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DETECTION OF NS3 AND NS4 PROTEINS IN HEPATOCYTES OF PATIENTS WITH CHRONIC HEPATITIS C

Objectives. To detect the antigenic determinants of native HCV proteins using monoclonal antibodies (Mabs) to recombinant NS3 and NS4 proteins (rps).
Methods. Interaction of Mabs with HCV proteins was estimated by immunohistochemical staining of cryostat liver sections obtained by needle biopsy from 14 patients with chronic hepatitis C (CHC). HCV RNA was detected by nested RT-PCR.
Results. Seven Mabs to NS3 helicase domain recognized at least four individual epitopes, three of which were conformational (CE) and one was linear (LE). Six anti-NS4 antibodies recognized five epitopes, two of which were specific to CE of 5-1-1 immunodominant region and three - to NS4A and NS4B LE. The Mabs revealed five previously unidentified epitopes of NS3 and NS4. HCV proteins were detected only in the hepatocyte cytoplasm. The number of hepatocytes stained by Mabs of different specificity varied considerably. Mab 6B11 to NS4 CE revealed HCV in all patients with detectable HCV RNA in the liver. There was no relationship between the ability of Mabs to recognize proteins in infected hepatocytes and their affinity for rps. Mabs to NS3 LE did not recognize this protein in the liver, while Mabs to 2 NS3 CE stained infected hepatocytes intensely. The expression of NS4A and NS4B varied in hepatocytes of patients with CHC of various severity.
Conclusion. The interaction of Mabs with proteins in HCV-infected cells is determined to a greater extent by epitope specificity and exposition of the corresponding B-cell epitope than by affinity for rps. The panel of Mabs obtained can serve as an effective tool for diagnostic purposes and for investigation of host-viral interactions at the cellular level in patients with CHC of various severity.

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