Reviewer's report

Title: Monocarboxylate transporter 4 (MCT4) and CD147 overexpression is associated with poor prognosis in prostate cancer

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Reviewer: Sven Perner

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The authors in the study elucidate the role of MCTs in prostate cancer. They individually evaluate the expressions of MCT1, MCT2, MCT4 and CD147 on both neoplastic and non-neoplastic tissue, further correlating it with patients’ clinicopathologic characteristics. The manuscript has been well written and the authors have aimed to study the correlation between the proteins and tumors in detail. However, there are some major limitations to this study.

Major Comments:

1. The main conclusion of this manuscript stating that MCT1/4 and CD147 are associated with features of unfavourable clinical course, is not novel, and has already been shown by Hao et al. The only new finding is the overexpression of MCT2 in prostate cancers, which revealed, besides younger age at diagnosis, no association with clinicopathological data.

2. The immunohistochemical evaluation of the TMA sections pertaining to cytoplasmic or plasma membrane staining seem to be very subjective. The manuscript would profit by including pictorial representations of scoring and staining intensity parameters for easier comprehension and clear definition. Also, the authors fail to state the reason for a combined scoring method. Was there a significant difference observed in the staining of a given area or a gradation in staining intensity?

3. The authors should explain why the positive cases were categorized into two groups (ISG and HSG). Also, this detail should be included in the methods and not the results section.

4. Referring to their introduction, it would be interesting to study the correlation of gp70 with MCT2 on neoplastic and non-neoplastic tissue. The gp70 antibody could be tested by IHC and then correlated to the patients’ clinicopathologic characteristics.

5. Contrary to the report by Hao et al., Gomes and collaborators found MCT1 to be expressed less intensively in neoplastic tissue as compared to benign tissues, suggesting a physiologically role of this protein. Still, the expression in tumours is reported to be associated with less favourable features. How do you explain this? The authors should expand their contrary finding in the discussion.

6. As suggested by the authors’ discussion, insight into the MCTs and CD147 expression in normal prostate tissue and PIN lesions would provide a better
understanding of protein function. This should be included in their study. Normal prostatic tissue is easily accessible through cystoprostatectomy material. Also, access to PIN lesions should not be a significant problem for the collaborating pathologists.

7. Figure 1 shows images with very faint IHC staining and counter staining. The image quality should be improved significantly.

Minor Comments

1. The authors very often use the term ‘correlation’ for MCTs and CD147. This word should be substituted with ‘association’ since a pure statistical association does not proof a correlation between two events.

2. Table 4 is not homogeneously formatted. The significant p-values should be made bold, thus making the significant results more eye-catching.

On the whole, this study has no biological explanation for the differences in protein expression and has been based on an a-priori formulated hypothesis. Therefore, this study has a marginal impact on the understanding of prostate cancer. In the conclusion, the authors state- ‘Importantly, since MCT4 and CD147 were associated with markers of poor prognosis, assessment of the expression of these molecules may help in the prediction of prognosis in prostate cancer’- This statement is too strong for a study where a small panel of antibodies were assessed on a cohort in order to expect a significant association.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.