Dear Editor,

Please find enclosed a modified version of my Microreview manuscript “The novel CRISPR-dCas9 based DNA demethylation system”. To address the concerns and comments raised by the 2 reviewers, I made the following changes to improve and clarify the manuscript. It is my hope that these changes make the manuscript acceptable for publication in Microreviews in Cell and Molecular Biology.

Sincerely,

Jiang Zhang

Reviewer B:

1. Briefly state if you found the comments of Reviewer 1 helpful or not.

As for the relevance/importance of this manuscript, the reviewer suggests that the Recent Progress Part should be in Introduction part. Basically, the Recent Progress part of this manuscript is about existing different ways of delivering the proteins that can demethylate DNA, which is TET1 in the manuscript, to specific sites in DNA. These introductions of the targeted demethylation methods are the foundations and directly connect to the novel application of CRISPR/dCas9 demethylation system. So most of the Recent Progress part should stay the way as it is but the introduction of TET family can be moved to Introduction part.

Also, the reviewer mentioned that the first paragraph of the Discussion part should be moved to Recent Progress. It is in some ways reasonable since it is mainly about all kinds of controls the author did, which should be part of the experimental results belonging to Recent Progress part. However, these controls are more crucial for proving the validity of the demethylation results and should be more suitable in the discussion part even though these controls take up more space in the selected paper.

The last paragraph shouldn’t be in Introduction part since it is about the suggestion of a new targeted demethylation method which the authors could work on in the future.

2. What changes did you make to your manuscript as a result of the comments of Reviewer 1?

I moved the first few sentences about the TET family to the Introduction part. Some spelling mistakes were corrected.

Reviewer C:

1. Briefly state if you found the comments of Reviewer 1 helpful or not.

It is true that some terms are not explained clearly which makes it difficult for people outside of this field to understand. However, some specific names like the name of the gene cannot be left

out because they are important for people who are researching in this field to know what exactly it is. So more explanations will be provided for some terms.

The reviewer mentioned that more about application/potential/background can be added to show relevance. But I am not sure sure what kind of application or potential or background I need to add and what kind of relevance do I miss. More constructive suggestions are expected.

As for the complains about the abstract, I agree that it is too long without hitting the theme with clarity. Also, some polish of the structure of sentences are indeed necessary for readability.

2. What changes did you make to your manuscript as a result of the comments of Reviewer 1?

Some structures of sentences were rearranged for readability. The abstracted was shortened for clarity by deleting some details and redundancies.