Reviewer's report

Title: Global gene expression analyses of bystander and alpha particle irradiated normal human lung fibroblasts: Synchronous and disparate responses

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Reviewer: Kevin Prise

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This manuscript reports studies of global gene expression patterns in directly irradiated and bystander cells. Specifically the authors have irradiated normal human lung fibroblasts with #-particles using a configuration where neighbouring non-irradiated or bystander cells are present. They report profile data 4 hours after irradiation, showing a significant p53 driven response in directly irradiated cells but a reduced response in bystander cells. In contrast both direct and bystander cells show a strong NFkB driven response which occurs over identical timescale. An intriguing finding is the observation of two waves of expression of some genes, immediately after irradiation and 4-6 hours later. The work follows on from previous elegant studies from the authors analysing gene expression profiles after irradiation and other work characterising bystander mechanisms. The manuscript is well written and presented and I only have the following minor suggestions.

1). Title, I feel this may be better as differential responses, rather than disparate?
2) Page 3, line 7, change “quite well” to “well”
3) Page 3, line 20, the authors could reference work showing differentiation also to occur as a potentially protective process. See for example Belyakov et al., 2006, Mutation Res., 597, 43-49.
4) Page 9. The authors discuss an increased variability in the bystander cells for both micronuclei formation and gene expression but are not specific as to what the extent of this is. A more quantitative analysis of how variable this is would be of benefit to the reader.

4) Figures 2 and 4. For the IPA pathways analysis it is not clear from the figures what the scale represents in terms of the fold changes, it looks like 12 to -4?
4) Radiation quality. The authors have previously presented studies of gene expression profiles after low LET radiation. Some comment on the likely role of radiation quality would be appropriate, even if it is simply to discuss differences between low and high LET for direct irradiation.

Level of interest: An article of outstanding merit and interest in its field

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