Immunodominant CD4+ T-cell epitope within nonstructural protein 3 in acute hepatitis C virus infection

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In acute hepatitis C virus infection, 50 to 70% of patients develop chronic disease. Considering the low rate of spontaneous viral clearance during chronic hepatitis C infection, the first few months of interaction between the patient's immune system and the viral population seem to be crucial in determining the outcome of infection. We previously reported the association between a strong and sustained CD4+ T-cell response to nonstructural protein 3 (NS3) of the hepatitis C virus and a self-limited course of acute hepatitis C infection. In this study, we identify an immunodominant CD4+ T-cell epitope (amino acids 1248 to 1261) that was recognized by the majority (14 of 23) of NS3-specific CD4+ T-cell clones from four of five patients with acute hepatitis C infection. This epitope can be presented to CD4+ T cells by HLA-DR4, -DR11, -DR12, -DR13, and -DR16. HLA-binding studies revealed a high binding affinity for 10 of 13 common HLA-DR alleles. Two additional CD4+ T-cell epitopes, amino acids 1388 to 1407 and amino acids 1450 to 1469, showed a very narrow pattern of binding to individual HLA-DR alleles. Our data suggest that the NS3-specific CD4+ T-cell response in acute hepatitis C infection is dominated by a single, promiscuous peptide epitope which could become a promising candidate for the development of a CD4+ T-cell vaccine.

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