Reviewer’s report

Title: URG4/URGCP promotes angiogenesis of human hepatocellular carcinoma through activating NF-kappaB signaling

Version: 3 Date: 20 January 2015

Reviewer: Moorthy Krishnan

Reviewer’s report:

This is a very nice piece of work and it is an excellent contribution towards HCC and NF-κB signaling pathway. The authors examine the relationship between URG4 and angiogenesis.

As a reviewer, I have following comments about the manuscript

Major Compulsory Revisions

1. Authors have examined the effect of over expression and Knock Down on URG4 gene in same cell line (QGY7703 and Hep3B). The authors should refocus the MS on utilizing the normal liver epithelial cells Lo2 or THILE3 for over expression studies. This study might support their claim that URG4 promotes angiogenesis in liver.

2. Authors have claimed that inhibition of NF-κB signaling blocks the promoter function of URG4 in HCC angiogenesis. In this experiment (Fig 5a) they used control vector and nondegradable IκB# mutant to register their claim. They have failed to show status of IκB# phosphorylation when they over express mutant form in both cell line.

Minor Essential Revisions

3. In material method section, authors should mention how they cloned the NF-κB promoter and mutant IκB# in luciferase vector.

4. Methods are appropriate but it is not well described. For example the generalized method was given for luciferase assay. Detailed experiment protocol should be given for different promoter assays (Fig 4A and 5A).

5. The authors used wrong term in fig 1B, 1C, 2C, 4C, 5B and 5C. It should be changed as “fold change”.

6. Densitometric Analysis should be given to Fig 1A, 2A and 3A.

Discretionary Revisions

7. Authors used Student’s t- test to evaluate the statistical significant between 2 different groups. The ANOVA might be helpful.
**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.