Reviewer’s report

Title: JNK signaling maintains the mesenchymal properties of multi-drug resistant human epidermoid carcinoma KB cells through snail and twist1

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Reviewer: Hiroshi Kajiya

Reviewer’s report:

This manuscript describes the role of JNK signaling on EMT, which transited epithelial cells into mesenchymal cells using MDR KB/VCR compared to KB parent cells. Although the manuscript is interesting in basal cancer research there are some important problems, which the authors need to address, described below.

Major Compulsory Revisions

1) There are many reports that TGF-beta induced EMT with invasion and migration and invasion in various kinds of cells. However, the present data have shown about the mesenchymal characteristics in only KB/VCR cells. Did the authors check the JNK signaling in response to the treatment of TGF-beta in KBR cells? If there are some reports about TGF-beta-induced EMT through activation of JNK signaling in KBR cells, the authors should cite the articles and they compare the characteristics in KBR/VCR to treatment of TGF-beta in the parent one. Otherwise you should examine yourself about treatment of TGF-beta in KBR cells. And the authors add the obtained results by TGF-beta treatment in KBR cells in Figures.

2) Although there are many kind of MAPK such as p38, Erk1/2 and Erk5/BMK1 the author stated only JNK signaling. The reviewer did not understand that why only JNK up-regulated in KBR/VCR cells. Did you check the other MAPK signaling in KBR/VCR cells? The authors should check and discuss them.

3) The data have shown that the inhibitor and siRNA of JNK downregulated the EMT biomarkers in KBR/VCR cells compared to the parent ones. These results indicated some molecules continuously activated JNK signaling, resulting in keeping mesenchymal cells in KBR/VCR cells. The authors should speculate what molecule is maintained the mesenchymal characteristics in KBR/VCR cells.

Minor Essential Revisions

1) Although the oncogenic function of JNK has known to be mostly based on the ability of phosphorylated c-Jun. However, how about is the activation of the other Jun family, such as JunB, JunD on EMT biomarkers in KB/VCR cells?

2) In Figure 2, how about is the morphology of KB/VCR cells after incubation with SP600125 a JNK inhibitor? Furthermore, the inhibitory effects (10 micromole, 24h) on EMT biomarkers were likely to be week. Did the authors check the other concentration and/or incubation time in the inhibitor?
Discretionary Revisions
1) page 3, final line; That phrase, to name a few, had better to change to such as.

2) page 5, line last 2; What kind of ABC transporters in expression the authors examine?

3) page 12, line 14; The phrase, with exemption should be changed to without.

4) page 13, line 3; The term, limiting had better to change to the silencing or knockdown.

5) page 14, line 11; The word, limiting had better to change to the silencing or knockdown.

6) page 15, line 11; The word, fresh should be changed to first or original.

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

Quality of written English: Not suitable for publication unless extensively edited

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.