Reviewer’s report

Title: Upregulation of MicroRNA-19b Predicts Good Prognosis in Patients with Hepatocellular Carcinoma Presenting with Vascular Invasion or Multifocal Diseases

Version: 2 Date: 5 May 2015

Reviewer: Albrecht Piiper

Reviewer’s report:

To the authors:

The levels of miRNAs might be useful to predict the prognosis of patients with HCC. The manuscript by Hung et al. examined the levels of miR-19b in frozen liver and tumor material from patients with vascular invasion or multifocal disease and correlated these parameters with clinico-pathological and survival data. It was found that the level of this miRNA was enhanced in the tumor samples as compared to the adjacent non-tumor samples. On the other hand miR-19b positively correlated with patient survival and disease-free survival. Moreover, the authors found that knock-down of miR-19b modulated the mRNA levels of NDGR1, EPCAM, HMGB2, Hif1A and MAPK14.

General comments:

The experiments appear to be technically well performed and the analyses look valid and the presentation is clear. Nevertheless, the additional prognostic value of miR-19b in these patients is not entirely clear as the comparison with the established scores (BCLC, CLIP etc.) has not been performed. Moreover, the study can gain considerable if the levels of the miR-19b target genes would also be determined in the patient material. As it is now, the relevance of the mRNAs found to be regulated by miR-19b remains unclear and the analyses somewhat superficial.

Essential:

1. Does miR-19b add additional prognostic information to the established prognostic scores?
2. Are there correlations between the levels of miR-19b and the putative target mRNAs in tumor material?
3. The references should cite the first valid description, e.g. of prognostic miRNAs in HCC. As I see it, this is not the case.
4. The source of the cell line is not provided.
5. Did the authors use a control-anti-miR in the transfection experiments?
6. The criteria applied in the selection of the tumor/normal liver pairs are not provided.

**Level of interest:** An article of importance in its field

**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