Cím:	IL28B CC GENOTYPE: A PREDICTOR OF RESPONSE TO INTERFERON IN CHRONIC AND IT IS ASSOCIATED WITH INCREASED TH1 CYTOKINE PRODUCTION OF ACT MONOCYTES AND LYMPHOCYTES
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AIM: The effect of IL28B polymorphisms on the outcome of chronic HCV genotype 1 infection, as well as the association between IL28B genotypes and the Th1/Th2 cytokine production of activated peripheral blood monocytes and lymphocytes were investigated.

MATERIALS AND METHODS: Total of 748 chronic HCV genotype 1 positive (HCV1) patients (365 male, 383 female; 18-82 years) have been enrolled; 420 of them were treated with PEG-IFN pus ribavirin (P/R) for 24-72 weeks, and 195 patients (46.4%) achieved sustained virological response (SVR). For genotyping studies, DNA was isolated from peripheral blood by standard desalting method. IL28B rs12979860 SNP was determined using Custom Taqman SNP Genotyping Assays. For cytokine studies, in 40 HCV patients TNF-α, IFN-γ, IL-2, IL-4 and IL-6 production by LPS-stimulated monocytes and PMA-ionomycine activated lymphocytes was measured from the supernatant of the cells, using FACS-CBA Becton Dickinson test. The cytokine levels were compared in the patients with different (CC, CT, TT) IL28B genotypes.

RESULTS: IL28B rs12979860 CC genotype occurred with lower frequency in HCV patients than in healthy controls (26.1% vs 51.4%, $p<0.001$). The patients carried T allele with higher frequency than controls (73.9%, vs 48.6%, $p<0.001$). P/R treated patients with the IL28B CC genotype achieved higher SVR rate, than those with CT (58.6% vs 40.8%, $p=0.002$), or who carried T allele (41.8%, $p=0.002$). LPS-induced TLR-4 activation of monocytes resulted in higher TNF-α production in patients with IL28B CC genotype compared to non-CC individuals ($p<0.01$). Similarly, increased TNF-α, IL-2 and IFN-γ production by lymphocytes was found in IL28B CC carriers ($p<0.01$)

CONCLUSION: IL28B CC genotype exerts protective effect against chronic HCV infection and may be a pretreatment predictor of SVR during P/R therapy. It is associated with

increased Th1 cytokine production of activated peripheral blood monocytes and lymphocytes, which may play a role in IFN-induced rapid immune control and sustained virological response of P/R treated HCV1 patients.

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