Reviewer's report

Title: Hepatitis C virus E2 protein involve in insulin resistance through an impairment of Akt/PKB and GSK3beta signaling in hepatocytes

Version: 2 Date: 9 May 2012

Reviewer: yuan-soon ho

Reviewer's report:

The manuscript from Hsieh et al. describes the potential role of E2 protein from HCV genotype 1b in T2DM. The authors have investigated the effects of HCV E2 on insulin signaling, and found that E2 has the ability to induce insulin resistance. The manuscript provided some interesting aspects of E2 function, especially with respect to SOCS3 upregulation. However, there are several defects in the data and their interpretation. My comments on the manuscript were as mentioned below.

Major criticisms:
1. Ikuo Shoji published a very nice paper in 2011 (Shoji et al, 2011) showing that HCV-induced down-regulation of GLUT2 expression and up-regulation of gluconeogenesis. This suggests that high concentration of glucose in HCV-infected hepatocytes, although interpretation of their data should be cautioned because they used a HCV J6/JFH1-infected cells. It seems that this too could be part of the discussion in this manuscript.
2. Figure 2 does not show much significant difference in IRS-1 status. Moreover, the actin bands too strong to make it difficult for loading comparison. The immunoblots should be done more clear, and quantification of each bands need to be done more precisely, with SD.
3. Figure 4: The effect of MG132 was not very significant. The immunoblots should be done more clear, it would help to include scanned data with lower actin level for proper comparison.
4. In Figure 5, the mark of phosphorylation is confusing. Please use uniform style for phosphorylation of Akt and GSK3beta in all figures and quantification of each band.

Minor criticisms:
In Figure 2C and 6B, the statistical analysis should be done between FLAG and E2.

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.