Reviewer's report

Title: Mouse model of carbon tetrachloride induced liver fibrosis: Histopathological changes and expression of CD133 and epidermal growth factor

Version: 1 Date: 16 December 2009

Reviewer: Frank Tacke

Reviewer's report:

Fujii et al describe experiments in which mice were treated with CCl4 per gavage, resulting in liver fibrosis and tumor formation. They also found upregulated gene expression of EGF, TGF, HSC markers and CD133 and conclude that CD133 might be involved in fibrosis progression or tumor formation.

Major Compulsory Revisions

1. It is very hard to believe that treatment with CCl4 per gavage leads to liver fibrosis and HCC development. CCl4 has been extensively used in the literature (typically i.p. injections for 6-8 weeks), but usually does not result in HCC. If this should be true, the authors need to provide compelling experimental evidence. To prove fibrosis formation: hydroxyproline assay, collagen or a-SMA Western Blot, collagen immunohistochemistry. For tumor formation: clonal analysis, macroscopic picture, gene profile from tumorous vs non-tumorous tissue.

2. The paper is solely descriptive, and the up-regulation of HSC-related genes in a fibrosis model is not surprising. If the authors believe that they have HCC development, they should differentiate gene expression profiles at time-point III for tumorous vs non-tumorous tissue.

3. It is completely unclear if the upregulation of CD133 has anything to do with HSC activation or proliferation. Therefore, clear immunohistochemical stainings are needed to assess CD133 in liver tissue and assess co-staining with activated HSC (e.g., by a-SMA staining). Many hematopoietic cells can express CD133 as well, this should be tested. Furthermore, it would be helpful to isolate primary cells from the treated livers, i.e. hepatocytes, HSC, endothelial cells and Kupffer cells, to assess which cell type expresses CD133. The use of cell lines is not helpful in this respect.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:
I declare that I have no competing interests