P1946
Poster Session VI
Viral hepatitis and HIV/HCV co-infection

EXPRESSION OF MX1, OAS1, PKR (EIF2AK2) AND TP53 GENES DURING TREATMENT OF CHRONIC HCV PATIENTS

B. Swiatek[1], **D. Januszkiewicz**[2], J. Rembowska[1], I. Bereszynska[3], J. Wysocki[3], I. Mozer-Lisewska[3], A. Kowala-Piaskowska[3], J. Nowak[1]

[1]Polish Academy of Sciences, Institute of Human Genetics, Poznan, Poland ; [2]University of Medical Sciences, Institute of Human Genetics, Poznan, Poland ; [3]Infectious Diseases Clinic, University of Medical Sciences, Poznan, Poland

OBJECTIVES: Interferon stimulated genes (ISGs) - *Mx1*, *OAS1* and *PKR* (*EIF2AK2*) play a key role in antiviral response against HCV infection. It is suggested that ISGs pre-activation is associated with anti-HCV treatment failure (not achieving of sustained virological resonse - SVR) . Moreover, it was observed that interferon may stimulate transcription of *TP53* gene. The aim of this prosective study was to examine the association between *Mx1*, *OAS1*, *PKR* (*EIF2AK2*) and *TP53* expression and response to pegylated interferon α + ribavirin treatment in CHC patients. **METHODS**: Genomic RNA, isolated from peripheral blood lymphocytes, was obtained from thirty-five chronic hepatitis C (CHC) patients (HCV genotype 1b) treated with pegylated interferon α and ribavirin (pegIFN-α + RBV). *Mx1*, *OAS1*, *PKR* and *TP53* expression levels were quantified by real-time PCR using TaqMan probes and were calculated by plotting the Ct value of samples to the calibration curve. They were then expressed as a number of copies. To determine treatment effects, serum HCV-RNA was measured by one-step quantitative RT-PCR with specific primers from 5'noncoding region. Analyses were performed before pegIFN+RBV administration (on the first day of therapy) and then at 4. and 12. weeks of treatment. All samples were run in triplicate. **RESULTS:** Rapid Virological Response (RVR) and complete Early Virological Response (cEVR) was achieved by 13 (37.1%) and 10 (28.6%) patients, respectively. 12 (34.3%) did not response to pegIFN and ribavirin combination treatment during 12 weeks (Primary Non-Response, PNR). The mean values of baseline viral loads were comparable in RVR, cEVR and PNR group (6.7, 7.3 and $3.5x10^4$ IU/ml, respectively). Median expression levels of classical ISG (*Mx1*, *OAS1*, *PKR*), but not *TP53*: increased during CHC treatment; was higher in Rapid Virological Responders compared to cEVR and PNR group before therapy; more noticeable increased in cEVR and PNR and than in RVR patients at week 4., was stable or poorly decreased in RVR, was stable or poorly increased in cEVR and noticeable decreased in PNR group between week 4. and 12. of therapy. **CONCLUSIONS:** Exogenous IFN can stimulate transcription of Mx1, OAS1, PKR (EIF2AK2) in PBL in CHC patients. Increase in ISGs expression at week 4. of therapy might depend on baseline HCV-RNA level and next changes on HCV presence. ISGs expression may predict outcome of pegIFN + RBV treatment – pre-activation of the endogenous interferon system is associated with RVR and thereby with high likehood of achieving SVR. Treatment failure during the first 12 weeks of anti-HCV therapy (PNR) may be related to noticeable decrease in ISG expression between week 4. and 12. It can be suggested that there is no association between TP53 expression and interferon action during treatment of CHC patients.

This research was supported by National Science Centre grant no 2011/01/B/N26/04258