Reviewer's report

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

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Reviewer: Barbara Pardini

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Second revision of the manuscript by Miwata et al (MS: 1208173965133018). The work of Miwata and coauthors has not been improved as requested from both the Reviewers.

In particular, the following points have still not been covered:

1) Both Reviewers were pointing out the reduced dimension of the population under study. We understand that it may not be possible to enlarge the sample group, but Reviewer 1 was suggesting to report some data from the literature (if any). Authors did not even consider this suggestion and they just reply in the same way to both Reviewers. In addition, the fact that they found significant differences it is not a sufficient reason for not enlarging the group of study. As it is the 2 groups are not comparable.

2) Both Reviewers recommended a rephrasing and rewriting of the Discussion and a clarification of the aim of the study in the Discussion. Authors did not touch anything in the Discussion: they just moved the last paragraph (a well know classification of colorectal cancer pathways) into the Introduction. Adding a sentence “A more detailed view is needed, of course” is not a sufficient revision. Moreover, the paragraph added in the Introduction did not help in clarifying the aim of the study: it is not clear yet the reason of the choice of the specific biomarkers selected.

3) Reviewer 1 was pointing out that the study analyzed somatic mutations and was asking not to use “genetic pathways” since it was not correct. Authors changed “genetic pathways” with “genetic alterations” which is misleading as the previous term.

4) Both Reviewers criticized Figures as they were of really poor quality. The justification given by authors was: “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.” What do these sentences mean?

5) Reviewer 2 asked for being more clear in the Abstract on the number of subjects analyzed. The suggestion has not been taken into consideration.

6) Reviewer 2 asked for a revision of the language by a native speaker. It is obvious that this has not been done since the reply to Reviewers is full of mistakes (for instance “we have fully understanding”) and all over the manuscript there are no changes of the previous errors found.
7) Reviewer 2 was pointing out the presence of a bias in the period of sampling of the 2 groups. The reply by authors considered only environmental exposure and cultural habits. The main problem from the epidemiological point of view in the comparison of small sampling of 12-years or of 2-years consist in differences in the diagnosis (in 12 years colorectal cancer prevention has improved lot), in the time distribution of samples recruitment (especially for 12 years long sampling, you can have 70% of samples collected in the first 5 years with methodologies that could be really different after additional 7 years especially in a developed country like Japan..). At least Authors should have considered and discussed this point among the limitations of the study.

8) From the epidemiological point of view colorectal cancer patients aged 50 years old are not considered early onset patients.. Again, Authors confused the terms. Early onset cancer samples are a group of patients having ALL an early age of onset. It is not a question of mean age. The two study group included in the study spanned a range of age comparable but it is the internal distribution of the age of cases that was different (you can see from the different mean). This difference would have been probably even more notable if Authors have shown median age.