

## Peer Review File

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### Review comments

The paper titled “Long noncoding RNA GPRC5D-AS1 in renal cell carcinoma: a molecular mechanism study” is interesting. Silencing the expression of lncRNA GPRC5D-AS1 can enhance the proliferation, invasion, and migration ability of renal cancer cell line 786-0, which can be weakened by the overexpression of lncRNA GPRC5D-AS1. However, there are several minor issues that if addressed would significantly improve the manuscript.

Reply: We also appreciate your clear and detailed feedback and hope that the explanation has fully addressed all of your concerns. In the remainder of this letter, we discuss each of your comments individually along with our corresponding responses. To facilitate discussion, we first rewritten your comments and then present our responses to the comments.

Comment 1: What are the relevant characteristics of the tumor microenvironment of renal cell carcinoma? What is the correlation between lncRNA GPRC5D-AS1 and the tumor microenvironment? What are the possible goals of future drug development? It is recommended to add relevant content to the discussion.

Reply 1: we have modified our text as advised. Changes in the text: see Page 12-13, line 325-336.

Comment 2: There are too few proteins related to proliferation, migration, and invasion in this study. It is recommended to increase the detection of related proteins.

Reply 2: we added some data Changes in the text: see Page 9-10, line 240-246.

Comment 3: There are many detection methods for cell proliferation, invasion and migration. If multiple methods are used, the results may be more reliable. It is suggested to add test results of other methods.

Reply 3: Thank you very much for pointing out this important issue. We agree with your opinion. Unfortunately, due to the limited time and funding, we did not supplement experimental validation. In this study, our aim is to preliminarily explore the molecular mechanism of lncRNA GPRC5D-AS1 in renal cell carcinoma. Even without this experiment, the article remains complete. Subsequently, we will conduct more in-depth research to determine the specific mechanism of this lncRNA in renal cell carcinoma.

Changes in the text: Due to limited time and funding, we were unable to supplement the experiment.

Comment 4: Can lncRNA GPRC5D-AS1 be used as a potential biomarker for patient risk

stratification and local regional metastasis in renal cell carcinoma? It is recommended to add relevant content.

Reply 4: we have modified our text as advised. Changes in the text: see Page 16-17, line 449-454.

Comment 5: There are many lncRNA that regulate the progression of renal cell carcinoma. Why did the author choose lncRNA GPRC5D-AS1 for research? Please describe the reason.

Reply 5: we have modified our text as advised. Changes in the text: see Page 4, line 85-86.

Comment 6: It is suggested that the research progress of lncRNA in renal cell carcinoma should be added to the discussion.

Reply 6: we have modified our text as advised. Changes in the text: see Page 12, line 309-324.

Comment 7: The introduction part of this paper is not comprehensive enough, and the similar papers have not been cited, such as “Prognostic value of immune-related genes in clear cell renal cell carcinoma, Aging (Albany NY), PMID: 31821170”. It is recommended to quote this article. Reply 7: we have modified our text as advised.

Changes in the text: see Page 15, line 412-420.

Comment 8: What is the impact of this study on the further treatment and prognosis of renal cell carcinoma? It is recommended to include relevant content in the discussion. Reply 8: we have modified our text as advised.

Changes in the text: see Page 16, line 421-432, line 442-447 We would like to take this opportunity to thank you for all your time involved and this great opportunity for us to improve the manuscript. We hope you will find this revised version satisfactory.