Author’s response to reviews

Title: Lineage relationship between prostate adenocarcinoma and small cell carcinoma

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PEER REVIEWER COMMENTS:

GENERAL COMMENTS: My understanding is that the authors aimed to dedifferentiate prostate cancer cells using stem cell transcription factors identified in a previous study to be expressed in drug-resistant prostate cancer cells.

The method section is well detailed. Previously, it was maybe a bit too detailed (i.e. cDNA cloning), but now it is of reasonable length.

- Thank you for this positive feedback.

Some data are over-interpreted, such as gene expression in Figure 1. I don't think one can conclude much on hB2M expression.

- Our interpretation of B2M expression is based on both gel electrophoresis and array results, as well as on results in our previous publication. As we responded previously, the array result provided a quantitative measurement of B2M expression levels.

Importantly, the authors use 293F as normal cells. 293F cells are derived from HEK293, cells that are transformed and express the viral oncoprotein E1A.
- 293F cells are “normal” in the sense that they are not cancerous i.e. they will not form tumors. This cell line is used in many biotechnology applications.

REQUESTED REVISIONS:

To assess hB2M expression correctly in Figure 1, the samples should at least be on the same gel for comparison. Ideally, qPCR should be performed to conclude in low expression levels of hB2M from the strom cells.

- We are comparing the levels of B2M to the levels of scTF within these xenograft lines, not between each line. The band intensity of B2M within each of the lines is lower than those of the other genes. These reactions were done at the same time. This was confirmed by query of RNAseq analysis of these lines (which is mentioned in the paper). In later figures, the lower B2M after transfection of different cell lines was compared to the level of neo because neo is expressed by all of the transfected cells. The intensity of B2M is lower than that of neo. Lower B2M was again confirmed by array results. We also showed that B2M expression increased when stem cells were induced to differentiate. We have included this data in a new figure (fig. 6). This shows a link between B2M expression and cell differentiation.