Reviewer's report

**Title:** Curcumin analogue T83 exhibits potent antitumor activity and induces radiosensitivity through inactivation of Jab1 in nasopharyngeal carcinoma

**Version:** 1  **Date:** 9 April 2013

**Reviewer:** Ingeborg Tinhofer

**Reviewer's report:**

The study of Pan and colleagues investigates the antitumor activity of the curcumin analogue T83 and its potential to inhibit Jab1 in nasopharyngeal carcinoma. The study is based on previous results from the same groups which revealed upregulation of Jab1 in NPC with a phenotype of radio- and chemoresistance.

**Major compulsory revisions:**

1) The rationale of the study is not given in the abstract and the main goals can only be delineated from the title. This information should be given.

2) The authors postulate that the antiproliferative and proapoptotic activity of T83 is based on its inhibition of Jab1. However, at doses at which significant growth inhibition was observed in clonogenic assays no effect on protein expression is visible in Figure 3 A. The authors should at least discuss this discrepancy.

3) It remains unclear to the reviewer why the authors used the cell line CNE2 for generating the radioresistant subclone CNE2R. In their previous study published in Oncogene, the defined CNE2 as radioresistant and concluded from a comparative expression analysis of three cell lines that high expression of Jab1 in CNE2 was responsible for their low sensitivity to irradiation. In contrast, the cell line CNE1 had lower levels of Jab1 and was more sensitive to cisplatin and irradiation. The authors should validate their recent data from CNE2 cells by using at least one other syngenic cell line model of radioresistance and should include CNE1 cells in these studies.

4) In line with point 2 a causal relationship between downregulation of Jab1 and radiosensitization by T83 remains questionable. The experiments presented in Figure 4 rather suggest that the inhibition of Jab1 by T83 is insufficient and/or not relevant for the observed effects on clonogenic growth. If the authors want to establish T83 as specific inhibitor of Jab1, they should demonstrate that ectopic overexpression of Jab1 reduces the sensitivity of cells to T83 treatment.

5) The reason for using such high doses for showing the differences in PARP and caspase-3 cleavage in figure 5E should be given. It would be more interesting to see whether there are any differences at those doses which have been used in the clonogenic survival assays.

**Minor essential revision:**
1) In figure 5 A-D, the same scale on the y-axis should be used, otherwise the graphs are misleading.

**Level of interest:** An article of importance 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.