Reviewer's report

Title: The correlation of WWOX, RUNX2, and VEGFA protein expression in human osteosarcoma

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Reviewer: Rami I. Aqeilan

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Paper by Yang et al investigated the correlation of WWOX, RUNX2 and VEGF in osteosarcoma using aCGH and immunohistochemistry on a relatively small number of samples. They found no correlation between WWOX and RUNX2, WWOX and VEGF but direct correlation between RUNX2 and VEGF.

Overall evaluation.

Before even judging this work, it requires extensive English editing to make it clear and readable. It is not understandable due to miss use of improper verb and tense of authors sometime refer to current findings or previous work. When referring to previous findings, authors should present perfect and when referring to new data, they have to use simple past. Several problems hindered this study pre-mature for publication:

Major points

1. The number of samples for genomic study is at best 10 though I could not see this in Table 2 (see below). This is a relatively low number to make any conclusion especially for correlation studies. This would make the conclusions of this article untrusted.

2. Authors stated in methods that they use 10 fresh osteosarcoma samples for aCGH while in Table 2, WWOX samples are 8; those for RUNX2 are 9 and those for VEGFA are 47!!! How can this be explained??

3. A positive correlation was found between VEGFA and RUNX2 only at protein level; VEGFA is already known as a target of RUNX2, however authors do not refer to it. It is to be expected thus to have this correlation.

4. Authors do not explain the association between RUNX2 gene amplification and loss of RUNX2 protein expression? This is very unusual!! Is it possible that there is an autoregulatory loop?

5. Authors stated that the lack of WWOX protein can promote RUNX2 expression, earlier in the text they stated that there is no significant correlation between WWOX and RUNX2 levels protein. They should check at which level RUNX2 is attenuated in RUNX2 gene copy number amplified samples.

6. There is no in vitro study to assess the association between the three gene to prove that actually high levels of RUNX2 can lead to higher VEGFA expression in osteosarcoma cells.
7. No clinical correlation studies on gene copy number amplification.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.