Peer Review File

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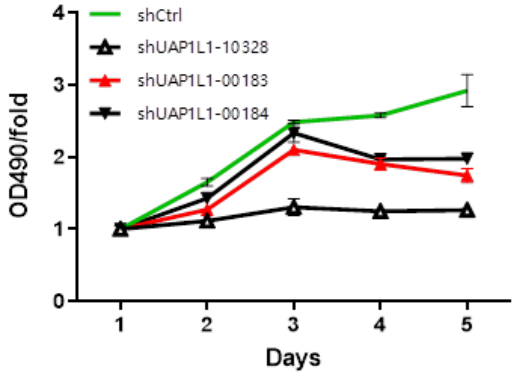
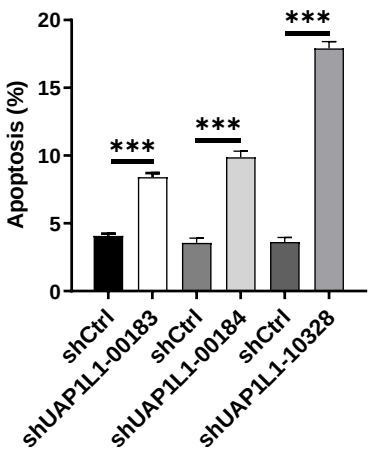
Reviewer A

The author studies the specific role of UAP1L1 in glioma. The finding was novel.

The author only uses one shRNA to knock down UAP1L1 in glioma cells, which could not avoid off-target effect. They should employ at least two different shRNA of UAP1L1.

Reply: Thanks for the kind suggestion from Reviewer.
Indeed, the off-target effect is a key factor that has to be excluded in the loss-of-function assays. Therefore, as suggested by the reviewer, 2 additional shRNAs (shUAP1L1-00183, shUAP1L1-00184) were prepared and the regulatory ability of 3 shRNAs on glioma cell phenotype was examined during revision period. As shown below, all 3 shRNAs possessed similar capability of inhibiting glioma cell proliferation and promoting glioma cell apoptosis. Therefore, we believe that the inhibition of glioma development by UAP1L1 knockdown in our study is not resulted from off-target effect. Still, we prefer to present the results of the shRNA with highest efficiency in our main text.
Changes in the text: Page7-8/L22, 1; P12/L16-17





Cell viability detected by MTT assay Apoptosis analyzed by flow cytometry

They should perform gain of function assay to study the role of UAP1L1 in glioma.

Reply: Thanks for the kind suggestion from the reviewer.
As indicated by the reviewer, gain-of-function assay is truly another important tool to investigate the role of genes in the development and progression of malignant tumors. However, our deduction and experimental results all clarified that UAP1L1 is a tumor promotor in glioma whose expression was fairly high in glioma. So we believe that gene knockdown model, other than gene overexpression model, is the better choice for demonstrating the functions of UAP1L1 in glioma. Of course, in our future work, we will examine gene expression in more glioma cell lines to select cell lines with relatively high gene expression for constructing gene knockdown model, and select cell lines with relatively low gene expression of constructing gene overexpression model.

It is better to explore the mechanism of how UAP1L1 promote cancer cell proliferation in glioma.

Reply: Thanks for the comments from the reviewer.
Frankly speaking, the mechanistic study is a weakness of this presented study. However, even so, we have applied a human apoptosis antibody array to preliminarily investigate the regulatory mechanism of UAP1L1 on glioma cell proliferation and apoptosis. The results showed that UAP1L1 knockdown induced the downregulation of cIAP-2, which is a well-known anti-apoptosis protein. Therefore, we have focused our future work on the regulation mechanism of UAP1L1 on cIAP-2, hoping to deepen the understanding of the function of UAP1L1 in promoting glioma.

Reviewer B

This study was to investigate the biological function of UAP1L1 in glioma. UAP1L1 is a novel biomarker in glioma, however this paper is lack of the mechanism of UAP1L1 in proliferation and apoptosis.

Reply: Greatly appreciate the positive comments and kind suggestion from Reviewer.

Frankly speaking, the mechanistic study is a weakness of this presented study. However, even so, we have applied a human apoptosis antibody array to preliminarily investigate the regulatory mechanism of UAP1L1 on glioma cell proliferation and apoptosis. The results showed that UAP1L1 knockdown induced the downregulation of cIAP-2, which is a well-known anti-apoptosis protein. Therefore, we have focused our future work on the regulation mechanism of UAP1L1 on cIAP-2, hoping to deepen the understanding of the function of UAP1L1 in promoting glioma.