

## **DIAGNOSTIC RELEVANCE OF THE HEPATITIS C VIRUS CORE AND NS3 PROTEINS**

The primary structure of the hepatitis C virus (HCV) core and NS3 proteins is relatively conserved. However, antigenic properties of these proteins derived from different HCV isolates vary considerably. To study the degree to which sequence heterogeneity affects the antigenic properties of the HCV core and NS3 proteins, 13 different synthetic genes encoding for core protein (2-120 aa) of genotypes 1 -6 and 6 different synthetic genes encoding for NS3 protein (1192 - 1457 aa) of genotypes 1, 2, 5 and 6 were assembled and expressed in *E. coli*. The core sequences were selected based on 2 criteria: significant evolutionary distances between each other, and representation by all 6 HCV genotypes. Six NS3 protein sequences were selected by first testing 12 recombinant proteins containing the NS3 immunodominant region derived from all 6 HCV genotypes against a panel of serum specimens obtained from patients infected with different HCV genotypes. Each recombinant protein was purified and tested against a panel of serum samples obtained from patients infected with different HCV genotypes, a panel of anti-HCV positive sera obtained from blood donors from Russia and Indonesia, and a panel of anti-HCV negative serum samples. The most immunoreactive NS3 protein detecting more than 90% of anti-HCV positive sera was derived from HCV subtype 6a. This protein was 88.1% homologous to a subtype 6a protein, which immunoreacted with only -50% of the anti-HCV positive sera. Ten out of 13 purified core proteins demonstrated strong immunoreactivity with up to 100% of anti-HCV positive sera of different genotypes. Several core and NS3 proteins were found strongly immunoreactive with some of anti-HCV negative by commercial assays but PCR positive serum specimens. Although a variable degree of genotype-specific antigenic reactivity was observed for all core and NS3 proteins, none of these proteins demonstrated strict immunoreactivity with the homologous HCV genotype; whereas, some closely related proteins derived from the same subtype or genotype immunoreacted with variable efficiencies with anti-HCV positive sera. In conclusion, these data suggest that diagnostic test development requires careful selection of sequence variants of antigens as diagnostic targets.

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