

Toll-like receptor-4 is involved in hepatic fibrogenesis in the course of non-alcoholic fatty liver disease

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Toll-like receptor-4 (TLR4) is actively involved in liver in the response to injury from a variety of etiologies. Recently TLR4 expression by hepatic progenitor cells (HPC) and biliary epithelial cells has been associated to the progression of liver damage in chronic HCV-related hepatitis (1). HPC compartment activation in ductular reaction (DR) is a feature of progressive disease also in non-alcoholic fatty liver disease (NAFLD) (2). We aimed to investigate the association among TLR4 expression, HPC compartment activation and histopathologic features of fibrotic disease progression in NAFLD. Seventy-four patients who had undergone liver biopsy were included and immunohistochemistry for TLR4 was performed on hepatic tissue samples. CK-7 was used to evaluate HPC, bile ducts (BD)/ductules of DR and intermediate hepatocytes; α -smooth muscle actin was used to quantify the activation of hepatic stellate cells (HSC) and of portal/septal myofibroblasts (MF). HPC in BD/DR were responsible for the highest TLR4 intensity of staining. TLR4-positive HPC and BD/DR correlated with fibrosis ($p < 0.01$ and $p < 0.05$), activity of MF ($p < 0.001$ and $p < 0.05$) and HSC ($p < 0.001$ and $p < 0.001$), portal and interface chronic inflammation ($p < 0.01$ and $p = 0.01$). The present study indicates the activation of the TLR4 expressing HPC compartment as important determinant of the progressive liver damage in NAFLD. TLR4 stimulation could represent one of the mechanisms directly linking the activation of HPC to inflammation and fibrosis in NAFLD.

References

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Key words

Toll-like receptor-4, fibrosis, nonalcoholic fatty liver disease, hepatic progenitor cells.