Reviewer’s report

Title: HBV-related hepatocarcinogenesis: the role of signalling pathways and innovative ex vivo research models

Version: 0  Date: 21 Apr 2019

Reviewer: Ming-Wei Lai

Reviewer’s report:

The authors reviewed the multiple signaling pathways contributing to the hepatocarcinogenesis of hepatitis B virus (HBV)-related hepatocellular carcinoma and compared the pros and cons of ex vivo models in the study of HBV infection and its long-term consequences, especially hepatoma.

Since this is a review article, not specifically a study on Wnt/Fzd signalling, I suggest changing the title to "Signalling pathways in HBV-related hepatocarcinogenesis and ex vivo research models".

The articles included many references. Please check if the cited references are correctly referred. For example, in Page 18, Line 434-435 "…. that can rescue a liver-defective mouse model [128]", the correct reference should be [129]. In Page 19, line 455-457, the authors depicted "The first report of human liver organoid culture and characterisation was in 2015 [135], and publication of infection studies are imminent". However, the cited reference is about pancreas organoid, not liver, despite that murine pancreatic tumor organoid orthotopic transplant did produce liver metastasis, with organoid culture (mM3L), it is not a human liver organoid. Please clarify this argument.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Unable to assess

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