Reviewer's report

Title: Effect of troglitazone on tumor growth and pulmonary metastasis development of the mouse osteosarcoma cell line LM8

Version: 1 Date: 23 November 2009

Reviewer: Olivia Fromigue

Reviewer's report:

The manuscript by Aizawa et al analyses the effects of troglitazone (TGZ) on a murine metastatic osteosarcoma cell line. The authors found that TGZ significantly reduces in vitro cell proliferation, cell migration and cell invasiveness. The authors also report a decrease in primary tumor mass, in neovascularization and microvessel density as well as pulmonary metastasis development in TGZ-treated mice compared to vehicle-treated group.

The paper is well written, the experiments are well designed, the results are convincing and appropriately interpreted. The references are adequate.

I thus highly recommend this study for publication in BMC Cancer.

Minor points:

1- Abstract : The Authors did not mention the inhibitory effect of TGZ on neovascularization and microvessel density.

2- Materials & Methods section : The Authors should homogenize the cell number at seeding and may rather specify cell number/cm2 instead of cell number/well or /plate.

3- Page 6 line 22 / page 7 lines 6 and 18 : The Authors should indicate that cells were treated "or not" with TGZ.

4- Page 13 line 20 : please define GW9662

5- Fig 3C, Fig 6B and page 15 line 1 : what form of MMP2 is detected on zymogramms? Does it reflect an increase in total inactive proform or an increase in active form of MMP2 (and thus an activation of the proMMP2 pool)?

The Authors should remind and discuss about the relationship between AKT phosphorylation/ activation level and MMP2 activity, previously described.

6- Fig 3A & B : How can the decrease in cell number (about 40% after 48h incubation in the presence of TGZ according to fig 2B) influence cell invasiveness and migration?

7- Fig 4A : The Authors should indicate the densitometric analysis of dose-dependent effect of TGZ on pAKT and total AKT levels. It could be interesting to indicate also the ratio of pAKT over total AKT (independently of
actin level). Is the dosage 10 µM TGZ really inefficient on pAKT/AKT ratio?

**Level of interest:** An article of outstanding merit and interest 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.