Reviewer's report

Title: Identification of gene-based biomarkers of alpha particle radiation exposure in human blood cells

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Reviewer: Nan Mei

Reviewer's report:

Re: Chauhan et al., “Identification of gene-based biomarkers of alpha particle radiation exposure in human blood cells”.

In this manuscript, the authors observed that alpha-particles and X-irradiation, with different dose rates and different LET radiation types, induced DNA damage as the increases in the alpha-H2AX signal; identified 31 genes as differentially expressed genes in three exposure groups after alpha-particle exposure; and validated these gene expression changes using X-irradiation and qRT-PCR. The following are the major concerns of this reviewer.

1. The information for each experiment is not clear in the Methods, Results, and Figure Legends. It seems the authors performed microarray analysis with validation in peripheral blood mononuclear cells (PBMC) and miRNA expression in white blood cells (WBC), both under alpha-particle exposure; conducted customized gene array in white blood cells after alpha-particle or X-irradiation; and determined DNA damage in white blood cells, with both irradiations. Please clearly mention the cell type used in each experiment (e.g., page 8, H2AX assay and page 15, DNA damage, only used “cells”).

2. Alpha-particle irradiation is major part of this study. Why the authors determined gene expression (31 common genes) in PBMC and miRNA expression (only one miRNA) in WBC after alpha-particle irradiation? What was the relationship between two expressions in two cell types? Do the authors consider miRNA expression in PBMC?

3. Since “the 31 gene panel was responsive in the alpha-particle exposed WBC and was shown to exhibit --- from X-irradiation cells, with no identification of alpha-particle specific transcripts” (Abstract), the authors did not identify any gene-based biomarker after alpha-particle irradiation. Therefore, they should consider changing the title.

4. Pages 15 and 16: the discussion about the differences in H2AX signal should move to Discussion.

5. Page 17, customised qPCR contains 31 genes from Figure 2 and 55 genes from the literature. However, it seems Figure 9 has 87 genes.

6. Figure 1 is not necessary in the main text. Please move it to supplementary Figures and Tables.

7. Figure 4: how many genes in each group (A, B, C)?
8. Figures 5-8 are basically same, should be combined as Figure 5A, 5B, 5C, 5D. It will save the space from similar figure legends.

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

'I declare that I have no competing interests'