Reviewer's report

Title: Androgen-regulation of the protein tyrosine phosphatase PTPRR activates ERK1/2 signalling in prostate cancer cells

Version: 4 Date: 7 October 2014

Reviewer: Lorna Harries

Reviewer's report:

Androgen-regulation of the protein tyrosine phosphatase PTPRR activates ERK1/2 signalling in prostate cancer cells. Munkley et al.

In this well written and interesting study, Munkley et al describe the androgen-regulation of the PTPRR gene, and provide evidence that decreased expression of this gene may be important in the progression of prostate cancer. This is an important finding from a well-executed study, and I have only a few comments.

Major compulsory revisions

1) Splicing patterns are commonly deregulated in prostate cancer. It would be interesting to see how many of the 226 novel androgen-regulated genes are alternatively spliced.

2) How was multiple testing accounted for in the pathway analysis? Did the authors use a False Discovery Rate (FDR) adjusted q value, and if so what cut off was taken as representative of statistical significance?

3) I would like to see more details of the deregulated genes; what were the effect sizes, 95% CIs and the p/q values?

4) What are the characteristics of the LNCaP cells – how representative are they of primary prostate tissue?

5) How were the doses and incubation times of androgen treatment determined? Are these levels physiologically relevant?

6) Why was PTPRR alone followed up functionally? What was the rationale for choosing this particular gene above the others identified from the pathway analysis for functional follow up?

7) Please can the authors give more details about the donors for the primary prostate samples in terms of age, ethnicity, tumour grade, drug treatment etc? Do these samples have heterogeneous patterns of PTPRR expression because the samples are dissimilar?

8) I am unsurprised that no differences are noted with HEK293 cells – these are embryonic kidney cells? Do the authors plan to look at other prostate cell lines?

9) How were the endogenous controls chosen? Were they shown empirically to be unresponsive to androgens? Did the authors check amplifications for
specificity given that SYBR green will bind any dsDNA?

Minor essential revisions

10) Minor point – there are a couple of places in the text where the symbols have become corrupted.
11) Minor point – please clarify on the graph axes precisely what is being measured – ie ‘PTPRR expression’ rather than ‘relative expression’
12) Page 6 line 15, please italicise ‘Spry2’ if referring to the mouse gene.

Overall, this is a very clear and interesting study, and I recommend publication following attention to these minor points.

Level of interest: An article of importance in its field

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'