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Lactoferrin regulate biliary epithelium growth and the activation of hepatic progenitor cell niche

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Lactoferin (Lf) is an iron-binding glycoprotein belonging to the transferrin family and it is present at high levels in breast milk and colostrum. This protein has many known functions and it is a potential antibacterial, antiviral, immunostimulatory, antioxidant, and cancer preventive agent.It has been seen that a 105 kDa Lf receptor (LfR) specifically mediates the effects of Lf in several different cell types (1). In human cholangiopathies, cholangiocytes are able to proliferate and replace the cell loss restoring the integrity of damaged biliary epithelium. However, when cholangiocyte proliferation is severely impaired, the activation of facultative hepatic progenitor cells (HPCs) takes place (2). The aims of our study have been i) to investigate the expression of Lf and LfR in cholangiocytes and in HPCs both in rats and in humans; and ii) to evaluate the *in vitro* effects of bLf on cholangiocyte proliferation and on HPC activation. Liver specimens have been obtained from normal (N=5) and bile duct ligated (BDL) (N=5) rats; from normal patients (N=5) and from patients with primary biliary cirrhosis (PBC, N=5); Specimens were processed for histology, immunohistochemistry and immunofluorescence. Moreover for the in vitro study small and large cholangioytes from mouse, human non malignant cholangiocytes (H69), and HPCs treated or not with lactoferrin were used. Our results showed that: i) cholangiocytes and hepatic progenitor cells express lactoferrin and its receptor, ii) cholangiocytes and HPC proliferation is enhanced by lactoferrin; iii) the treatment with lactoferrin determine the commitment of HPCs towards cholangiocyte fate; this commitment is characterized by HPC morphological and phenotypical changes. Our current findings suggest that modulation of lactoferrin may be an important therapeutic tool for managing the proliferation of cholangiocyte and the activation of progenitor cell compartment in biliary disorders.

References

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Keywords

Lactoferrin; cholangiocytes; hepatic progenitor cells.