Expression of Brain Derived Neurotrophic Factor (BDNF) and of its receptors in biliary epithelium: correlations with proliferation and apoptosis

Giorgio Vivacqua¹, Anastasia Renzi¹, Antonio Franchitto¹, Guido Carpino¹, ² and Eugenio Gaudio¹

¹Dept. of Anatomic, Histologic, Forensic and Locomotor Apparatus Sciences, Sapienza University of Rome
²Dept of Health Sciences, University of Rome Foro Italico

Cholangiocytes are the cells lining the biliary tree from canals of Hering to larger bile ducts. At morphological level, we can distinguish small and large cholangiocytes, which result heterogeneous also at functional and proliferative levels (Alpini et al., 1998). Proliferating cholangiocytes are modulated by several factors including neurotrophins (Alvaro et al., 2008). BDNF is a neurotrophin expressed in the nervous system but produced also by different types of epithelial cells and by progenitor cells of neuronal and mesenchymal origin (Prakash et al., 2010). Our aim was to investigate the expression of BDNF in the biliary epithelium.

The expression of BDNF and of its two receptors (TrkB and p75NT) was detected through immunohistochemistry and immunofluorescence in the biliary epithelium of normal and bile duct ligation (BDL) rat liver and of human cholestatic liver diseases. BDNF and its two receptors are expressed by small, large cholangiocytes and by Hepatic Progenitor Cells (HPC), both in normal and BDL rat livers. During BDL, the expression of BDNF and of its receptors correlates with the proliferation rate of small and large cholangiocytes. Indeed, during first two weeks of BDL, BDNF, TrkB and p75NT are highly expressed and proliferation prevails on apoptosis. After three weeks of BDL, BDNF and TrkB are slightly expressed while p75NT expression remain high and apoptosis prevails on proliferation. In vitro studies confirmed that BDNF and its receptors are expressed by small and large rat cholangiocytes. Also in human samples BDNF and its receptors are expressed in biliary epithelium, with a different intensity during chronic cholestasis.

Our results suggest that BDNF plays a role in the remodeling of biliary tree during experimental cholestasis and cholestatic liver diseases.

References


Keywords

BDNF, neurotrophins, cholangiocytes, experimental cholestasis, neuroendocrine cells, liver diseases.