FOXP3 expression in hepatitis C virus-specific CD4+ T cells during acute hepatitis C

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BACKGROUND & AIMS: Down-regulation of hepatitis C virus (HCV)-specific CD4 (+) T-cell responses is a hallmark of chronic viral persistence in acute hepatitis C. FOXP3(+)CD25(+)CD4(+) regulatory T cells can modulate HCV-specific immune responses in vitro, but the role of virus-specific regulatory T cells in the pathogenesis of chronic viral persistence is unknown. METHODS: Two novel HLA-DR15 tetramers were synthesized to study the kinetics and phenotype of FOXP3(+) expressing HCV-specific CD4(+) T cells from 10 patients with acute hepatitis C and 15 patients with chronic hepatitis C. RESULTS: In acute hepatitis C, generally only a low percentage of HCV-specific CD4(+) T cells expressed FOXP3(+) (mean of 2.5% in patients with self-limited acute hepatitis C vs 2.4% in patients with evolving chronic hepatitis C). Although distinct but short-lived increases in virus-specific FOXP3(+)CD4(+) T cells occurred in 3 patients (30%, 26%, and 7% of tet(+) CD4(+) T cells, respectively), these did not correlate with the evolution of chronic hepatitis C. HCV-specific FOXP3(+) CD4(+) T cells displayed a distinct phenotype, with only 10% expressing CD25 and 40% being CD127low. Interestingly, this phenotype of FOXP3(+)CD4(+) T cells was already expanded in bulk CD4(+) T cells in patients with chronic hepatitis C. CONCLUSIONS: Although short-lived increases in HCV-specific FOXP3(+)CD4(+) T cells occur during the course of acute hepatitis C, we could not demonstrate an association of HCV-specific regulatory T cells and persistent viremia.