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DIAGNOSTIC RELEVANCE OF SEGUENCE OF HETEROGENEITY OF THE HCV NS4 MOSAIC PROTEINS

The NS4 protein is one of the most variable HCV proteins. At the same time information regarding the influence of genetic heterogeneity of NS4 protein on the efficiency of antibody detection is insufficient.

AIM: To study how the sequence heterogeneity affects on the immunoreactivity of HCV NS4 proteins.

OBJECTIVES AND METHODS: 4 different synthetic genes encoding epitopes of NS4 protein were assembled by PCR from synthetic oligonucleotides and expressed in E. coli as mosaic proteins. All proteins comprise two epitopes from 1712-1733 (genotype 1a, 3a, 5a) aa and 1921-1940 aa (genotype 1a, 1b, 2b, 3b) in different combinations. Heterogeneity of amino acid sequences of NS4 artificial mosaic proteins was 32-70 %. Immunoreactivity of these artificial proteins was evaluated by testing well defined anti-HCV positive (n=72) and anti-HCV negative (n=82) samples in ELISA.

RESULTS: All proteins were strong immunoreactive. NS4-1 (2b, 5a) had the most level of immunoreactivity and detected anti-HCV in 65.3 % of positive samples. NS4-2 (1a) had the lowest immunoreactivity and detected anti-HCV in 58.3 % of samples. NS4-3 (3a, 1b) determined anti-HCV in 62.5 % of samples, NS4-4 (1b, 3b) – in 63.9 % of samples. Complex of four proteins NS4-1, NS4-2, NS4-3, NS4-4 made possible to detect anti-HCV in 84.7 % of positive samples.

CONCLUSION: These results show that heterogeneity of primary structure as a effect on the antigenic properties of the HCV NS4 protein and suggest that diagnostic test development requires careful selection of sequence variants of antigens as diagnostic targets.