Reviewer's report

Title: Periostin is up-regulated in high grade and high stage prostate cancer

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Reviewer: Karl Chai

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The question posed by the authors was well defined, i.e., to evaluate for epithelial and stromal expression of periostin in human prostate cancer specimens for determination of any association or correlation with clinical parameters. The methods used were appropriate and well described. Periostin expression in human prostate cancer specimens was evaluated by immunohistochemistry using a periostin-specific antibody that had been previously cited by others. The human prostate cancer specimens of the training and test cohorts included in the tissue microarrays were described with detailed specific information. The IHC scoring was specifically and clearly described. The statistical methods were also clearly described and appropriate. The IHC images were presented with good tissue morphology and the staining intensities were appropriately represented, i.e., epithelial versus stromal; negative versus weak, moderate, and strong staining. The data reporting was done appropriately with the complete and detailed description and categorization of the prostate cancer specimens. The discussions and conclusions were supported by the data.

• Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

• Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Some minor language issues should be addressed. The following is a list of a few examples but not a complete list. The authors should make an effort at further polishing the language.

1. In the Abstract, under Conclusions, an “interesting” target for therapeutic interventions is a poor choice of word. The same word (“interesting”) was used in the same context on Page 10, Line 8 from the bottom. A change is suggested.

2. Page 3, Line 2, “mice” should be “mouse”.

3. Page 7, Line 12, “equal” should be “equal to”.

4. Page 16, Line 7, “insert” should be “inset”.

• Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

1. The authors should make the presentations of the results more consistent throughout the article to assist the readers in getting the most precise and
relevant information from the study. For example, in the Abstract the description of epithelial periostin staining was “Strong epithelial periostin expression was detectable in 142 of 418 (34.0%) of prostate carcinomas”. In the Results, the descriptions were “189 (58.2%) cases had an IRS equal or below 3 (median 3)” and “Only in 7.4% of cases the IRS for the epithelial periostin expression was above 6”. The reader will have to rely on the two tables to put together the information referred to in the Abstract by adding the “Periostin epithelial high” columns of the two cohorts (6 + 136 = 142).

2. Likewise, for the benign tissues, the Abstract states that “strong epithelial periostin expression was detectable in 11 of 38 benign prostate glands (28.9%)”. In the Results, these were described as “14 (36.8%, median IRS 2) (displayed) no epithelial periostin expression”. Along with that, 24 (63.2%, median IRS 0) were said to have displayed no periglandular stromal periostin expression. The readers are once again left with a small mathematical challenge before the authors’ ideas are clearly conveyed. It will help the authors’ delivery a great deal if these data presentations are re-sorted. Further, what’s the epithelial staining status of the 24 benign tissues w/o periglandular stromal staining? Also, what’s the periglandular stromal staining status of the 14 benign tissues w/o epithelial staining? In other words, how many are "double negatives"?

3. Outside of the two cohorts, the 20 metastatic, 19 hormone resistant, and 38 benign prostate tissues were not very well described. Major conclusive remarks were made of the data gathered from these tissues, so they should be better described. In particular as the journal does not have page limit issues, there should be more detailed descriptions of these tissues.

4. Prior to this manuscript, only one report by Tsunoda et al. was published on periostin expression in the prostate, with data gathered from a much smaller group of patients. This prior study was acknowledged and described by the authors. The difference in the observed results, however, was not explained. The study by Tsunoda et al. reported an association of prostate cancer (epithelial cell) periostin over-expression with low Gleason scores (6-7), but not with high Gleason scores (8-10). The authors of this manuscript reported an association of high epithelial periostin expression with high Gleason scores (8-10) in the test cohort but not the training cohort. A discussion of this difference in the observations between the two studies should be included in the manuscript. A discussion on the Gleason score/epithelial periostin expression association differences between the two cohorts in this study is also merited.

**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.