Immunomodulatory effects of pegylated interferon-α and Ribavirin on Th1 and Th2 cytokine responses to chronically infected hepatitis C patients

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Introduction: Hepatitis C virus (HCV) is a life threatening human pathogen. Chronicity of the disease leads to cirrhosis, hepatocellular carcinoma and end-stage liver disease. Clearance of the virus is characterized by a vigorous, persistent T-cell response. Standard treatment involves a combination of pegylated interferon-α (PEG-IFN) and ribavirin, Mechanisms for the observed synergistic effects of the two drugs are still not well understood, but in addition to direct antiviral mechanisms, immunomodulatory effects of both drugs seem to be important with a possible shift from Th2 to Th1 cytokine profiles in successfully treated patients.

Aim & Method: This study will determine Th1 and Th2 cytokine responses to infection with the major HCV genotypes, before, during and after treatment with PEG-IFN and ribavirin. The proliferative response of peripheral blood mononuclear cells to mitogen will be assessed by measuring uptake of radioactive thymidine and the production of Th1 type and Th2 type cytokines by ELISA.

Results: We have inducted a total of 36 patients (27 responders and 9 non-responders). There were a significant increase in the levels of Th1 type cytokines IFNγ, IL-17A and IL-17F between responders and non-responders. IL-4 and IL-6 anti-inflammatory Th2 cytokines is produced at significantly higher levels in non-responders. The ratios involving IFNγ and IL-4 showed interesting differences. At baseline measurement, IFN/IL-4 and IFN/IL-10 ratios were 18 and 10 fold higher in responders. Likewise, at the end of the treatment, IFN/IL-4, IFN/IL-6 and IFN/IL-10 ratios were 90, 80 and 50 fold respectively higher in responders as compared to non-responders.

Conclusion: Our data suggests that, Th1 biased reactivity and poor Th2 response state appears to be associated with drug effectiveness. In other words, we suggest that the host cytokine profile can either dampen or aid the immune viral response to recent and future drug therapy

Biography
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