Reviewer's report

Title: Differences in the genetic pathway(s) between Vietnamese and Japanese colorectal cancers

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Reviewer: Barbara Pardini

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The work of Miwata and colleagues investigated the frequency of selected mutations in K-ras gene, in mtDNA and MSI-H status in a group of colorectal cancer cases from Vietnam. Authors compared these frequencies with those measured in another group of colorectal cancer cases from Japan and found significant differences among the 2 groups in terms of frequencies of the selected mutations.

Besides the study may have some potentialities, after a careful reading it appears a very weak study.

Major points:

1) The Vietnamese study population is quite small in comparison with the Japanese and this discrepancy emerge especially in the context of MSI-H status (27 versus 130). Moreover, in the abstract is stated that 60 Vietnamese CRC were compared with 233 Japanese CRC but in none of the reported analyses are reported such numbers for the Japanese cohort.

2) I think that it would be also important to evaluate the mutational status also considering the corresponding “healthy tissue” of the patients since there could be an over representation of familiar cases.

3) Another aspect to be considered consists in the high differences in the 2 populations: Vietnamese CRC are distinctly different from the Japanese CRC investigated for age distribution (10 years of difference in the mean!!) and for tumor location and histology. Even if in some analysis the distribution is not significantly different, I would consider carefully a comparison of predominantly Colon cancers (the so called “right side tumor” in the paper) (Vietnamese) against predominantly rectal cancers (the so called “left side tumor “ in the paper) (Japanese). Personally, I really do not like this classification since there are several studies that reported clear genetic and molecular differences among colon and rectal cancer tissues.

4) Authors never considered also that the 2 groups were collected in quite different periods: Vietnamese CRC in the period 2009-2011 and Japanese in 1998-2010. I think that also this aspect should be also carefully considered because especially environmental exposures and cultural habits (lifestyle, diet etc) could be quite different when considering a 2-years or a 10-years lapse.

5) Figures are not really clear (especially figure B and C). I may suppose that these presented are among the best pictures obtained, then I have some doubts
that the observed different frequencies in mutations could be due also to a misinterpretation of the gels.

6) Finally, in the manuscript authors never justified or explained why Vietnam has been compared with Japan. Besides the availability of samples there should be other reasons (ethnicity, common history, lifestyles etc)

Minor comments:

1) All over the text authors underlined the high frequency of CRC at early age in Vietnam. However, the studied population is far from being at early age, because the age range is 32-79 (similarly for the Japanese). Authors should be more careful in the Introduction and in the Discussion sections.

2) A revision of the language by an English native speaker is recommended since various section are redundant and not clear.