

PTH-116

REDUCED NK CELL CYTOTOXICITY IN HEPATITIS C INFECTION IS ASSOCIATED WITH REDUCED LEVELS OF CYTOTOXICITY MARKERS NKP30 AND NKP46

doi:10.1136/gut.2011.239301.517

T P I Pembroke,^{1,*} I Rees,¹ K Gallagher,¹ P Mizen,¹ E Wang,¹ A Godkin¹ ¹*Infection Immunity and Biochemistry, School of Medicine Cardiff University, Cardiff, UK*

Introduction *Background:* Infection with hepatitis C virus (HCV) results in life long chronic infection in the majority of subjects, indicating the virus has developed immunoevasion strategies. Treatment with interferon α (IFN α) and ribavirin is effective in clearing HCV in approximately 40% of genotype 1 and 80% of genotype 2 and 3 infected patients. Results from previous studies are inconclusive regarding the effects of HCV infection on natural killer (NK) cell function.

Aims To phenotype and assess cytotoxicity of NK cells derived from HCV exposed subjects and healthy controls using multi-parameter flow cytometry.

Methods Mononuclear cells were extracted from heparinised blood samples and liver biopsies where available. NK cells were phenotyped using a panel of monoclonal antibodies to natural cytotoxicity receptors NKp30, NKp46, NKG2D and CD16. Cytotoxicity was measured by surface expression of CD107a (indicating degranulation) after stimulation with IFN α and Huh 7.5 cells or K562 target cells.

Results Cytotoxicity was strikingly impaired in HCV infected subjects (genotype 1 more than 3) compared to healthy controls. The steady state expression of cytotoxicity receptors NKp30 and NKp46 correlated to the frequency of cells that degranulated. However, these cell surface receptors were down regulated by stimulation, thus rendering direct comparison at the single cell level not possible. Expression of NKG2D did not correlate with increased CD107a expression and the proportion of cells expressing NKG2D did not alter after activation with IFN and target cell lines. The percentage of NK cells expressing NKG2D was increased in HCV infected subjects.

Conclusion NK cell function is impaired in patients with chronic HCV infection. The authors found that the level of NK cytotoxicity is associated with NKp30 and NKp46 but not NKG2D prior to activation with IFN.

Competing interests None.

Keywords hepatitis C virus, immunology, natural killer cell.