Author's response to reviews

Title: Oleanane triterpenoid CDDO-Me induces apoptosis in multidrug resistant osteosarcoma cells through inhibition of Stat3 pathway

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Sabina Alam, PhD
Senior Scientific Editor of BMC series journals

Dear Dr. Alam

We appreciate the constructive comments and suggestions from both you and the reviewers regarding our manuscript, "Oleanane triterpenoid CDDO-Me induces apoptosis in multidrug resistant osteosarcoma cells through inhibition of Stat3 pathway" (MS: 2018554733007574). We have addressed each of the reviewer’s concerns point by point while including additional clarifications. We have also made changes in the manuscript as a whole. Specific responses to the reviewers’ criticisms are listed below.

Referee 1.
Reviewer: Cheryl A London

The authors are commended for making substantial revisions to the manuscript in response to the concerns of all reviewers. There are only two minor comments.

Minor Essential Revisions

1. We have previously evaluated the U2OS line for IL-6R and have found very low expression by RT-PCR, while both gp130 and oncostatin M receptor are expressed highly, suggesting that IL-6 is unlikely to have much of an effect on these cells. Indeed, we have found that most of our OSA lines respond to Oncostatin M but not IL-6. While it is possible that different passages of this line
express the IL-6R to varying degrees, it would be appropriate to actually demonstrate STAT3 phosphorylation following IL-6 stimulation.

Response: We appreciate the reviewer’s suggestions. We have previously reported on the phosphorylation of Stat3 on U-2OS by IL-6. (Clin Cancer Res 2006; November: 6844-52, Mol Pharmacol 2007; 72: 1137–114,).

2. While the authors have calculated the CI to demonstrate synergy, they have not provided the methods for this. This should be included in the manuscript.

Response: We have added an additional paragraph on calculation of CI in the Methods section (Page 10).

We hope these changes will now make this manuscript acceptable for publication in BMC Cancer.

Respectfully,

Zhenfeng Duan