Reviewer’s report

Title: Co-culture of primary human tumor hepatocytes from patients with hepatocellular carcinoma with autologous peripheral blood mononuclear cells: Study of their in vitro immunological interactions.

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Reviewer: Frank Tacke

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This manuscript describes the culture of primary parenchymal cells from normal human liver and HCC specimens. Furthermore, the authors conducted co-cultures with autologous PBMCs.

1. Although I acknowledge the technical value of the culture of primary parenchymal human liver cells, I believe the work is preliminary at present. The FACS plots are not convincing at all, and the MHC-II expression of the “hepatocytes” indicates that there might be “contamination” by other cells. The authors only mention negative staining for CD14 or CD3, but this should be shown. The quality of the presented FACS data is rather poor (likely due to the low numbers of cells retrieved from human tissue), but this makes the data difficult to interpret. I think it is important to show that (a) no cell doublets were measured (FSC-W), and (b) all “hepatocytes” stain negative for CD45 (leukocytes), endothelial and HSC markers. Furthermore, immunohistochemistry for typical KC and HSC markers (e.g., CD68, decorin) should be performed.

2. The co-culture experiments are, to my opinion, difficult to interpret. The co-staining of CD8 and HLA-DR is not convincing, because the compensation appears not appropriate. How should CD8+ cells and hepatocytes/HCC cells “communicate”? Why do both populations upregulate MHC-II? I strongly doubt that these observations are truly relevant. More functional assays would be needed to confirm that these observations are not artefacts, but related to pathogenically relevant mechanisms.

3. Co-cultures of hepatocytes / tumor cells with defined immune cell subpopulations (e.g., isolated by MACS) are needed to identify and delineate the interactions.

Level of interest: An article whose findings are important to those with closely related research interests

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.