Author's response to reviews

Title: GLUT1 gene is a potential hypoxic and prognostic marker in colorectal cancer patients

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Author's response to reviews: see over
Object: MS: 2086800294216368 - GLUT1 gene is a potential hypoxic marker in colorectal cancer patients.

Thank you for considering our manuscript for publication in your journal. We have revised it according to your reviewer’s comments.

To Reviewer # 1 (Dr. Cornelis Sier):

We deeply appreciate your effort and patience in reviewing our manuscript. You have given us a great deal of invaluable comments. All of our authors are also grateful your suggestions. Detailed explanations and replies to your comments are as follows:

Major Compulsory Revisions:

Question 1: Remove from the manuscript (including the title) all claims regarding the prognostic value of GLUT1.

Answer: Thank you. We have gladly eliminated all claims regarding the prognostic value of GLUT1 form the manuscript (including the title). (Line 1, p. 1; Line 24, p. 3; Line 14, p. 22)

Question 2: Carefully check the data in Table 4 to ensure that the calculations are correct.

Answer: We appreciate this comment. We have carefully checked the details, and have corrected these errors, including overexpression for HK1 60%, PGK1 70%, and PGK1 90% instead of 70%, 80% and 80%, in Table 4, and rewritten the related descriptions in the revised version (Lines 4 and 5, p. 17 and Table 4).
**Question 3:** Please include additional discussion of the data obtained from peripheral blood.

**Answer:** Thank you suggesting this. We added a description of the data obtained from the peripheral blood to the Discussion (Line 15–20, p. 22).

**Minor Remarks:**

**Question 1:** Abstract: The background section should indicate that this study is about colorectal cancer. The same goes for the cell lines used in the methods section.

**Answer:** Thank you for pointing this out. In the background section and methods section of this draft, we now indicate that this study is about colorectal cancer (Lines 5 and 7, p. 3).

**Question 2:** Check spelling of words like tumor(i)genesis.

**Answer:** Thank you for pointing this out. We corrected this mistake in the revised version (Line 22, p. 5).

**Question 3:** There are now 3 sentences in the introduction describing the aim of the study and they are not corresponding.

**Answer:** We appreciate your mentioning this. We rephrased these sentences in the Introduction section (Lines 6 and 10, p. 7).

**Question 4:** Word ?addition?missing after CO2 (page 8, line 21)?

**Answer:** Yes, thank you. We have added the word “addition” after CO2 (Line 22, p.8).

**Question 5:** Too many decimals for SE (page 10, line 7, 19, and 20, e.g. 51.5\(\pm\)4.

**Answer:** We are glad to accept the comment and reduce the decimals for SE (Line 7, 19, and 20, p. 10).
Question 6: The reference to Figure 6 at page 16 is incorrect.

Answer: We appreciate your mention of this. We have corrected this mistake in the revised version (Line 9, p. 17).

Question 7: Figure 1 should be simplified by omitting the first 2 columns (control) because the actual controls in this experiment are the data for normoxia. Actually, if normoxia are put at 100%, than only the last 4 columns are necessary in this figure.

Answer: We agree, so we will modify Figure 1 to omit the first two columns in the revised version (Figure 1).

Question 8: Tables 5 and 6 should be one table.

Answer: We appreciate this comment. We modified Table 5 and 6 to be one table and we have rewritten the table reference in the revised version (Lines 3 and 5, p. 18; Table 5).

Question 9: The significant P-value of GLUT1 (0.004) in Table 5, which actually forms the center of the paper, is over-interpreted: When the same statistical procedure is used for UICC groups II and III the P-value is actually 0.94, indicating that the previous significance is completely depending on the low number of patients in group I.

Answer: We appreciate your mention of this. We have added the additional descriptions of the data obtained from the peripheral blood in the Discussion section (Line 15~17, p. 22).

Question 10: Quality of written English: Needs some language corrections before being published

Answer: Language corrections have been done.
To Reviewer # 2 (Dr. Gemma Dominguez):

We deeply appreciate your effort and patience in reviewing our manuscript. All of our authors also appreciate your insightful comments. Our detailed explanations and responses to you comments are as follows.

**Minor comments**

**Question 1**: Misspelling: - page 5, line 22: tumorgenesis should be changed to tumorigenesis and - page 21, line 11: GTUT1 should be changed to GLUT1

**Answer**: Thanks for pointing this out. We have corrected those two misspellings in the manuscript (Line 22, p.5; and line 12, p.21)
To the Editor:

We have removed the second sentence of the Competing interests statement so that it now reads; “The author(s) declare that they have no competing interests.” (Line 2, p. 25).

Again, we deeply appreciate the reviewers for their effort in reviewing our manuscript. I eagerly look forward to your reply.

Sincerely yours,

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