Author's response to reviews

Title: Generation of a selectively cytotoxic fusion protein against p53 mutated cancers

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Author's response to reviews:

Dear BMC Cancer,

Please find enclosed our revised manuscript with the details of the response to reviewers’ requests listed below. We have addressed all the mayo concerns and some of the discretionary items. We hope it is now suitable for publication in your journal. Best wishes and thanks for your help. Dr Deonarain

Reviewer-1 (Ghavami)

1. The thematically-related figures (Fig. 4 to 7) describing the animal therapy experiments have been combined into a single figure. This new figure is called Figure 5.

2. We have used HCT116 background cell lines with different p53 and p21 statuses in order to study the effects of delivering p21 using Antp-p21. These cell lines were the kind gift of Professor Vogelstein who is an acknowledged world expert in the study of p53 in colorectal cancer. Against a co-genic background, it can be seen that restoration of p21 tumour suppression function in p53-deficient and p21-deficient cell lines leads to tumour cell death, an effect which is more pronounced in the presence of chemotherapy. This outcome is explained in the text as a new Figure 3 and in the body of the text (page 9 and page 13). A new reference (28) has been inserted).

3. The experimental data from the original figures 5 and 6 (now Figure 5c/d and 5e/f) have been further explained in the main body of the text (page 11). The inclusion of Table also helps understanding.

4. Table 1 (description of therapeutic regimens used, page 7) was in the manuscript but was missed. We have uploaded it as a separate table.

5. Discretionary requests: We have also refined the figure legends to make them understandable as stand-alone items. However, we have not been able to do any cancer stem cell markers and discuss this data. The role of p21 in the maintenance of stem cells and cancer stem cells is less well understood and we feel that the mechanism of Antp-p21 action through the stem cell pathways would
require a lot more investigation.

Reviewer-2 (Widlak)

The major revision requested also asked us to study the effects in a cogenic cell model (item-2 above), so this has been done as explained.

Minor revisions:
1. As also requested above (in 1), some figures have been combined to make the paper more compact
2. As also requested above (in 3), figures 5 and 6 have been explained better
3. As also requested above (in 4), Table 1 has been included.
4. Any duplication in the figure legends and text has been removed.
5. We have noted the comments on toxicity and made a reference as such (page 13-14).