Response to Reviewer 3 Comments

**Point 1:** In this manuscript, the authors study the anticancer activity of Ailanthone and some hallmarks of its pro-apoptotic properties on two melanoma cell lines. Ailanthone is extracted from a Chinese traditional plant and has been reported to exhibit several biological activities including anti-cancer. The biological studies are well described and results appear to be sound. The results and discussion parts are well presented and conclude on the interaction with the PI3K/Akt pathway and mitochondria mediated apoptosis.

**Response 1:** Thanks for the comments.

**Point 2:** The author should precise in the Materials and Methods section the origin of the samples of Ailanthone. If the samples used for the biological studies are obtained further to an extraction process, data on the identity and quality of the samples should be provided.

**Response 2:** Thanks for the comments. Ailanthone (Cat no. SA9130, purity: ≥98%) was purchased from Solarbio Life Sciences (Beijing, China). We have added this information in the Materials and Methods section. Please refer to line 83-84 in the updated manuscript.

**Point 3:** For the cell proliferation assay, the authors should calculate the IC_{50} obtained on the two different melanoma cell lines.

**Response 3:** Thanks for the suggestions. We had calculated the IC_{50} obtained on the two different melanoma cell lines and added the values in the Results section. Please refer to line 154 in the updated manuscript.

**Point 4:** As a conclusion, the study appears to be relevant and sound, the manuscript needs only minor revisions.

**Response 4:** Thanks for the comments. We had tried our best to address the above comments by careful revision using point-by-point fashion to improve the quality of our manuscript. Please refer to the revisions above.