Dear editor,

Thank you very much for your e-mail and the enlightening comments of the reviewers. We are pleased to answer the reviewer's questions and have revised the manuscript accordingly. We hope that those changes will make the manuscript acceptable for publication in World Journal of Gastrointestinal Oncology.

The revised manuscript has been resubmitted online. We thank you for the consideration and look forward to your reply.

Yours sincerely,

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On behalf of all authors
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Response to the reviewer' questions

Before answering the questions raised by the worthy reviewer, we would firstly like to thank the reviewers for their appreciation and critical review along with excellent good suggestions. This will improve the quality of the article and will make it more understandable for the readers.

Reviewers' comments:

Reviewer #1: This is a well written and presented manuscript. All the component sections are well drafted. The statistical analysis is appropriate and result presentation in prose and figures are acceptable. Article citations are current and relevant to the topic. Key findings in this study are that long noncoding RNA RP5-881L22.5 (lncRNA RP5-881L22.5 is expressed more in digestive system cancers namely gastric, oesophageal and colorectal cancers (CRC) compared to normal tussues. Among the CRC cases, some had differential higher expression than others and this influenced hosts' tumour immune response parameters inversely whereas cancer cell invasiveness was directly correlated to marker expression. Thus the study suggests from its hypothesis that lncRNA RP5-881L22.5 could play a remarkable role in CRC carcinogenesis and progression. From the submission, the authors hypothesize that RNA RP5-881L22.5 has prospects of being a drug target in combating immune checkpoints mounted by tumour cells. Other possible pathogenetic roles may become clear with additional studies.These conclusions are well supported by the data from this study. However, the following concerns would require attention.

1. Authors need to provide keywords for the study.

Response: Thank you very much for your suggestion. These keywords had been listed in the manuscript.

2. Acronyms need to be stated in full meaning when first used to make reading and understanding smooth and easy. One that may be easily overlooked by the authors is in the first sentence of the third paragraph of the introduction section "200 nt". This may not be an abbreviation, either way, it needs to be revised.

Response: Thank you very much for your suggestion. The abbreviation had been listed in the manuscript. 200 nt means 200 nucleotides.

3. Authors should please state in the result section what proportion of CRC tissues had high and low RNA RP5-881L22.5 respectively. This will strengthen their position on increased marker expression in CRC and will make it easier for future researchers to compare with their own observations.

Response: Thank you very much for your suggestion. It is very important. we have made correction in the revised manuscript. All 448 colorectal cancer tissue samples were divided into a high expression group and a low expression group according to the median expression of RP5-881l22.5 with 224 tissues in each group. The 62 specimens of patients in stage IV were divided into a high expression group and a low expression group according to the median expression of RP5-881l22.5 with 31 tissues in each group. Eighty specimens of patients in the N2 stage were divided into a high expression group and a low expression group according to the median expression of RP5-881l22.5 with 40 tissues in each group.

4. Still on the result, no difference in survival was found between high and low expressing tumors. However, a subset of tumours with advanced stage showed better survival despite high marker expression. What could explain this?

Response: Thank you very much for your suggestion. we have made corrections in the revised manuscript. We believe that this may be because the expression of inhibitory receptors on the surface of T cells in the RP5-881l22.5 high expression group is reduced, so T cells in the tumor microenvironment of these patients show relatively stronger antitumor immune activity. Of course, there may also be other key mechanisms related to RP5-881l22.5 expression that leads to this difference in prognosis, which provides a way to explore for further research on immunotherapy of advanced tumors with rp5-881l22.5 as a marker.

5. The citation in the result section needs not be there. Its absence does not alter the information provided. Authors to consider removing it and recasting the sentence.

Response: Thank you very much for your suggestion. we have made corrections in the revised manuscript.

6. Authors to please revisit the reference section. It needs to be organized to remove repetitions

Response: Thank you very much for your suggestion. we have made corrections in the revised manuscript.

Reviewer #2: Dear authors Your manucript „The potential role of long noncoding RNA RP5-881L22.5 as a novel biomarker and therapeutic target of colorectal cancer,, is interesting and intriuging. It belongs to the new wave of ideas, and retrospectivelly tested importance of long noncoding RNA RP5-881L22.5. The manuscript is well organized, relativelly well written, clear with apprppriate tables and figures and propper citation. Methodology is well described, and results were clearly presented. It will be interesting to comment lack of correaltion with the T stage and lack of difference in survival between high and low groups according to RP5-881L22.5 expression levels. There is not described limitation of the study.

Response: Thank you very much for your suggestion. Our description is indeed not clear enough. We have made corrections in the revised manuscript. We believe that this may be because the expression of inhibitory receptors on the surface of T cells in the RP5-881l22.5 high expression group is reduced, so T cells in the tumor microenvironment of these patients show relatively stronger antitumor immune activity. Of course, there may also be other key mechanisms related to RP5-881l22.5 expression that leads to this difference in prognosis, which provides a way to explore for further research on immunotherapy of advanced tumors with rp5-881l22.5 as a marker.

Reviewer #3: No comments