Prediction of Hereditary Nonpolyposis Colorectal Cancer using mRNA MSH2 Quantitative and The Correlation with Nonmodifiable Factor

Manuscript #: 63022 | Review Response Letter

The authors would like to extend their highest appreciation to the editor and reviewers for their kind evaluation and appraisal to improve the manuscript. We (the authors) have taken into accounts all of the concerns portrayed by both reviewers and accordingly made satisfactory modifications. Please note that changes have been amended to the manuscript. Hereby, we depict our augmentation to the manuscript.

Editor:

1. Please respond to the reviewer's comments (View attachments 63022_ReviewReport).
   Thank you. We have accordingly responded to the editor's and reviewers' comments and made satisfactory modifications in the manuscript.

2. The content of the core tip part needs one paragraph, and the number of words is controlled between 50-100 words.
   Thank you for the reminder of the core tip section. We have appended the 100 words core tip paragraph before the "Introduction" section on page three.

3. The part of the "Article Highlight" needs to be rewritten. Each heading (Research background; Research motivation; Research objectives; Research methods; Research results; Research conclusions; Research perspectives) in this part needs one paragraph and cannot be divided into sections. Citing documents is not allowed.
   We appreciate the editor's reminder for the "Article Highlight". The authors accordingly have concocted the highlight with one paragraph within each heading. Please see page twelve.

4. Please provide the Figures cited in the original manuscript in the form of PPT. All text can be edited, including A, B, arrows, etc.

5. Please provide the table in the manuscript again in Word.

   We have accordingly provided the tables in the manuscript after the "Footnotes" section. Please note that some changes have been implemented.

6. According to the manuscript you provided, it needs to be revised after rechecking. Please read the attached CrossCheck report for details. Similar sentences with other articles (highlighted in the CrossCheck Report), please rephrase these sentences. Our editorial policy states the overall similarity should be less than 30%, the overlapped section should be less than 5% in single papers, including author's own work.

   Thank you for the advice. Similarities within the earlier version of the manuscript is directed toward author's previous work on akin topic. Nonetheless, adjustments have been made to reduce the similarity in the manuscript.

7. Please add page number to CONSORT 2010 checklist of information to include when reporting a randomised trial

   Thank you for the reminder on study type guideline. However, after careful deliberation among all authors, we think that the study is more suited as an observational study opposed to a randomized trial. There is no randomness and any intervention in this study. The tissue biopsy and MSH2 mRNA gene quantification are done for all respondents.

   The main point of the study relies on the risk factor assessment toward the hereditary and sporadic respondents coming from the CRC group which are undoubtedly observational. Consequently, the authors follow the STROBE guideline and items list in preparing and revising the study, akin to the information stated in the "Footnote" section on page nineteen. The authors have understood the STROBE statement for observational study. Thereafter, the authors have prepared and revised the manuscript according to the statement and items checklist.

Reviewer 1:

1. This is an interesting and meaningful study, and I recommend accept.

   We appreciate the interest of the reviewer on the study.

Reviewer 2:

1. MSH2 mutations have been reported previously to contribute to HNPCC. MSH2 has already been examined at the DNA, RNA, and protein levels in some studies. Therefore, this paper lack novelty.

   The authors thank the reviewer in highlighting the relations of MSH2 to HNPCC. We acknowledge that many earlier studies have indeed prove the after-mentioned relationship. However, current paper is not only about the association of MSH2 toward HNPCC. MSH2 mRNA gene expression merely acts as a cut-off technique to distribute the CRC respondents into hereditary and non-hereditary group.

   The novelty of current study lies on the establishment of definite cut-off regarding the MSH2 mRNA gene expression for categorizing the hereditary status of CRC, 11059 fc. Then, as per the authors knowledge, this is the first study about the MSH2 mRNA quantitative gene expression not just to HNPCC but its hereditary characteristics. Further, this study develops easier to implement probability equations in determining the hereditary status compared to previously established criteria with hard to collect or implement variable(s).

2. HNPCC is a complex genetic disease with polygenic alters, it's hard to say whether detection of the single MSH2 mRNA can help much in HNPCC prediction.

   Thank you. We understand the reviewer's concern about the polygenicity of HNPCC. However, findings on several studies indicates indirect involvement of MSH2 even for other gene relations to HNPCC. For instance, to reduce the risk of HPNCC, MSH6 must bond with MSH2 first and form the MutSα complex and do DNA repair. MSH2 chosen for its being almost in the center for any link to HNPCC.