Reviewer's report

Title: Irradiation-induced telomerase activity and gastric cancer risk: a case-control analysis in a Chinese Han population

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Reviewer: Sean AM Cleary

Reviewer's report:

The report by He et al. is well written, concise, and describes a straightforward series of experiments. The authors report differences in radiation-induced telomerase activity in peripheral lymphocytes in a series of gastric cancer cases and controls. The objectives and hypothesis of the project are relevant clearly stated. The statistical analysis was appropriate and well controlled for differences between cases and controls.

Major Compulsory Revisions:

1. The authors state that their findings support the hypothesis that inherited increased radiation-induced telomerase activity is a risk factor for gastric cancer. I do not think the experiments performed can fully support that hypothesis and needs to be qualified by expanding on the limitations of the study. First, since blood was drawn in gastric cancer cases after diagnosis we cannot determine whether telomerase activity was increased prior to the development of cancer. In other words, is increased telomerase activity a cause of cancer or the result of a systemic response to malignancy. The latter hypothesis cannot be excluded since increased telomerase activity is seen in activated lymphocytes. Therefore it cannot be determined whether the results of the study are simply a marker of cancer or a risk factor for cancer development.

2. The authors state in their objectives (p4) that they designed this experiment to investigate inherited discrepancy of radiation induced telomerase activity. There is no aspect of the study which addresses whether the observed differences in telomerase activity were inherited or not. Given the issues raised in comment #1, the authors cannot differentiate between inherited differences in telomerase activity and acquired differences in activity either as a result of associated factors (age/smoking/H.pylori) or in response to the development of cancer itself. Th role of heritability could be determined by testing telomerase activity in blood-relatives of gastric cancer patients vs controls. Either the authors should provide additional experimental evidence of ‘heritability’, revise their objectives, or address this weakness in their study.

3. It would be helpful if the authors provided some indication as to whether they examined the clinical and pathologic characteristics of the malignancies among the cases. Some reports have associated telomerase activity with microsatellite instability while others have noted higher telomerase activity with increasing tumour stage. If telomerase activity did not correlate with clinical stage or tumour
characteristics, this would be easy to do and helpful to the readers.

Minor Essential Revisions

1. The authors do not provide any information on a-priori statistical power calculations to determine the magnitude of difference in telomerase activity which could be reasonably detected by their study. This information should be provided.

Discretionary Revisions

1. The authors used H.pylori antibody to determine H.Pylori status. It is unclear how many cases/controls had active H.pylori infection vs those who had previously treated infection. This information may be useful as active infection may increase telomerase activity in circulating lymphocytes.

2. The authors should comment on the accuracy of their assay compared to more recently developed fluorescent real-time PCR based assays.

I recommend:
Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of Interest:
An article whose findings are important to those with closely related research interests

Quality of written English:
Acceptable

Statistics:
Yes, and I have assessed the statistics in my report.

Conflicts:
I declare that I have no competing interests