Title: Identification of genes regulating migration and invasion using a new model of metastatic prostate cancer

Version: 1
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Reviewer: Frank Claessens

Reviewer's report:

Major comments

1. The establishment of the DU145-derived lines here described has already been reported in the paper from this group in Sci Reports 2013. Figure 1 and 2 of the here submitted manuscript are very similar (partly identical) to Fig 1, A, B and C from the published paper. Also in that paper, Western blots are shown for EpCam, vimentin, Ecadherin and Cytokeratin, for which in the submitted manuscript immunohistochemistry now demonstrates the same changes.

New for this manuscript is the gene expression data (versus the miRNA data in the Sci report) and the tests on effects of siRNA on cell motility and invasiveness.

I suggest therefore that the manuscript be rewritten now that the other work is published.

First paragraph: PSA screening is no longer accepted by FDA. Please enter this important information here.

2. There is a conceptual compromise made during the generation of this model for which the rationale is unclear: DU145 cells were injected in the prostate of nude mice. After 4 weeks or longer, the sentinel para-aortic lymph node was minced, and human cells growing out of homogenized lymph nodes were reinjected into prostate again. Why are cells taken from the lymph nodes reinjected in the prostate? This is different from the situation in patients, where there is obviously communication between the prostate (tumor) and the draining lymph nodes, but the route back (cfr to reinjecting cells back into the prostate) is less obvious. This should be well explained in the discussion.

3. Page 6: ‘DU145 cells … still have AR.’ This is a controversial statement. Except for this 2006 paper the authors refer to, most people that tried to detect AR in DU145 were unsuccessful. It is crucial therefor to prove with appropriate qRT-PCR that there is AR mRNA present in these cells. Otherwise it would be better to leave out this statement and rather emphasize the fact that DU145 cells might represent a dedifferentiated state and thus be a good model for AR-mCRPC which arises after enzalutamide and/or abiraterone treatment.

Minor essential points

1. In the introduction, some details on how the original DU145 cell line was established should be discussed.
2. On p.14 ‘metastatic incidence varied’ Do the authors mean ‘local metastasis’, or did they check for metastasis in bone and soft tissues?

3. On p.17, the ref 25 is used. Apparently, the new metastatic model presented in the her submitted manuscript is also presented in that paper. It is unclear how much overlap there is between ref 25 and this study.

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.

Declaration of competing interests:

'I declare that I have no competing interests'