Peer Review File

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Reviewer A

Comment 1: Why the author only uses qPCR to detect IFITM10 expression levels in patient tissue samples? Why not combine with other methods to test, the results will be more reliable in that case.

Response 1: Thank you for your opinion, because the experiment cost is limited. The funding is not enough to support our sequencing of all the tissues. Therefore, we can only use TCGA database to screen the differential genes, and use qPCR method to verify in a large number of tissues.

Comment 2: In this paper, it is best to supplement the research on bioinformatics analysis, such as GO analysis or KEGG analysis. This is more conducive to support the conclusion of this paper.

Response 2: Thank you for your opinion. We used GSEA to analyze gene function in the experiment. The result of this analysis is based on KEGG database analysis. Go is very limited in the analysis of single gene function. We supplement the protein interaction network of IFITM10 based on STRING.

Changes in the text: page8 line165-172. We constructed the protein interaction network of IFITM10 by string and listed top 10 interactant proteins (Fig 7). In these related proteins, the low expression of interferon regulatory factor 6(IRF 6) is closely related to the poor prognosis of gastric cancer.(27) Ubiquitin C-terminal hydrolase-L1 (UCHL1) can activate HIF-1 α, which is a new tumor therapeutic target. (28) SCNN1A is highly expressed in ovarian cancer and is closely related to the poor prognosis of ovarian cancer. (29) IFITM10 can interact with these proteins and genes to participate in these tumor related pathways, which also shows that ifitm10 has certain research potential in cancer.

Comment 3: The sample size in the database is relatively limited. How to avoid the influence of this factor?

Response 3: Thank you for your opinion. As we have only 62 clinical specimens, we have simultaneously analyzed 375 tcga-stad databases with relatively sufficient data and obtained similar results. This makes the results relatively accurate. We will also gradually accumulate tumor specimens for larger sample size studies in the future.

Comment 4: The research on gene signal pathways in this article is only a list of a

few signal pathways, and specific research and screening of signal pathways should be increased.

Response 4: Thank you for your opinion. In the experiment, we only used GSEA to analyze the possible regulatory pathway of IFITM10. Due to the problem of funding and time, we can not carry out the next functional test. Therefore, we have relatively few studies on the pathway. We supplement the protein white interaction network of ifitm10, and further discuss the role of ifitm10 in the signaling pathway.

Comment 5: There are still some weak points in this paper. It is suggested that the author increase the possible mechanism analysis. This is more conducive to support the conclusions of this study.

Response 5: Thank you for your opinion. In the experiment, we only used GSEA to analyze the possible regulatory pathway ofIFITM10. Due to the problem of funding and time, we can not carry out the next functional test. Therefore, we have relatively few studies on the pathway. We supplement the protein white interaction network of IFITM, and further discuss the role of ifitm10 in the signaling pathway.

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Comment 6: The function research of the gene should be increased.

Response 6: Thank you for your opinion. Due to the problem of funds and time, we can not carry out the next functional test. Therefore, we supplement the protein interaction network of IFITM10 and further analyze the role of ifitm10 in the signaling pathway. In addition, we supplemented the analysis of ifitm10 in exobase. We found that IFITM10 is highly expressed in exosomes of digestive system tumors, which also indicated that ifitm10 had good diagnostic potential.

Changes in the text: page6 line147-149. We found that ifitm10 was highly expressed in exosomes from colon cancer, pancreatic cancer and liver cancer(Figure 5). Although there is no such study in gastric cancer

Reviewer B

Comment 1: If there is a potential as an early diagnostic marker of IFITM10 shown in the title, IFITM10 mRNA/protein needs to be examined in samples available at the time of diagnosis, e.g., patient peripheral blood, etc. There are quite a few specific gene products derived from tumor tissue that differ between stages. The authors' claim that IFITM10 is associated with early diagnosis is ill-founded.
Response 1: Thank you for your opinion. Due to the lack of peripheral blood samples and related databases, we did not carry out more convincing tests. A large number of previous studies have shown that the genes highly expressed in peripheral blood and other body fluids are highly expressed in tumors, and most of the genes entering body fluids are secreted by exosomes. We found that ifitm10 was highly expressed in exosomes of colon and pancreatic cancer by exobase analysis, and ifitm10 was highly expressed in early gastric cancer. Therefore, we speculated that ifitm10 has certain diagnostic potential.
Changes in the text: page6 line6-8. We found that ifitm10 was highly expressed in exosomes from colon cancer, pancreatic cancer and liver cancer(Figure 5). Although there is no such study in gastric cancer

Comment 2: The statement that “T is associated with IFITM10” is also unsubstantiated; T indicates the size of the primary tumor. There is no difference in the expression of IFITM10 in terms of “tumor size” among the authors' in-house samples. Nevertheless, there is a difference in the expression of IFITM10 in the T classification. It is natural to assume that this is related to other factors that have not been measured. Gastric cancer is a highly heterogeneous disease. It is nonmeaningful to discuss IFITM10 expression levels by unnaturally combining heterogenous gastric cancer subtypes.
Response 2: T stage generally represents the depth of tumor invasion. This index is given by the pathology department according to the current guidelines. We found that the expression of ifitm10 is related to T stage in the experiment, and the deep correlation needs to be discussed in more in-depth experiments. Due to the limitation of funds and time, we can not complete this work for the time being.

Comment 3: Due to the significant statistical immaturity of the descriptions, all figures and texts should be verified by a statistician before submission.
Statements that could be read as arbitrary data exclusions are found in the removal of patient data from the TCGA-STAD cohort and the removal of IFITM10 outliers. I disagree with like this act without scientific descriptions.
Response 3: Due to the lack of pathological information of some patients in TCGA-STAD database, forcing these patients to be included will lead to imprecise results

and unable to carry out logistic regression, so we only objectively delete patients with incomplete pathological information. All the icons in this paper were statistically analyzed by SPSS and R.