Reviewer's report

Title: Dietary Flaxseed Administered Post-Thoracic Radiation Treatment Improves Survival and Mitigates Radiation-Induced Pneumonopathy in Mice

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Reviewer: Kei Iwamoto

Reviewer's report:

This manuscript evaluates the efficacy of a flax seed diet in the mitigation of radiation-induced lung sequelae. This is a well-executed study that should prove important for improving treatment of radiation injury in the lungs, and possibly in general, not only in the event of a nuclear accident or terrorist attack but also during radiation therapy. The study continues from the author’s previous work on dietary flax seed’s ability to protect lung when administered before irradiation. In this manuscript, they show a remarkable effect of dietary supplementation after irradiation on inflammatory response in the lung. Overall, there are no major problems. The following are some minor questions that need to be addressed:

Minor Essential Revisions

1) Should mention in figure 1 legend and materials and methods page 7 that the mice were maintained on the diet after initiation until termination. Page 12, first paragraph; it needs to be clarified whether the mice were maintained on their respective diets for 4 months or each group was on the diet for 19, 16, 14, 12, or 10 weeks – the latter appears to be the case (according to figure 1), but the text seems to imply the former. It becomes clear after reading the entire article, but there is ambiguity in the beginning, which needs to be corrected.

2) What is the HVL of the x-rays? Or if the HVL is unknown, give the manufacturer of the x-ray tube.

3) In the survival plot, ‘n’ is given as 20 and 30 for unirradiated and irradiated groups, respectively. Does this mean 10 mice each for the 0% FS and 10%FS groups and 5 mice each for the irradiated groups? Was this repeated for the second independent experiment so that actually there were 40 and 60 mice used total?

4) There are misspellings and grammatical mistakes throughout the manuscript. Some, but not all, have been listed here: Page 4, incomplete last sentence of first paragraph; Page 10, line 5, “pre-adopted” should be “pre-adapted”; Page 12, top, it should just be “results” not “results and discussion”; Page 12, 4 lines from bottom “let” should be “led”; Figure 2 legend, last line should be deleted; Figure 3, the dotted line described in the legend is missing; Page 17, line 1, “o significant” should be “a significant”; Page 21, first line, second paragraph “leeds” should be “leads”…
Discretionary Revisions

1) What is the significance of ED versus EL levels in the plasma? It is interesting that the EL/ED ratio increases in the FS+IR (0 wk) and FS+IR (+6 wks). Is there any radiation-induced metabolic significance to this? Certainly others have shown that the anti-oxidative potency of EL and ED are different; interestingly, although ED may be a stronger antioxidant, EL appears to be more effective against tumor cell lines. Additionally, regardless of the ratio, it is clear that irradiation decreases plasma ED levels and increases EL levels.

2) Change in body weight as a function of time would be much more informative than final body weight at the end of the study, since mice are continually dying throughout the 4 months and the thoracic irradiation will probably cause transient changes in weight as waves in cellular responses come and go during the 16 weeks, which may be modified by the diet as well.

3) Considering all the time and resources used to measure numerous cytokines, a more extensive discussion and interpretation of the results would be helpful.

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

Quality of written English: Needs some language corrections before being published

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.