by quantitative rt-PCR. Different signalling pathways were analysed by westernblot and electromobility shift assay (EMSA). Furthermore, supernatants from KC and LSEC cultures stimulated with IFNs in the presence or absence of IL-10 and TGF-β were analyzed in antiviral assays (LCMV). IFN-α induces a number of ISGs (e.g. IFT1; IFI47, Igtp) in murine LSEC but not KC. Furthermore the expression of Cxcl10 is highly induced by IFN-γ both in murine KC and LSEC but not in hepatocytes or spleen cells. Similarly several other ISGs were activated differentially in parenchymal and non-parenchymal liver cells, like Nos2 which seems to be stimulated only in KC. Regarding the kinetic of activation of Stat1 by IFN-α we show the maximum of phosphorylation in KC occurs after 5 minutes and in LSEC after 60 minutes. Pretreatment of KC and LSEC with IL-10 or TGF-β strongly suppressed ISG induction by IFN-α and led to a marked suppression of the antiviral function of IFNs.

In conclusion, our data show for the first time that the interferon response of liver cells is cell-type dependent and can be suppressed by anti-inflammatory cytokines. These data deepen our understanding about the local regulation of the innate immune response in the liver which is of particular interest for the pathogenesis of acute and chronic viral hepatitis.

**ANALYSIS OF THE EX VIVO INTERFERON-α RESPONSE IN PATIENTS WITH CHRONIC HEPATITIS B AFTER INITIATION OF ANTIVIRAL THERAPY WITH ADEFOVIR**

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**Background and Aims:** The currently approved therapeutic regimen for treatment of chronic hepatitis B include interferon-alpha, lamivudine and adefovir. However, only a minority of patients treated with these agents has a long-term sustained response with 'cure' or eradication of the virus. Patients with a high viral load in particular only very rarely respond to IFN therapy. We therefore aimed to determine whether PBMC from HBV patients with a high viral load have a suppressed IFN response and if the response to IFN is modulated by treatment with the nucleotide analogue adefovir.

**Methods:** PBMC were isolated from 30 patients with chronic hepatitis B that received de novo therapy with adefovir before and at week 4, 8, 12 and 24 of therapy. The cells were stimulated for 12h with 10, 100 and 1000 U/ml IFN-α2. Total RNA was isolated and analyzed by customized cDNA arrays that cover a large proportion of known interferon-inducible genes. Significant results were checked by quantitative rT-PCR where appropriate. Viral load and clinical parameters were assessed in parallel correlated with expression data.

**Results:** When baseline responses to IFN were compared no significant differences were detectable between patients with high and low viral loads (cut-off: 1 x 10^7 copies/ml). There was no difference when patients with good and weak antiviral responses were compared (cut-off: 2 log drop in viral load at week 8). Overall the IFN response of the majority of ISGs remained stable over the period of the study.

**Conclusions:** The ex vivo IFN response in PBMC of patients with chronic hepatitis B is not influenced by high viral load or antiviral treatment. This may indicate that the reduced clinical response to IFN that is observed in patients with high viral load is specific for target cells (i.e. hepatocytes) of this treatment rather than the effector arm (immune system). Alternatively, it is possible that exogenous HBsAg and/or HBeAg is responsible for the reduced IFN response in patients with a high viral load. This hypothesis is currently being tested.