

## Point-by point response to the Reviewers' comments

### Reviewer #1:

1.The section on alternative RNA splicing and its different types。 Five standard forms of AS events are mentioned in the third paragraph, including retained intron (RI), your acronym is RI, and in the fourth paragraph, your acronym is IR. Please consider if there is any clerical error.

**Response.** Thank you for your guidance. There are two words for this alternative splicing event, including Retained Intron (RI) and Intron Retention (IR). In this manuscript, IR acronym was mistakenly written without its full name. To eliminate any confusion both names and their acronyms are added.

2.The section on alternative splicing analysis tools。 Admittedly, choosing the right Alternative splicing analysis tools can play a very important role. However, while there is a strong connection between the Alternative splicing analysis tools and alternative splicing, I don't think this section is very supportive of your title. It is just a tool for analysis. With or without such tools, selective splicing has important implications for various physiological and pathological functions of stem cells. This part is a little bit redundant.

**Response.** Thank you for addressing your suggestions concerning the alternative splicing tools. By reviewing the literature, we found that it has not been published a comprehensive review article to address newly developed tools and their specific features. So, we decided to add this section in order to include all aspects relevant to alternative splicing in one article.

### Reviewer #2:

1. Some abbreviations are not shown at the first time.

**Response.** Thank you for your guidance. We tried to check and edit all of abbreviations.

2. The section "Knowledge gap in alternative RNA splicing in stem cell research" may be revised to include the comprehensive insights in stem cell, or otherwise change the section title to depict the computation in cancer

**Response.** We appreciate your suggestion as it helped us to revise the unclear and misleading title. The title has changed to “The challenge of Alternative RNA splicing analysis in cancer research”.