Author's response to reviews

Title: Targeting mTOR/p70S6K/glycolysis signaling pathway restores glucocorticoid sensitivity to 4E-BP1 null Burkitt Lymphoma

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Author's response to reviews: see over
Dear Editor,

We would like to submit the enclosed manuscript entitled "Targeting the mTOR/p70S6K/glycolysis signaling pathway restores glucocorticoid sensitivity to 4E-BP1 null Burkitt lymphoma cells", which we wish to be considered for publication in BMC Cancer.

Glucocorticoid (GC) resistance is a therapeutic problem with an unclear molecular mechanism in lymphoid malignancies. Increasing evidence indicates that rapamycin can restore GC sensitivity in lymphoblastic malignancies by prevention of 4E-BP1 phosphorylation.

Interestingly, we found that, in 4E-BP1 null (rapamycin resistant) Burkitt lymphoma Raji cells and xenograft nude mice, combined rapamycin with dexamethasone can effectively reverse GC and rapamycin resistance and inhibit cell growth by inducing caspase dependent and independent cell death and G_0/G_1 cell cycle arrest. Our results showed that inhibition of mTOR/p70S6K/glycolysis signaling pathway is the key point of therapy in reversing GC resistant in Burkitt lymphoma patients. More important, the study provides further insight into the molecular mechanisms involved in rapamycin reversing GC resistance.

Considering that GC resistance is a very common phenomenon in treating lymphoid malignancies and clinically the main cause of treatment failure, we believe that this manuscript will be interesting to general readers of BMC Cancer.

All authors have seen the manuscript and approved to submit to your journal. The material has not been published or is not under active consideration by another journal. The research was conducted in accordance with the guidelines established by the internal Institutional Animal Care and Use Committee and Ethics Committee guidelines of Sichuan University.

Thank you very much for your attention and consideration.

Sincerely,

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