

Format for ANSWERING REVIEWERS

September 6, 2013

Dear Dr. Ma:

Please find enclosed the edited manuscript in Word format (file name: Revision - 5062)

Title: Cathepsins mediate tumor metastasis

Author: Gongjun Tan, Zhengke Peng, Jinping Lu, Faqing Tang

Name of Journal: World Journal of Biological Chemistry

ESPS Manuscript NO: 5062

We thank you and the reviewers for your careful reviews and constructive comments again. Incorporating your suggestions, we modified appropriately the manuscript including Tables and manuscript structure, and addressed each comment point by point below.

Reviewer 1

In this review, Tan et al. described a role of cathepsin family, especially in the tumor metastasis and invasion. Although authors well explained the function of cathepsins, this review is needed minor revision before acceptance. Major comments: 1) This review is a bit unreadable though each cathepsin is explained in detail. Authors should show Table 1 in the page 4, for example, "The cathepsin family consists of cathepsin A, B, C, (Table 1).", for supporting readers to refer. 2) The conclusion or expert opinions should be included as the last section. 3) Perspective concerning treatment for cancer patients by targeting of cathepsins may make this review much better.

Response: Thanks! We thank this reviewer for the positive and constructive comments.

1) This is a good suggestion, incorporating your suggestion, we have prepared a table to express cathepsin family members, **Table1**.

2) Thank! We added "**Conclusion**" in the last section.

3) Thank! This is a construction suggestion. We also add a section "**2.8 Cancer therapy targeting cathepsins**".

Reviewer 2

It would be better if authors could revise their manuscript as following: 1) for part 1. cathepsins family and their function: summarizing this part and expressing it in a table would be a lot easier for readers to understand and a small paragraph of description may be needed to highlight the differences of sub-types of cathepsins. 2) for part 2. cathepsins

mediate cancer metastasis: Making re-arrangement of subtitles in the order of the processes of tumor invasion, for example, moving the part 2.5 before part 2.2.

Response:

- 1) Thanks! We have prepared **Table 1** to express cathepsin family members
- 2) Thanks! Incorporating your suggestion, we have made re-arrangement in the order of the processes of tumor invasion, moving the part 2.5 before part 2.2.

Reviewer 3

The authors reviewed the role of various Cathepsins in cancer. General Comments: 1. Overall, the review article is well written and very organized. The table provided in the review is a nice summary of the role of Cathepsins in cancer. 2. The article contains information for various Cathepsins. However, the majority of the review focuses on Cathepsin B, which was already extensively reviewed by Gondi et al. in January of this year. In addition, there are not many recent references cited in this review. There are several recent manuscripts published that focus on the role of other Cathepsins in cancer (late 2012 – 2013). This review would be much stronger if the authors include some of this more recent information. 3. Since autophagy eventually use lysosomes as the final destination to degrade the intracellular/extracellular contents, it will be nice to discuss the relationship of the increased cathepsin activity and autophagy observed in the high metastasis cancers. Whether autophagy activity is also higher in these cancers. It has been reported that autophagy can also degrade collagen and thus it will be nice to add a session to discuss the possible relationship of cathepsin and autophagy that the authors have been discussed. 4. The title should be changed to “Cathepsins Mediate Tumor Metastasis”.

Response:

- 1) We thank this reviewer for the positive comment
- 2) Thanks! This is a good suggestion! We added some novel ideal and recent references.
- 3) Yes, this is a constructive suggestion. We added “**2.7 Cathepsins and autophagy**”.
- 4) Thank! The title has been changed into “Cathepsins Mediate Tumor Metastasis”

Thank you again for publishing our manuscript in the World Journal of Biological Chemistry

Sincerely,


2013-9-6

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and Xiangya Hospital, Central South University