Reviewer's report

**Title:** Consequences of the cooperation between macrophages and the breast cancer cells MDA-MB-231 for angiogenesis. Proposed molecular mechanism and effect of tetrathiomolybdate.

**Version:** 2  **Date:** 19 December 2009

**Reviewer:** Cheryl Jorcyk

**Reviewer's report:**

Discretionary Revisions:
1) Perhaps an additional human breast cancer cell line, besides the MDA-MB-231 line, should have been included in the results, along with a discussion of the global importance of the data obtained from the authors' model system.

Major Compulsory Revisions:
1) The number of embryos/group used in the CAM assay was not described for Figure 1. There is no quantitative or statistical analysis of this data. There is only a single photograph for each group, and the quality of the photographs is inconsistent between them. There are no controls present, such as recombinant VEGF.

2) The cytokine array in Figure 4 was not performed in duplicate or quadruplicate. Furthermore, while Figure 2 suggests that coculture of MDA-MB-231 cells and macrophages results in a decrease in TNF# expression by ELISA, this is not confirmed by the cytokine array, putting the array data into question. Likewise, according to the array data, coculturing MDA-MB-231 cells and macrophages does not increase VEGF expression. This is not thoroughly explained in the Discussion section, as IL-6 and other cytokines produced by tumor cells/macrophages result in increased HIF1# resulting in increased VEGF expression in a non-hypoxic environment (Xu, Q et al, Oncogene 24, 5552-60, 2005).

In summary, while the authors present data to support an interesting question, some of the data is not statistically significant. The limitations of the results are not discussed adequately. Sections of the manuscript use poor English and could be improved, including the Title and the Abstract.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**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. CLJ