

Peer Review File

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Reviewer A:

1. The authors described the relevance of KIF23 level and PDAC patients' overall survival and progression-free survival rates, but whether the participants in the study cohort received treatment and the details of their treatment were not mentioned.

Reply1: From the perspective of the longer survival time of patients, chemotherapy should be used. You can check the specific information through GEPIA and TCGA databases.

2. You mentioned that KIF23 positive staining was localized in the nucleus, but figure 2A showed that positive staining was localized in the cytoplasm, which was contradictory, and the "low" or "high" expression in figure 2 was not explained clearly.

Reply 2: KIF23 positive staining should be located in the nucleus. This is an editorial error. I have replaced the correct picture; in the article, we have explained that the KIF23 immunohistochemical grade is divided into four grades according to the staining intensity, and the low expression is 0 And 1+, high expression is 2+ and 3+.

3. The reason why you chose CDCA8 as KIF23's downstream molecule needs further explanation, are there better choices?

Reply 3: In this article, we found that KIF23 affects pancreatic cancer in terms of proliferation, so we mainly choose genes for proliferation; in Genecards we find the mechanism diagram of the interaction between KIF23 and multiple genes (Figure 6B in the article), and find the proliferation-related gene CDCA8 It is obviously related to it.

Finally, tense changes and the mistake in grammar existed, which added to the confusion in reading.

Additional more specific comments follow.

1. "Despite we have treatment strategies..." -the word "despite" is usually followed by nouns rather than clauses.

I have modified

2. Line 57 and 58. "The occurrence of pancreas"-I think the authors mean "The occurrence of pancreas cancer", perhaps?

I have modified

3. Line 58. "imbalanced diet, and obesity"- the " ," could be omitted.

I have modified

4. “Figure 1”-the figure is too blurry, I think a clearer picture would be more friendly to readers.

I have replaced with a clearer picture

5. “We also report that knock down of KIF23 decreased...” - “report” should be “reported”.

I have modified

6. “Figure 2” – it would be better to provide explanation for “Figure 2B”, and the same problem exists in “Figure 8B”

I have added an explanation to the picture

7. “Supplementary Figure S1A” and “Supplementary Figure S2A” need more specific explanation.

I have modified

8. Line 246. “The expression level of KIF23 protein in the control group was obviously more than that in tumors” – “more” should be “higher”. The same problem also exists in line 249.

I have modified

Reviewer B:

1. Cell cycle assay should be made in addition to cell proliferation experiments. Cell cycle-related proteins(cyclin A/B/C/D/E, p21, p27, CDK2/4/6) should be detected in WB.

2. Does KIF23 affect death receptor mediated apoptosis? Additional pro-apoptotic factors(eg. FasL, TNFa, TRAIL) should be added to test the effect of KIF23 on death receptor mediated apoptosis.

3. Does KIF23 affect the expression of other apoptosis related mitochondrial proteins, for example: Bcl-2, Bcl-XL, Bax, Bim, Bad, IAPs?

4. Does KIF23 affect cell migration and invasion of tumor cells?

Reply: We have done pre-tests related to cell migration, invasion, apoptosis, and cell cycle before, and the results are negative: there is no statistical difference between the experimental group and the control group, so we only show the results of the differential proliferation. Of course, if you need me, I can send you the relevant experiment results.

5. What is the detailed mechanism of KIF23 regulating the cell proliferation of tumor cells. Does Flurbiprofen affect AKT, Ras, Src and NF-kB signaling?

Reply: Due to funding, time and energy constraints, the specific mechanism needs to be further studied and completed in the future. There are currently published similar articles about 3-4 points as follows:

Zhang XG, Zhang T, Li CY, Zhang MH, Chen FM. CD164 promotes tumor progression and predicts the poor prognosis of bladder cancer. Cancer Med. 2018 Aug;7(8):3763-3772.

[Neural precursor cell expressed, developmentally downregulated 8 promotes tumor progression and predicts poor prognosis of patients with bladder cancer.](#)

Tian DW, Wu ZL, Jiang LM, Gao J, Wu CL, Hu HL.

Cancer Sci. 2019 Jan;110(1):458-467. doi: 10.1111/cas.13865. Epub 2018 Dec 10.

6. Expression of KIF23 in cancer tissues of 10 patients and their corresponding noncancerous mucosal tissues should be analyzed by IHC and western blot.

Reply: In this paper, the expression levels of KIF23mRNA in cancer and adjacent to cancer have been compared in the GEPIA database, and the data are true and valid. We used 82 samples of tumors in our hospital to compare the immunohistochemical protein levels of the corresponding tissues adjacent to the cancer, but because there are no fresh tissue samples, it is impossible to perform related WB experiments.

7. Poor writing and experiments design. The results of this experiment are not reliable. The author needs to provide all the original data including WB image.

Reply: We can provide compressed packages of original data