Peer Review File

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Reviewer A

To reviewer A:

First, we would like to thank the Reviewer A for their recognition of our research and the many substantive suggestions they have put forward. After careful consideration, we found your suggestions very valuable, and we accepted almost all of them and made changes that will make our article better. Finally, thank you again for your advice.

Comment 1: In the "Methods" section, the authors should use subheadings to separate different bioinformatics tools, such as "GEPIA2" and "TIMER2," and clearly provide detailed parameters used for analysis.

Reply 1: We have modified our text as advised.

Changes in the text: Please see Page 6-7 , line 112-123.

Comment 2: The authors should include appropriate citations for "GEPIA2" and "TIMER2".

Reply 2: We have modified our text as advised.

Changes in the text: Please see Page 6-7 , line 115 and line 117.

Comment 3: Differential expression of OGDHL at the protein level should be explored. The human protein atlas (HPA) and/or UALCAN databases can be used for this purpose.

Reply 3: We have modified our text as advised.

Changes in the text: Please see Page 7 , line 124-128. Please check Figure 1F-H.

Comment 4: As the data in this study rely solely on the TCGA-KIRC dataset, it is recommended to perform survival analysis with other publicly available datasets for validation.

Reply 4: We are sorry that we were not able to do this fully. First, we did try to look at many GEO datasets, and almost no ideal dataset could meet the requirements, often lacking prognostic outcome data. To compensate for this shortcoming, we selected a dataset with a larger sample, 72 paired samples of primary tumors and para-cancerous tissues. To analyze the differential expression of OGDHL, the results showed significant statistical significance.

Changes in the text: Please see Page 6 , line 108-111 and Page 9, line 174-176. Please check Figure 1E.

Comment 5: The authors should provide more detailed information on the gene list and parameters used for the enrichment analysis.

Reply 5: We have modified our text as advised.

Changes in the text: Please see Page 8 , line 147-148. Please check Please see the list

of differential genes (|Log2FC| > 1, P < 0.05) in file named “supplement 1”.

Comment 6: The criteria used to separate patients into high- and low-OGDHL expression groups should be clearly described.
Reply 6: We have modified our text as advised. The criteria for all high- and low-expression groups were defined based on the median expression level of OGDHL in KIRC samples. We also mentioned it in the article, but perhaps in a less prominent position. So, we refer to it again in the methods section.
Changes in the text: Please see Page 7-8 , line 137-138.

Comment 7: The cited references in the "Discussion" section are in Chinese. Appropriate English-language references should be provided.
Reply 7: First, we are very sorry about this problem. Secondly, we would like to make it clear that the references we cite are all in English, not in Chinese. This is because when we use the Chinese version of word, there are some mistakes in the use of cross-references, resulting in the Chinese error prompt text in the discussion section. Now, we have solved that problem.
Changes in the text: Please see Discussion.

Comment 8: The manuscript contains numerous typographical errors, and the authors should revise the language to improve readability. English-language editing is highly recommended.
Reply 8: We apologize for the trouble this issue has caused you. With the help of experts and editors, we have found many details of the problem, and now it has been corrected. We have polished the English language in a professional platform for language.

Comment 9: The statement "However, immune system development was suppressed." in the Abstract (Page 3, line 43) should be removed as it may not be directly related to the study.
Reply 9: We have modified our text as advised.
Changes in the text: Please see Page 3 , line 54.

Comment 10: The result presented in Figure 2E and relevant texts on page 8, lines 140-143 could be excluded if they do not contribute significantly to the main findings of the study.
Reply 10: We have modified our text as advised.
Changes in the text: Please see Page 7, line 132-134 and Page 10, line 193-196.

Reviewer B

To reviewer B:
First of all, thank you very much for the Reviewer B's recognition of our research. The reference suggestions you gave us are of high academic value, which has expanded our

vision, and we can see that there is a certain correlation between our studies, which makes our article richer. Ultimately, we found that we have similar insights on glutamine, and there is great potential for further research in the future.

Comment 1: In this study the authors investigated the role of OGDHL in ccRCC, through bioinformatics analyses. This is a well performed study with interesting results. I have some comments: Renal cell carcinoma (RCC) is essentially a metabolic disease characterized by a reprogramming of energetic metabolism (PMID: 36960789; PMID: 30983433, PMID: 36430837, PMID: 36310399). In particular the metabolic flux through glycolysis is partitioned (PMID: 29371925, PMID: 28933387, PMID: 25945836), and mitochondrial bioenergetics and OxPhox are impaired, as well as lipid metabolism (PMID: 30538212; PMID: 32861643, PMID: 29371925, PMID: 36430448). In this scenario it has been shown that OGDHL is an important regulator of cell metabolism. These findings should be referenced and discussed.
Reply 1: We have modified our text as advised.
Changes in the text: Please see Page 14-15, line 304-318.

Comment 2: In addition, renal cell carcinoma is one of the most immune-infiltrated tumors (PMID: 31527133, PMID: 30738745). Emerging evidence suggests that the activation of specific metabolic pathway have a role in regulating angiogenesis and inflammatory signatures (PMID: 32345771, PMID: 28359744). Features of the tumor microenvironment heavily affect disease biology and may affect responses to systemic therapy (PMID: 37189689; PMID: 33265926; PMID: 36902242; PMID: 37373581). OGDHL can modulate immune cell infiltration and regulate immunoflogosis. These processes should be better discussed.
Reply 2: We have modified our text as advised.
Changes in the text: Please see Page 15, line 336-349.