Reviewer's report

Title: Decreased PCSK9 expression in human Hepatocellular Carcinoma

Version: 2  Date: 20 November 2014

Reviewer: cedric le may

Reviewer’s report:

In this study, Bhat M. and colleagues have compared PCSK9 expression levels in hepatocellular carcinoma (HCC) and adjacent hepatic tissues. Using immunohistochemistry, they observed that PCSK9 staining was significantly less expressed in HCC compared to adjacent tissues. Furthermore, PCSK9 staining was not correlated to the grade of tumor but did significantly correlate with the stage of fibrosis. Unfortunately, these interesting finding was poorly validated by quantitative real time PCR. Indeed, the authors only observed a trend for a decreased PCSK9 expression in HCC compared to adjacent tissues. Finally they did quantify circulating PCSK9 by ELISA in patients with HCC and control patients without HCC. They reported that serum PCSK9 levels were significantly increased among patients with HCC compared to control patients.

In absence of LDLr staining or LDLr protein quantification in HCC or adjacent tissues, it is difficult to evaluate and extrapolate the functional and physiological relevance of these findings.

It is crucial to further explore the putative link between PCSK9 and HCC regarding the development of PCSK9 inhibitors. However, the data presented in the actual manuscript are to date insufficient.

Major Compulsory Revisions

1. The strongest data have been obtained from immunohistochemistry, it would be important to reinforce the quantification by adding representative pictures from HCC and control tissues stained for PCSK9.

2. A western-blot analysis of PCSK9 in HCC and HCC tissues should be added to validate the immunostaining experiments.

3. Finally, as PCSK9 expression is reduced in HCC but the circulating PCSK9 levels is increased in HCC patients compared to non HCC control patients, it is necessary to measure in HCC the real effect on cell surface LDLr. Thus, it is required to quantified by immunohistochemistry and western blot the LDLr protein levels in HCC and adjacent tissues.

Minor Essential Revisions

1. The authors should precise whether patients included in the study received any pharmacological treatment.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.