Reviewer’s report

Title: Symbiotic energy metabolism based on lactate shuttle can sustain prostate cancer progression

Version: 1 Date: 1 August 2013

Reviewer: Fatima Baltazar

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The manuscript describes a symbiotic energy metabolism mediated by lactate between prostate cancer cells and associated stroma.

General comments: the findings are interesting, supporting the symbiosis in energetic metabolism between cancer cells and associated stroma, however they are not novel since they are very similar to the ones of Fiaschi T et al. (Cancer Res 2012, 72:5130-5140, ref. 27 in the present paper) in prostate cancer.

Major Compulsory Revisions:
1. The authors should make clear what is the novelty of the present manuscript when compared to the paper of Fiaschi T et al.
2. Abstract. The way the abstract it is written is it somehow confusing. Without reading the full paper is difficult to understand what has been done. It needs to be re-written.
3. Results. Line 321. The authors say that MCT4 was expressed in the central zone of cell aggregates, which could be the result of local hypoxia. How big are these aggregates? Does it make sense in 2D cultures? Please comment.
4. Figure 3A. The increase in MCT1 protein is not clear. The authors should quantify the bands to check.
5. Figure 4B. The increase in MCT4 protein is not clear.
6. Results. Results with WI-38 cells are shown but they were not mentioned in the Materials and Methods section.
7. Since MCT1 is also expressed in non-tumoral tissue, the effect of MCT1 inhibition should also be tested in normal prostate cells to better understand the consequences of MCT1 inhibition.

Minor Essential Revisions:
1. Figure 1E. There are no statistics to compare the treated conditions with the control ones.
2. There are several English incorrections throughout the text, which need to be corrected.

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