Peer Review File

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Reviewer Comments

This is an interesting study and can provide new information on the mechanisms that colorectal cancers promote proliferation will hopefully become useful in the clinical setting. Please respond to the following comments and questions:

Comment 1.

Abstract: Please, the first time you write words with acronyms, detail what they mean "GO, KEGG, ECM".

Reply 1.

We appreciated the Reviewer's comments. We have now added details of words with acronyms in the abstract according to the requirement (Page2, line30 & line31 & line40).

Comment 2.

Introduction:

- The same for the word "MDAR".
- More generally, the authors should explain the differences between colon cancer and rectal cancer. Although I suspect that the two groups have not been divided, it is important to describe that they are two entities with different characteristics regarding diagnosis, treatment and prognosis. If possible, it would be interesting to compare the expression of TTI1 in both groups.

Reply 2.

Thanks for the Reviewer's comments. We have now added detail of the word 'MDAR' according to the requirement (Page5, Line97).

In our work, we generally focused the role of TTI1 in colorectal cancer. We added the correlation analysis between TTI1 expression and cancer occurrence site (Table 1), colon cancer patients and rectal cancer patients take a similar proportion and there is no significant difference between TTI1 expression and sites of cancer.

Comment 3.

Material and methods:

- Ethical statement: You must specify if the patients had to sign an informed consent.
- Colorectal tissues collection: Why do you indicate that 53 colorectal tissue samples were analyzed if the total sample is 98 patients and 50 controls?

Reply 3.

Thanks for comments from the reviewer. Our work was approved by the Ethics Committee of the Army Medical University and every step of this work strictly met the requirement of the Chinese Ethics Committee of Registering Clinical Trials (clinical trial register no.ChiCTR2000033078).

We first screened out TTI1 as a novel gene in GEO database (GSE44076) and GSE44076 contained micro-array information of 98 patients and 50 controls. Then we verified TTI1 expression in colorectal cancer tissues of 53 patients in our department.

Comment 4.

Results:

- TTI1 is up-regulated in CRC: A further description of the characteristics of the patient sample, as well as the control sample, is needed. It would be very interesting to differentiate between rectal and colon cancer due to the therapeutic and prognostic implications they have. If this was not done, the reason should be justified.

Reply 4.

Thanks to your comments. We described the characters of patients in the table as the supplement material. We also add the type of colorectal cancer in the table. However, there was no significant difference of TTI1 expression between colon cancer and rectal cancer. The prognostic implications of TTI1 was shown in Figure.S2B&C.

Comment 5

Discussion:

- Please review and contrast the following sentences, “Less invasive screening rather than colonoscope is becoming an effective mean to increase survival rates” and “However, innovative treatments are usually unable to prevent patients from dying in three years”.
- It is not necessary to summarize the results section, it becomes repetitive and does not add anything to the discussion.
- Check the text, repeat too many times "moreover".

Reply 5.

Thanks to your comments. We have removed the sentence “Less invasive screening rather than colonoscope is becoming an effective mean to increase survival rates” (Page16, line336) and “However, innovative treatments are usually unable to prevent

patients from dying in three years" (Page16, line338). And we removed unnecessary 'Moreover' (Pge16, line333; Page17, line366 &368; Page18,line383 & 385).