Author's response to reviews

Title: Differences in the genetic alterations between Vietnamese and Japanese colorectal cancers

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Author's response to reviews: see over
Dear Editor,

We are pleased to submit the revised version of our manuscript:

MS No: 1208173965133018  
MS Title: Differences in the genetic alterations between Vietnamese and Japanese colorectal cancers

We have revised the manuscript according to the comments from editors and reviewers.

Point-by-point response to reviewer

# Reviewer 1: Rashmi Prasad

Major

1) As the reviewer pointed out, the Vietnamese population is quite small in comparison with the Japanese. We have fully understanding of the problem. However, we can find significant differences in frequencies of genetic changes including K-ras and mtDNA mutations and MSI-H between Vietnamese and Japanese. If we could not find significant differences, we would have added the case number.

2) We added the sentences to make clear why the 3 mutations were specifically selected (shown in blue).

3) We changed the “genetic pathways” to “genetic alterations” in the title (shown in blue).

4) We deleted the sentences related to GWAS studies.

5) We revised the Discussion and Conclusion sections.

Minor

1) We think that these tables should be present form but not supplementary data. Supplementary data should be more detailed ones.

2) Figures B and C are images of microsatellite assay. The assay shows ladder-like or smear-like band shadows. Therefore, the bands seem to be unclear, but not unclear.
# Reviewer 2: Barbara Pardini

**Major**

1) As the reviewer pointed out, the Vietnamese population is quite small in comparison with the Japanese. We have fully understanding of the problem. However, we can find significant differences in frequencies of genetic changes including K-ras and mtDNA mutations and MSI-H between Vietnamese and Japanese. If we could not find significant differences, we would have added the case number.

   We examined MSI-H in the 60 Vietnamese CRCs. Unfortunately, only 27 cases were informative in the analysis. We used formalin-fixed, paraffin-embedded specimens, and the DNAs may be degenerated. Therefore, informative cases were limited.

2) We also have understanding that we should have examined genetic changes in corresponding normal tissues. Unfortunately, we could not have corresponding normal tissues of Vietnamese CRCs. If we could have them, we would have examined much more genetic changes.

3) As the reviewer pointed out, there are differences in the Vietnamese and Japanese patients with CRC. High incidence of early-onset (patients under 50 years of age) and poorly-differentiated histology seems to be crucial characteristics of Vietnamese CRCs. We showed the high frequencies of K-ras and mtDNA mutations and MSI-H may be another characteristics of Vietnamese CRCs.

4) The reviewer mentioned that environmental exposure and culture habits could be quite different when considering a 2-years or a 10-years lapse. Is it true? If so, the disease demographics would change year by year. We think that the difference would be small.

5) Figures B and C are images of microsatellite assay. The assay shows ladder-like or smear-like band shadows. Therefore, the bands seem to be unclear, but not unclear.

6) We added the sentences to make the aim of this study clear (shown in red).

**Minor**

1) As the reviewer pointed out previously, the mean age of Vietnamese patients with CRCs were younger than that of Japanese patients by 10 years in the present study. It is natural that we underline the high frequency of CRC at early age in Vietnam.

2) The manuscript was revised by a native researcher again.

We now hope that our paper will be suitable for publication in *BMC Gastroenterology* and look forward to hearing from you concerning your editorial decision.
Yours sincerely,

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