Cím:	Increased baseline proinflammatory cytokine production in chronic hepatitis C patients with r ribavirin
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Background: Chronic hepatitis C (CHC) patients achieving rapid virological response (RVR) on PEG-IFN/ribavirin (P/R) therapy have high chance of sustained virological response (SVR). To analyze host immunological factors associated with RVR, viral kinetics, phenotype distribution and Th1/Th2 cytokine production by peripheral blood mononuclear cells (PBMC) were studied prior to and during P/R therapy. **Methods:** TNF-α, IFN-γ, IL-2, IL-6, IL-4 and IL-10 production by PBMC were measured after Toll-like receptor 4 (TLR-4) or phorbol myristate acetate /Ionomycin stimulation in 20 healthy controls and in 50 CHC patients before receiving and during P/R therapy. RVR was achieved by 14, complete early virological response (cEVR) by 19 patients and 17 patients were null-responders (NR). **Results:** Patients with RVR showed an increased baseline TNF-α and IL-6 production by TLR-4 activated monocytes and increased IFN-γ, decreased IL-4 and IL-10 production by lymphocytes compared to non-RVR patients. SVR was also associated with increased baseline TNF-α production and decreased IL-10 levels compared to patients who did not achieve SVR. Baseline IL-2 production was higher in cEVR compared to NR patients. Antiviral treatment increased TNF-α, IL-6 production by monocytes and IFN-γ secretion by lymphocytes and decreased IL-4 and IL-10 production by lymphocytes in cEVR compared to NR patients. **Conclusion**: RVR was associated with increased baseline proinflammatory cytokine production by TLR-4 stimulated monocytes and by activated lymphocytes. In null-responders and in patients who did not achieve SVR both TLR-4 sensing function and proinflammatory cytokine production were impaired, suggesting that modulation of TLR activity and

controlled induction of inflammatory cytokine production may provide further therapeutic strategy for CHC patients non-responding to P/R treatment.