

## Peer Review File

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### Reviewer A

This is an important review on EMT and cancer metastasis. Reference citation and a whole manuscript should be carefully re-checked. The references 72 and 73 are not in the reference list.

**Reply: Thanks to your comment and we have got the mistake corrected. We are sorry for this kind of mistake and we have checked the references carefully.**

### Reviewer B

**Thank you for your patient suggestions! We've looked and the researches which concentrate on adrenal cancer metastasis are not comprehensive so it's hard to introduce an adrenal-focused review and we've suggested deeper study on this field.**

Comment 1: In the abstract section, it would be better to add some background information about EMT and metastasis, and thus, to put the paper in a right context.

**Reply 1: This is a pertinent suggestion and we have added some information in the text. It really enhances the integrity of our manuscript and thank you for the suggestion.**

**Changes in the text: We added some introduction of EMT in the Abstract part, hoping this will improve the readability. (see page2, line20-24)**

Comment 2: In the section of “Treatment of metastasis”, the authors comprehensively listed all common non-target treatment strategies. Making a figure/table to compare the advantage/disadvantage of each treatment method would make this section more reader-friendly.

**Reply 2: This suggestion does help us to put the treatment strategies more clearly and orderly and thank you to bring it up.**

**Changes in the text: We have got this part 1.3 Treatment of metastasis in a table in place of literal description. (see page4-9)**

Comment3: The table of Gene and EMT is not comprehensive. Some key EMT-regulate genes, such as ZEB family, have not been included.

**Reply3: This is an important point and thank you for this comment. It is a big miss for our review and we have added the key genes to the table, hoping this supplement could make the table more comprehensive.**

**Changes in the text: In 2.3.1 Gene and EMT, we added the ZEB family. (see page10)**

Comment4: In the table in the section of “Cancer targeted therapy of EMT”, the authors listed a few targets for the current treatment. However, the relationship between these targets and EMT is unclear. For example, how let-7 and miR-34 are involved in EMT and what’s the consequence of EMT by targeting these two members? Moreover, this is the major section of this review. I would make the table more comprehensive. For instance, include the information about the current status of these targets (in preclinical study, under clinical trials, or have been approved).

**Reply4: Thank you for your careful reading and we agree that this is a very important part of the manuscript. We have added the precised target of therapy,**

**some mechanism and more details of them. Thank you again for your specific and constructive suggestion.**

**Changes in the text: in 2.4Cancer targeted therapy of EMT, we got the table more comprehensive and added more information of these therapies, such as clinical effects and mechanism. (see page20-21)**

Comment5: The title of the review is about EMT and cancer metastasis, however, the authors spent a lot of efforts to introduce the detection of metastasis and non-target treatments (surgery, chemo-, radiotherapies) of the disease. On the other hand, the content about EMT is general and superficial. I would expend the EMT part and make other sections concise.

**Reply5: Thank you for this suggestion and we have considered it carefully. Here is the reason why we arrange the content like this. Our manuscript focuses more on the molecules which are linked to EMT and cancer metastasis, and other introduction about EMT is mature and adequate, our description of more EMT itself may lead to repeat of contents. Also, the detection and treatments seem to need a collection and they do have a close connection with molecules concerning EMT, moreover, they are essential to clinical application. Thanks again for your careful reading.**

Comment6: The manuscript needs to be checked completely for English to avoid any grammatical errors.

**Reply6: Thank you for this comment and we have carefully reviewed the English in this manuscript and checked it twice. Thanks again for your patient and helpful recommendations.**

**Changes in the text: We have reviewed carefully in this whole manuscript, and made some modifications. We have kept the track changes in the revised**

**manuscript.**