Peer Review File

Review Comments:

Reviewer A:

Ma Tao et al comprehensively assessed the significance of alterations of the CBX family member genes, CBX1-8, in gastric cancer (GC) by silico analysis. The authors observed that overexpression of CBX3-6 and underexpression of CBX7 mRNAs was significantly associated with the poor prognosis and survival of GC patients. In addition, CBX1 mRNA was significantly related to the poor prognosis of GC patients who received adjuvant 5-fluorouracil-based chemotherapy. These findings indicate the CBX family members are useful biomarkers for GC. Although the study using public databases is interesting, several questions arisen in the present version.

Comments:

1) The authors should further analyze the relationship between each CBX gene and clinicopathological factors such as histology and metastasis, if possible. Table 1 shows that CBX mRNA levels are associated with histologic grades, such as intestinal type.

Reply 1:

We gratefully appreciate for your valuable suggestion. We have added the relationship between CBX family mRNA expression levels and
tumor grades.

Changes in the text:

We added some sentences and one figure about the relationship between CBX family mRNA expression levels and tumor grades. (see Page 10, line 2-8 and figure 4).

2) Page 11, paragraph 3.5. the mutation rate of CBX was very high (45%) in GC. However, Figure 7A almost shows "mRNA high". Does "mRNA high" mean "mutation"? I think that other word, such as "alteration", should be used. Otherwise, many scientists will confuse that somatic mutation rate CBX is 45% in GC.

Reply 2:

Thank you for your comment. "mRNA high" does not mean "mutation". "mRNA High" in this case implies higher expression than the average patient. mRNA z-Scores (RNA Seq V2 RSEM) is compared to the expression distribution of each gene tumors that are diploid for this gene. And mRNA expression z scores (RNA Seq V2 RSEM) were obtained using a z-score threshold of ±2.0. Using "mutation" is indeed confusing, and we have replaced "mutation" with "alteration".

Changes in the text:

We have modified our text as advised. (see Page11, line16-19)

3) CBX7 was underexpressed in GC. Figure 7A show that 6% of cases had high mRNA expression and no other alterations were detected in other cases. Why is CBX7 downregulated in cancer cells?

Reply 3:

Thank you for your comment. In figure 7A, mRNA expression is compared to the average patient. "mRNA High" in this case implies higher expression than the average patient. But the expression of CBX7 mRNA was significantly lower in tumor than in normal people.

4) All the immunohistochemistry data on Figure 3 are directly obtained from the photographs of the Human Protein Atlas. We often refer the data of Human Protein Atlas and perform IHC by ourselves, but never show original photographs of Human Protein Atlas in the manuscript. I think that the figure 3 should be deleted. However, if the authors want to show them and the editors agree it, the authors should add more information in the figure legend. "Analyses conducted using the Human Protein Atlas" is very short figure legend, giving us question what the authors analyze in this figure.

Reply 4:

Thank you for your comment. We have deleted the figure 3 and related content.