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: Gabriella Czifra

Reviewer’s report:

The authors study the role of #1D-adrenoceptors and transient receptor potential vanilloid type 1 in prostate cancer cell proliferation. They show that these receptors co-expressed 40% of DU145 and 50% of PC3 prostate cancer cell lines. They describe the cooperative role of #1D-adrenoceptors and transient receptor potential vanilloid type 1 in NA-induced proliferation of PCa cells and they show the crucial role of PLC-PKC-ERK pathways in cell proliferation of prostate cancer.

Major Compulsory Revisions

1) Figure 1: How can you explain that „just” 40% of DU145 and 50% of PC3 co-expressed both receptors? Both cell line are androgen insensitive. Did you use any androgen sensitive cell line for example LNCaP cells? The expression of #1D-adrenoceptors and transient receptor potential vanilloid type 1 depend on the androgen sensitivity? Could you show the co-expression of #1D-AR and TRPV1 in benign prostate hyperplasia (BPH) and advanced prostate cancer (PCa) tissues?

2) Figure 2: The bicalutamide is a non-steroidal anti-androgen and it can bind to androgen receptor (AR). The mRNA expression of #1D-adrenoceptors and transient receptor potential vanilloid type 1 decreased in neoadjuvant treated PCa. How can the authors explain this result? What is a connection among #1D-adrenoceptors - transient receptor potential vanilloid type 1 and AR receptor?

3) Figure 6: The authors show that the PLC-PKC-ERK signal pathways play a role the NA induced cell proliferation of PC3 cells. They register that inhibition of these signals (alone) reduce the cell growth. These signals are parallel or successive? What happen if you use these inhibitors combination (Chelerythrine, PD98059, U73122) with NA?

4) Figure 7: I suppose the author used the transient gene silencing. How did you check the double gene silencing? I think you have 3 population of cells i)
si#1D-adrenoceptor, ii) siTRPV1 and iii) si#1D-AR/siTRPV1. How many percent of cells is double gene silenced? Did you check for example by FACS or immunocytochemistry?

Minor Essential Revisions
1) Figure 1 A and B: I don’t think that the authors have to show the negative control here (GARB-PE – RAG-FITC). If they want to show it they can in additional file.

2) Figure 4: You should write the molecular weight of ERK and p38 (Fig. 4B) and the molecular weight of the protein standard (Fig. 4C) at the western blot figures.

3) Figure 5: same comment as at Fig. 4!

Discretionary Revisions
1) Figure 4: I think the p38 is a correct form and not the „P38”.

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