Author's response to reviews

Title: Cancer cell adaptation to chemotherapy.

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Author's response to reviews: see over
Dear BMC Cancer

Re: Manuscript ID 1088111205166407

We are grateful to the reviewers for their helpful comments, and are delighted that reviewer 1 has recommended acceptance of the manuscript. We have responded to the comments from reviewer 2 and made some further revisions to our re-submitted manuscript. The changes are summarised in the points listed below.

We have responded to the general comment from Dr S E Bates (Reviewer 2) by toning down our conclusions to suggestions and by removing the final paragraph of the introduction. In response to the specific comments, we have made the following changes and hope that this improves the clarity of the manuscript:

1. We have added text to the 1st paragraph of the results section stating that Figures 1b-e illustrate results from tumor-derived cells from multiple ovarian carcinoma patients taken pre- and post chemotherapy. At the end of paragraph 1, we have stated more clearly that the results in Figure 1f were obtained using tumor cells obtained from a single ovarian carcinoma patient: this is also stated in the figure legend.

2. We have moved Figures 1g-h to create a new Figure 2a-b. This means that Figure 2a-h is now Figure 3a-h, and the text references to these figures have been changed.

3. Reviewer 2 was previously keen to have all of the immunohistochemistry presented in the paper as a table, as photographs would only provide examples from individual patients. We concur and have provided the table as asked. The numbers are small and the results are not normally distributed: we therefore chose to present a median and range for the histoscore. The text is correct, and we have amended the Table 4 legend to state (n=16), instead of (n=11). Histopathology is a subjective discipline and immunohistochemistry is at best semi-quantitative. The H-score is one of several ways of tackling this problem, but does not represent a measurement – just a subjective assessment. The use of descriptive wording in the text should not be confused with statistical tests, which we feel to be inappropriate here, and we have amended the text accordingly to ensure that the word “trend” is not misinterpreted by removing the offending phrase from page 12 (results section).

4. We have added text to the newly renamed Figure 3 (old figure 2) legend stating that the numerical data corresponding to the graphs in the Figure 3 form part of Table 5. The samples in figure 1 are ATP-TCA results from matched samples before and after clinical treatment, while
the results shown in figure 3 show the results for single samples exposed to drugs in vitro for six days. There is therefore no relationship between these data.

5. ECF is epirubicin + cisplatin + 5-fluorouracil. This was previously first mentioned in the background, we have now added the definition of this regimen to the results section of the abstract.

We hope that the paper will now prove suitable for publication and look forward to hearing from you soon.

With best wishes

Yours sincerely

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