Reviewer's report

Title: Functional p53 is required for rapid restoration of daunorubicin-induced lesions of the spleen

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Reviewer: Margareta Wilhelm

Reviewer's report:

In this manuscript Herfindal and colleagues describe that p53 is required for rapid restoration of daunorubicin-induced lesions in the spleen. The authors have treated p53 knockout and wt mice with daunorubicin and compared the onset of apoptosis and recovery after treatment. There are some concerns the authors have to respond to before publication, see comments below;

General comments:
The manuscript need to be more carefully edited, in several places it is not clear whether they have used one or more mice in their experiments, often refers to mouse instead of mice. Also trp53 vs p53 nomenclature is not consistent

The statistical data analysis need to be clarified ? In the bar diagrams there are stars which may be indicating significant values; however the p value cut off point (0.05, 0.01 etc) was not mentioned and no reference has been made to any significant values in the text.

Specific comments:

Figure 1
(A) The first sentence has to be changed, authors refer to (A) and (B) being wt and ko mice but this is not as it is in the figure.
1. The amount of apoptosis overall is relatively low, would like to see how much total cells death occurs, including necrosis.
2. It is not clear whether the cells were sorted for spleen-derived leukocytes before being treated or was the whole heterogeneous population used to investigate apoptosis. If not sorted then one should perhaps not refer to the population as spleen-derived leukocyte but rather splenocytes.
3. Spontaneous cell death can occur during the mechanical dissociation of primary tissue, a control or vehicle only sample should be included
4. Not clear why IDA was used, is it a positive control? Clarify in text or in figure caption. Also IDA concentrations and source is not mentioned in materials and method section.
(B,C)
1. A small figure legend would make it easier to grasp this results better
2. The right plot representing spleen weight after ionizing radiation is not explained in material and methods at all (time of exposure, strength of radiation etc.). Its relevance is not clear, how is it linked to the findings and contribution of this paper. Moreover, the number of mice used for this experiment (n=2) is too few to make any conclusions.

3. Why were the animals anesthetized rather than euthanized when the spleen was removed? And if anesthetized, what form of anesthesia was used?

Figure 2

For orientation purpose low magnification images of the spleen sections would be good. How were the pyknotic nuclei quantified? Were they counted in a specific area or within specific dimensions of the section? Do the stars in the bar diagrams refer to significant values? Then what are the p values and what is the p value cut off point (0.05?)?

(A)

1. What was observed in animals treated for more or less than 3 days? What is the significance of using 3 day, does it have clinical relevance, if so need to be mentioned.

2. What was observed in the red pulp sections with these stains, why were the lymph nodules (white pulp) investigate here?

(B)

1. Is this white or red pulp section?

2. N=1? Were there more of these observations of this kind, if so need to be mentioned otherwise result lose significance.

3. The two arrows are pointing to two different things.

4. I recommend this figure either is clarified and improved on.

(C)

1. The H&E images for p53WT do not correspond to the graphed data. The 4h graphed date shows more lipofucsin pigments and 24h less; the opposite is evident in the H&E images.

2. What was observed in white pulp regions of the spleen?

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

Quality of written English: Not suitable for publication unless extensively edited

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

Declaration of competing interests:

I declare that I have no competing interests