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Hepatic progenitor cell activation is influenced by liver macrophages in the progression of non-alcoholic fatty liver disease

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Non-alcoholic fatty liver disease (NAFLD) is one of the most important causes of liver-related morbidity in children. In NAFLD, the activation of hepatic progenitor cells (HPC) is a central event in the progression of liver injury (1). The aim of the present study was to evaluate the cross-talk between HPC activation and polarization of liver macrophages in the progression of pediatric NAFLD. 32 children with biopsy-proven NAFLD were included. 20 out of 32 patients were treated with docosahexaenoic acid (DHA) for 18 months and biopsies at the baseline and after 18 months were included (2). HPC activation, macrophage subsets and Wnt/β-catenin pathway was evaluated by immunohistochemistry and immunofluorescence. Our results indicated that in pediatric NAFLD, pro-inflammatory macrophages were the predominant subset. Macrophage activation was correlated with NAFLD Activity Score, HPC activation, and portal fibrosis; DHA treatment determined a macrophage polarization towards an anti-inflammatory phenotype in correlation with the reduction of serum inflammatory cytokines and with the up-regulation of macrophage Wnt3a expression; macrophage Wnt3a expression was correlated with β-catenin phosphorylation in HPCs and signs of commitment towards hepatocyte fate. In conclusion, macrophage activation seems to have a key role in driving HPC response by Wnt3a production in the progression of pediatric NAFLD.

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References

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Keywords
Non-alcoholic fatty liver disease; stem cells; liver; WNT.