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Poster Session VI
Viral hepatitis and HIV/HCV co-infection

IFN-ALPHA RECEPTOR-1 UPREGULATION IN PBMC FROM HCV NAÏVE PATIENTS CARRYING CC GENOTYPE. POSSIBLE ROLE OF IFN-LAMBDA

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Objectives: IL-28B gene polymorphisms predict better therapeutic response and spontaneous clearance of HCV. Moreover, higher expression of IFN-lambda has been reported in patients with the rs12979860 CC favourable genotype. The study aim was to establish possible relationships between IL-28B rs12979860 genotypes and expression of IFN-alpha receptor-1 (IFNAR-1) in naive HCV patients, and to explore the possible role of IFN-lambda.
Methods: IFNAR-1 mRNA levels were measured in PBMC from naive patients with chronic hepatitis C with different IL-28 genotypes. The ability of IFN-lambda to up-regulate the expression of IFNAR-1 was established in PBMC from healthy donors carrying different IL-28B genotypes.
Results: Lower IFNAR-1 mRNA levels were observed in PBMC from naive patients as compared to healthy donors. In healthy donors IFNAR-1 mRNA levels were independent from IL-28B genotype, while in HCV patients an increasing gradient of expression was observed in TT vs CT vs CC carriers. In the latter group, a direct correlation between IFNAR-1 and endogenous IL-28B expression was observed. Moreover, IFN-lambda up-regulated IFNAR-1 expression in normal PBMC in a time-and dose-dependent manner, with a more effective response in CC vs TT carriers.
Conclusion: Endogenous levels of IFN-lambda may be responsible for partial restoration of IFNAR-1 expression in HCV patients with favourable IL-28 genotype. This, in turn, may confer to CC carriers a response advantage to either endogenous or exogenous IFN-alpha, representing the biological basis for the observed association between CC genotype and favourable outcome of either natural infection (clearance vs chronicization) or IFN therapy.