Reviewer's report

Title: Cross-talk between alpha1D-adrenoceptors and transient receptor potential vanilloid type 1 triggers prostate cancer cell proliferation.

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Reviewer: Barbara Seliger

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The manuscript by Maria Beatrice Morelli and co-authors determined the role of the #1D-adrenoreceptors (#1D-AR) and the transient receptor potential vanilloid type 1 (TRPV1) expression pattern in both prostate carcinoma cell lines as well as tumor lesions as well as the effect of #1D-AR/TRPV1 signal transduction on cell growth. The authors demonstrated an increased expression of both receptors in prostate carcinoma cell lines and lesions when compared to benign specimens. Treatment with noradrenalin enhanced calcium flux and signal transduction pathways associated with cell proliferation, which could be inhibited by #1D-AR and TRPV1 inhibitors or by siRNA-mediated downregulation of both receptors. Although these data suggest that #1D-AR and TRPV1 might be novel targets for treatment of prostate cancer, there are a number of issues, which have to be addressed by the authors:

Major Compulsory Revisions
1. The differential frequency of TRPV1 and #1D-AR receptor expression suggested a heterogeneous population of prostate cancer cell lines. Please provide the mean specific fluorescence intensity and the number of experiments performed. Double staining of both receptors would have been more appropriate using flow cytometry and antibodies labelled with distinct fluorescence.
2. The quality of figure 1 should be enhanced.
3. Please provide further information regarding the prostate cancer lesions analysed.
4. The time course analyses in Figure 4 showed an altered pERK activation. Please discuss why P38 expression is not altered.
5. Please give information about the percentage of inhibition of both receptors by siRNA. The discussion should be shortened.

Minor Essential Revisions
6. There exist a number of typos throughout the manuscript.

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

Quality of written English: Acceptable
**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 interest.