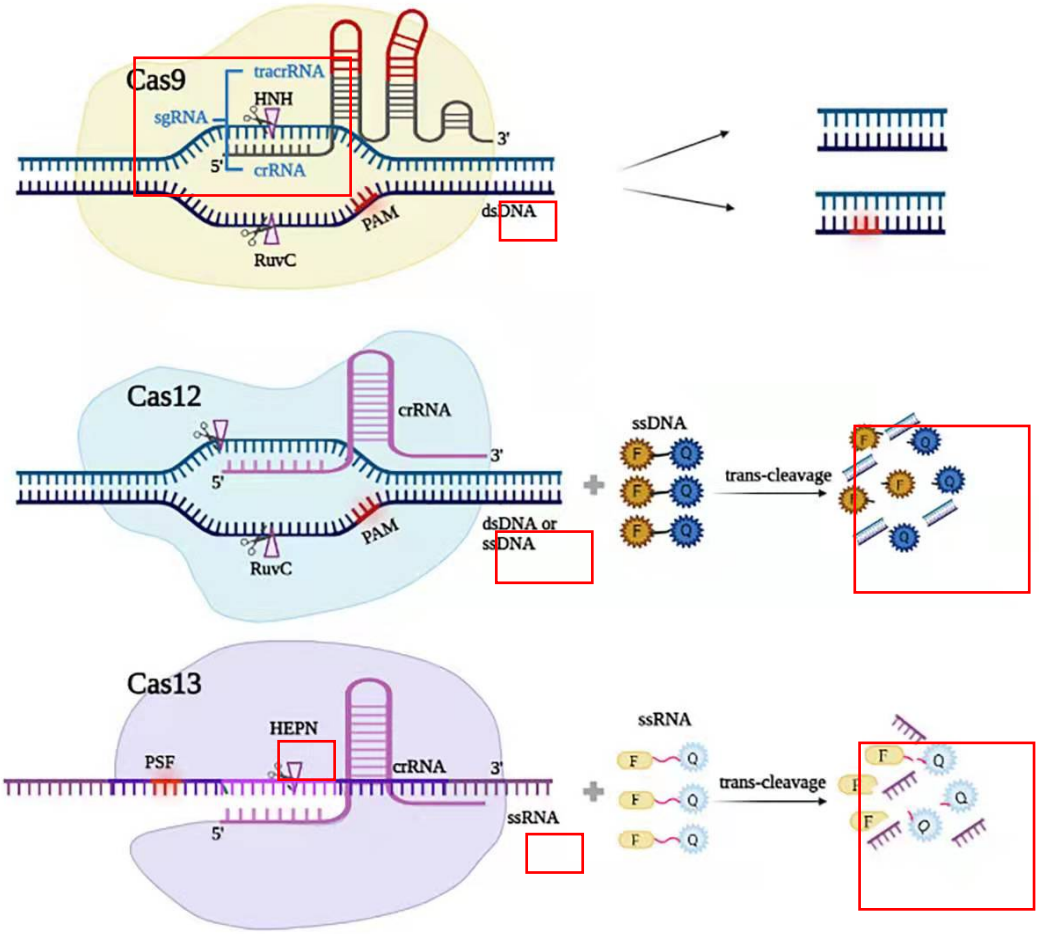
Dear Editor,

We are truly grateful to your and other reviewers' critical comments and thoughtful suggestions on our manuscript. Based on these comments and suggestions, we have made careful modifications on the original manuscript. Following your suggestions, we have made a second linguistic polish of the article. We feel appreciated for the proofreading by sagesci. All changes made to the text are in yellow color. We hope the new manuscript will meet the standard of the Journal. You will find our point-by-point responses to the reviewers' comments questions below. We hope that these revisions are satisfactory and that the revised version will be acceptable for publication in *World Journal of Clinical Cases*. Thank you very much for your work concerning our paper. Wish you all the best!

Reviewer #1:

1. Figure 1 gives just collateral activity of Cas9, Cas12, Cas13. This figure must include general mechanisms of gene editing by CRISPR/Cas in detail.

Description of modification: In response to expert opinions, we added content on the cleavage mechanism of Cas9 and added content on the cis-cleavage of Cas12 and Cas13; see the following figure for details, and the modified content is in the red picture box.



2. The authors well reviewed regarding diagnostic applications. However, a review for tumor

pathogenesis would like to include detect epigenetic changes as well as genetic changes.

Situation description: In response to expert opinions, we reviewed the articles on the application of CRISPR system in the pathogenesis detection of tumors in recent years, but there are too few articles on epigenetic and genetic changes in gene editing, which have been included as far as possible.

3. Therapeutic applications are not enough discussed. If the authors don't want to add sentences for therapeutic applications, they can add figure and/or table for delivery strategies or clinical trials. Alternatively, they can remove section for therapeutic applications.

Description of modification: In response to the opinions put forward by experts, we added the application of Cas12 protein in the treatment of clinical diseases in the article, enriching the content of this chapter.

4. In 'Challenges facing the application of CRISPR/Cas technology' section, the authors don't suggest solutions to overcome 'off target effect' or 'safety issues'. This point might be due to insufficient review for therapeutic applications.

Description of modification: In response to the opinions put forward by experts, we have made re-adjustment for the content of improving off-target effects, from three aspects: (1) predicting off-target sites; (2) optimizing the design strategy of sgRNAs; (3) changing the structure of Cas enzyme, stating and summarizing, and this chapter is reviewed in a deeper level.

Reviewer #2:

The review gives a new overview related to the current advanced scientific pieces of evidences that CRISPR/Cas technology is being contributed to clinical practice. The conclusion of the review provides a clear summary of the topic. But the Author has to discuss the recent developments of the technology in detail. So the review seems to be limited in quantity.

Suggestions on revision: According to the opinions of experts, we have consulted the literatures in recent years, supplemented the clinical disease treatment, off-target effect, etc., and the number of cited articles has also increased.