Reviewer's report

Title: SOX4 inhibits GBM cell growth and induces G0/G1 cell cycle arrest through Akt-p53 axis

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Reviewer: Fumiharu Ohka

Reviewer's report:

The authors reveal that upregulated SOX4 stabilizes p53 and results in cell cycle arrest in GBM cell lines. It is evaluable that the authors demonstrate their hypothesis clearly in vitro study, using Cre-loxP system. However reviewer thinks that the authors need to discuss about the significance of SOX4 in glioma-genesis. Additionally, the authors need to analyze several points as described below.

Major Compulsory Revisions:

1. The authors reveal that SOX4 is tumor suppressor. However they showed that SOX4 expression is upregulated in GBM samples, compared with normal brain. They need to discuss about this inconsistency. In GBM patients, is upregulated SOX4 correlated with good prognosis?

2. The authors showed that SOX4 is correlated with maintaining stemness of glioma stem cells, via TGF-b signaling. This suggested that SOX4 enhanced stemness feature in GBM tumors. Is this phenomenon tumor suppressive?

3. Is expression level of endogenous SOX4 in GBM cell lines, such as U87, LN229, T98 and so on, higher than those of normal cells?

4. The authors suggest that SOX4 activates p53 function via downregulation of post-transcriptional regulation factor, such as MDM2, AKT. They also need to analyze whether SOX4 alters transcriptional level of p53 mRNA or not, using RT-PCR or expression microarray data.

5. CDK2 is essential for G1/S transition. Upregulation of CDK2 by overexpression of SOX4 might be inconsistent with cell cycle arrest which is caused by SOX4. The authors need to discuss about this inconsistency. Additionally, in supplemental table 2, CDK2 is not contained. The authors need to check this list.

Minor Essential Revisions:

6. In Figure 2A and 3A, the authors reveal the expression levels of HA in control cells, using anti-HA antibody. At least in one figure, they need to show the expression level of endogenous SOX4 using anti-SOX4 antibody.

7. In page 11, 15, spelling of RT-PCR and GBM are incorrect, respectively.
Level of interest: An article whose findings are important to those with closely related research interests

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.