Author's response to reviews

Title: P-LAP/IRAP induced cell proliferation and glucose uptake in endometrial carcinoma cells via insulin receptor signaling

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Author's response to reviews: see over
Thank you very much for your efforts regarding our manuscript entitled "P-LAP/IRAP induced cell proliferation and glucose uptake in endometrial carcinoma cells via insulin receptor signaling". The comments raised by the referees were carefully reviewed, and our manuscript was modified according to their suggestions. We hope that the manuscript is now acceptable for publication in "BMC cancer".

Sincerely yours,

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Reviewer 1

We appreciate your helpful comments to improve our manuscript. Our responses point by point to the comments are shown below:

Major Compulsory Revisions

1) As you suggested, the sentence overstated the results of our study. This part has been revised in Discussion on page 16, line 13.

2) As you noted, it is important to show the relationship between IR or IRS-1 staining levels and tumor grade advancement. In our study, neither the IR nor IRS-1 staining levels showed any correlation to tumor grade advancement. We added this sentence in the Results on page 11, line 16-17.

3) As you suggested, it is important to examine the relationships between the expression of P-LAP/IRAP and those of GLUT4, IR, and IRS-1 in immunostaining. However, in this study, we only found that P-LAP/IRAP and GLUT4 were associated with progression of the tumor grade. This explanation was added to the Discussion on page 15, line 11-13.

Minor Essential Revisions

1) Thank you very much for your helpful advice regarding our lack of a description of the presence of serum. We added a sentence to Material and Methods on page 9, line 18.

2) Thank you very much for your advice regarding our lack of a description of the treatment time for insulin and wortmannin. We have inserted explanations in the figure legends of Figs. 5, 6.

3) Thank you very much for your guidance. We have corrected this throughout the manuscript.

Discretionary Revisions
1) As you noted, the GLUT4 band on Western blotting is somewhat indistinct. We blotted total membranes. We are considering improving the blotting methods to obtain distinct bands in future study.

2) As you suggested, the measurement of cell proliferative activity in a lower concentration of serum may have produced better results. We used a normal concentration of serum, but are also considering using a low concentration of serum in future study.

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Reviewer 2
We appreciate your productive comments to improve our manuscript.
Our responses point by point to the comments are shown below:

1) As you pointed out, it is important to analyze the phosphorylation of insulin receptor and insulin receptor substrate 1. The comparison of A-MEC, A-MEC-pc, and A-MEC-LAP cells showed similar degrees of phosphorylation. These results are additionally shown in Fig. 5. This explanation was added to the Results on page 13, line 9-10.

2) According to your suggestions, the manuscript was edited by a native English speaker.