

Portal and interface chronic inflammation are associated with the progenitor cell compartment activation during NAFLD

Simone Carotti¹, Umberto Vespasiani-Gentilucci², Andrea Onetti-Muda³, Giuseppe Perrone³, Antonio Picardi², Sergio Morini¹

¹Laboratory of Microscopic and Ultrastructural Anatomy, University Campus Bio-Medico, Rome, Italy

²Clinical Medicine and Hepatology Unit, University Campus Bio-Medico, Rome, Italy

³Department of Anatomical Pathology, University Campus Bio-Medico, Rome, Italy

Background and aim: During nonalcoholic fatty liver disease (NAFLD), portal and interface chronic inflammation (PCI and ICI) are strongly associated with fibrosis by activation of hepatic stellate cell (HSC)s (Brunt et al., 2009; Vespasiani-Gentilucci et al., 2014). However, the determinants of PCI and ICI observed in NAFLD remain to be elucidated. Since portal and periportal ductular reaction is related to disease progression, we aimed to investigate if PCI and ICI are associated with hepatic progenitor cell (HPC) compartment activation. **Methods:** Fifty-two NAFLD patients were studied. NAFLD activity score, fibrosis, PCI and ICI were histologically evaluated. HPCs, intermediate hepatobiliary cells and bile ductules/interlobular bile ducts were evaluated by immunohistochemistry for CK-7, CK-19 and EpCAM. HSC and myofibroblast (MF) activity were determined by immunohistochemistry for α -SMA. **Results:** PCI and ICI strongly correlated with HPC compartment activation and with the activity of MFs ($p \leq 0.001$). Lobular inflammation, ballooning and HPC compartment activation were all associated with both PCI ($p < 0.01$) and ICI ($p < 0.05$) by univariate analysis. In the multivariate models, HPC compartment activation was independently associated with PCI and ICI (OR 4.4, 1.7-11.5; OR 3.4, 1.5-7.9, respectively). **Conclusions:** During NAFLD, PCI and ICI are strongly associated with HPC compartment activation and this association is likely one determinant subtending the strong association between PCI/ICI and fibrosis.

References

- [1] Brunt EM et al. (2009) Portal chronic inflammation in nonalcoholic fatty liver disease (NAFLD): a histologic marker of advanced NAFLD. Clinicopathologic correlations from the nonalcoholic steatohepatitis clinical research network. *Hepatology* 49:809-20.
- [2] Vespasiani-Gentilucci U et al. (2014) Hepatic toll-like receptor 4 expression is associated with portal inflammation and fibrosis in patients with NAFLD. *Liver Int.* Mar 20. doi: 10.1111/liv.12531.

Keywords

Portal inflammation, fibrosis, nonalcoholic fatty liver disease, hepatic progenitor cells.