An intrahepatic transcriptional signature of enhanced immune activity predicts response to peginterferon in chronic hepatitis B

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Differences in intrahepatic gene expression patterns may be associated with therapy response in peginterferon-treated chronic hepatitis B (CHB) patients.; We employed gene expression profiling in baseline liver biopsies of 40 CHB patients (19 HBeAg-positive; 21 HBeAg-negative) treated with peginterferon and adefovir for 48 weeks, and compared expression patterns of combined responders (HBeAg loss, HBV-DNA <2000 IU/ml, alanine aminotransferase normalization after 1 year of treatment-free follow-up) with non-responders. Genes identified by transcriptome analysis in 15 biopsies were confirmed in 25 additional biopsies by RT-qPCR.; Transcriptome analysis demonstrated significant differences in expression of 41 genes between responders and non-responders. In responders, pathway analysis showed specific upregulation of genes related to the immune response, including chemotaxis and antigen processing and presentation. Genes upregulated in responders exhibited strongest similarity with a set of genes induced in livers of chimpanzees with acute Hepatitis B infection. Differential expression was confirmed for eight selected genes. A 2-gene subset (HLA-DPB1, SERPIN-E1) was found to predict response most accurately. Incorporation of these genes in a multivariable model with HBeAg status, HBV genotype and baseline HBsAg level correctly classified 90% of all patients, in which HLA-DPB1 and SERPIN-E1 were independent predictors of response.; We identified an intrahepatic transcriptional signature associated with enhanced immune activation which predicts therapy response. These novel associations could lead to better understanding of responsiveness to peginterferon in CHB patients, and may assist in selecting possible responders to interferon-based treatment.
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