IJAE
Vol. 120, n. 1 (Supplement): 94, 2015
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Reelin expression by hepatic stellate cells and ductular reaction in HCV related liver fibrosis

Simone Carotti[1], Michelina Maria Amato[2], Giuseppe Perrone[2], Umberto Vespasiani-Gentilucci[3], Claudio Pellegrini[2], Antonio Picardi[3], Andrea Onetti-Muda[2], Sergio Morini[1]

[1] Laboratory of Microscopic and Ultrastructural Anatomy, University Campus Bio-Medico, Rome, Italy – [2] Department of Anatomical Pathology, University Campus Bio-Medico, Rome, Italy – [3] Clinical Medicine and Hepatology Unit, University Campus Bio-Medico, Rome, Italy

Reelin is a secreted extracellular glycoprotein that is thought to guide migrating neurons during brain development and maturation cooperating with Disabled-1 (Dab1), an adaptor protein obligate effector of reelin signalling pathway (1). Reelin is also expressed in human liver by hepatic stellate cell(HSC)s that following liver injury become activated, migrating and fibrogenic cells (2). The cross-talk between HSCs and other cells such as those of ductular reaction (DR) is believed to rule liver fibrogenesis leading to cirrhosis (3). In order to better understand the role of reelin in human liver tissue with ongoing fibrosis, we aim to analyse the hepatic reelin expression and its relationship with the main histological determinants of the disease activity and severity. Eighty-one liver biopsies of patients with chronic hepatitis C were studied. The expression of Reelin, Dab1, and HSC markers was investigated by immunohistochemistry and immunofluorescence. The Knodell histology activity index and DR score were evaluated. Activated HSC were frequently reelin positive and a statistical correlation was found between the number of reelin positive HSCs and Knodell's stage (r= 0,3; p<0,05). Dab1 was expressed by cells of DR and the number of reelin positive HSCs correlated with DR score in mild/moderate fibrosis (r=0,4; p<0,05). Since reelin expression by HSCs correlates with increasing fibrosis and DR, whose cells in turn express Dab1, it might act as mediator in DR activation by HSCs. Further studies are needed to test reelin as useful biomarker for liver fibrosis assessment.

References

[1] Rice DS et al. (2001) Role of the reelin signaling pathway in central nervous system development. Annu Rev Neurosci.;24:1005-39.
[2] Samama B et al. (2005) Reelin immunoreactivity in lymphatics and liver during development and adult life. Anat Rec A Discov Mol Cell Evol Biol.;285(1):595-9.
[3] Carpino G et al. (2013) Role of hepatic progenitor cells in nonalcoholic fatty liver disease development: cellular cross-talks and molecular networks. Int J Mol Sci.;14(10):20112-30.

Keywords
Reelin; hepatic stellate cells; fibrosis; HCV chronic hepatitis; ductular reaction.