Reviewer's report

**Title:** Role of loss of full length CtBP1 expression in malignant melanoma

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**Reviewer:** Adam Riker

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BMC Cancer, Review of:
Reviewer: Adam I. Riker M.D., F.A.C.S.

Title: Role of loss of full length CtBP1 expression in malignant melanoma

Authors: Andreas Winklmeier, Ina Poser, Keith Hoek, Anja Bosserhoff

Summary:

This study describes the loss of CtBP gene expression (wild type), with the induction of a novel splice variant that has not been previously identified in human melanoma. The significance of this finding seems to be that the loss of CtBP is related to the invasive and migratory capacity of melanoma, via the downstream regulation of LEF/TCF components and related genes, such as MIA.

Points to be discussed:

1. Is the question posed by the authors well-defined?
   • Moderately defined. The authors have already looked into the loss of CtBP1 expression in human melanoma with subsequent increase in MIA activity. They wish to evaluate a more general role of CtBP1 and to identify associated/regulated genes. (DR)

2. Are the methods appropriate and well described?
   • Yes. However, only a single melanoma cell line is utilized. Would strengthen manuscript to evaluate other melanoma cell lines, in order to define what is the approximate percentage of melanoma cell lines that exhibit loss of CtBP1. (MC)

3. Are the data sound?
   • Yes. However, although co-immunoprecipitation is one way of showing the interactions between CtBP1-splice and TCF4 and snail, are there other methods to show this? Molecular-based methods? (DR)
   • Although migration and invasion assays are shown, it would greatly strengthen the manuscript if in vivo data/analysis were present. Is it possible to inject stable transfectants of wtCtBP1 into nude mice, in order to see the in vivo effect of CtBP1 upon tumor growth? (DR)
   • Did the authors look at other assays, such as a basic scratch assay? (DR)
   • Would recommend that invasion data be shown for figure 2. (MC)
• Why do the authors limit their search to the melanoma array data GDS1989? Why not look at other related data sets that would greatly expand their ability to identify relevant genes involved in this unique loss of CtBP1? Many are available for public use through recently published articles (Riker, Kashani-Sabet, Hoek, Jaeger, Spatz etc). (DR)

• It would be interesting to see what other tumor histologies possess this CtBP1 splice-variant. Indeed, would show this data and colon cancer cell data. Possibly perform similar experiments on a non-melanoma cell line to see if the expected effects are similar. (DR)

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
• Two data sets are utilized and discussed, GDS1989 and Hoek et al (ref.#11). Would make clear reference as to how the readers may access these data sets for future use, as this is not clear. (ME)

5. Are the discussions and conclusions well-balanced and adequately supported by the data?
• Somewhat. The conclusions made could be greatly strengthened by adding some of the suggested experiments above. (MC)

6. Are limitations of the work clearly stated?
• No. The authors should point out the limitations and weaknesses of this study. (MC)

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
• Somewhat. They comment that further studies are necessary to understand the function and role of CtBP1 splice variants in carcinogenesis. They do not state who will be doing this work. (ME)

8. Do the title and abstract accurately convey what has been found?
• Yes. However, would re-word the title because it is awkward as written, ie: Role of loss of… (ME)

• Also, ALL melanomas are malignant and therefore would not use malignant melanoma, as is throughout the manuscript. This is a misnomer. Would change title to ….human melanoma. May use non-metastatic, vs. metastatic, invasive vs. non-invasive etc… but would NOT use malignant vs, benign melanoma as there are no benign variants that I know of. (ME)

9. Is the writing acceptable?
• Yes. There are a few typographical and grammatical errors throughout, however, these are fairly minor in nature. (ME)

Discretionary Revisions (DR)

Minor Essential Revisions (ME)

Major Compulsory Revisions (MC)
**Level of interest:** An article whose findings are important to those with closely related research interests

**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