requires careful selection of sequence variants of antigens as diagnostic targets.

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