PTH-076

MOLECULAR AND FUNCTIONAL CHARACTERISATION OF HEPATIC SLAM CD229 AND ITS IMPLICATION IN THE DEVELOPMENT OF HEPATOCELLULAR CARCINOMA

doi:10.1136/gut.2011.239301.477

H Bouhlal,[1,*] R Nyga, F Cartier, C Ossart, L Lamotte, D Chatelain, J P Marolleau, K Lassoued, H Bouhlal [1]*Immunology, INSERM U925, Amiens, France*

Introduction Hepatocarcinoma (HCC) is a cancer whose molecular mechanisms are still widely unknown. In this study, the authors show that the signalling lymphocyte activation molecule (SLAM) CD229 initially known to be expressed at the surface of certain immune cells, as well as its adaptor proteins SAP and EAT-2, are expressed in hepatocytes. A comparative analysis of the expression level of these proteins between normal and tumorous hepatocytes, together with an analysis of the function of the receptor, points to its potential role in the oncogenesis of hepatocarcinoma.

Methods The expression of CD229 (mRNA and protein) in the samples (n=10) of normal liver and HCC collected on patients in the Digestive Surgery and Pathological Anatomy Units (Amiens Teaching Hospital) or in Huh-7 and Hep-G2 cell lines was assessed through flow cytometry, western blotting, confocal microscopy and real time PCR. The molecular interactions between CD229 and its protein partners have been analysed by co-immunoprecipitation. To end with, the study of the proliferation of the cells which do or do not express CD229 has been carried out through CFSE.

Results The authors show for the first time the expression of the CD229 molecule in the hepatocytes, whose sequence is similar to that initially described in immune cells. The expression levels of CD229 are one fourth as high in Huh-7 and Hep-G2 cell lines as in normal hepatocytes. Similarly, the expression rate of CD229 decreases in tumorous cells compared to peri-tumorous cells in the same subject (n=10, $p<0.05$). The authors also show the expression of SAP and EAT-2 proteins which play the role of adaptor molecule to initiate a signal

transduction triggered by the activation of CD229. Hepatic CD229 also recruits tyrosine kinase Lyn – and not Fyn as previously shown in lymphocytes. Moreover, this receptor is functional because its stimulation divides the proliferation of Huh-7 cells by three at the utmost.

Conclusion Our results highlight the specific expression as well as the functionality of SLAM CD229 receptor in hepatocytes. The low expression level of this receptor in HCC compared to normal hepatocytes, combined to its inhibiting effects on the proliferation of hepatocytes following its stimulation or over expression, points to its implication in the hepatic carcinogenesis process.

Competing interests None.

Keywords EAT-2, hepatocellular carcinoma, SAP, SLAM CD229.