

Peer Review File

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Reviewer A

Comment 1: This review summarizes the effects of M6A methylation on the regulation of non-coding RNAs and their impact on cancer. The review provides an extensive summary of non-coding RNAs and m6A functions in various cancers. I find this review comprehensive, though since there is a lot of information, and lots of non-coding RNAs, it may be helpful to the reader to organize/cluster the information somehow. Perhaps add a table or two summarizing the effects of each non-coding RNA change in M6A, and their effects on gene expression, in each of the mentioned cancer types.

Reply 1: We feel great thanks for your professional review work on our article. We have carefully considered your valuable feedback and made the following response: Our article mainly focuses on the m6A methylation site on ncRNA. The only change of ncRNA in m6A discussed in this review is the addition of a methylation site, so the content is not enough to form a table. If you would like us to summarize the functional changes of ncRNA influenced by m6A regulatory factors, we have already summarized the relevant information in **Figure 1**. In addition, due to the large number of downstream genes affected by ncRNA in different types of cancer, after discussing with other researchers, we believe it is difficult to summarize the relevant content into a table. We would appreciate your kindest understanding. Thank you again

Comment 2: M6A has versatile functions that act very differently depending on the regulation of different reader proteins. For example, in row 69-74 Mettl3 is mentioned to enhance m6A and enhance stability. However, some papers covering m6A in mRNA point that m6A most often reduces stability (Geula et al, Science, 2015). Since these effects are opposite to one another, this should be pointed out and discussed, possibly through highlighting the different effects of m6A reader proteins. Perhaps adding a figure that highlights the different functions of m6A readers, writers, and erasers can also help.

Reply 2: We feel great thanks for your professional review work on our article. As you are concerned, a figure that highlights the different functions of m6A readers, writers, and erasers really needed to be added. According to your nice suggestions, we have modified our text as advised (see Page 3, line 58-60) and added a figure (Fig a1) to our draft at Page 4, line 63-72. Meanwhile, the number of the following pictures has also been modified. Our additions to the manuscript are given in the red text with underline.

Changes in the text: Page 3, line 58-60; Page 4, line 63-72; Page 14, line 282; Page 22, line 455; Page 23, line 475; Page 25, line 507.

Reviewer B

Comment:

In the main text, please add the **Conclusions** section. Or you can modify the Discussion section to **Conclusions**.

Reply: Thank you for the suggestion, we have modified the Discussion section to Conclusions. Change in the text: Page 22, line 499.

Comment:

Figures

- All abbreviations in figures and legends should be explained. M6A in Figure 1 for example. Please check all abbreviations and provide the full names in the corresponding legends.
- Figure 2 is not clear enough. Please provide it in higher resolution.
- Please check if the following citations should be **Figure 4**.

prognostic indicators for malignant tumors in various cancers, including gastric cancer, bladder

cancer, and breast cancer. This review article provides an overview of these findings (Figure 3).

- The citations of figure 2, 4, and 5 are missing in the main text. Please check and add.

Reply:

- We have added the full names of all abbreviations in the corresponding legends.
- The new version of Figure 2 with higher resolution has been provided in the attachment of the email.
- We feel sorry for our carelessness. We have modified the citation to "Figure 4" in the

manuscript (see Page 20, line 463).

- The citation of each figure has been added to the manuscript separately (see Page 3, line 63; Page 12, line 272; Page 20, line 445; Page 20, line 463; Page 21, line 471).

In addition, we have made the following changes:

- An explanation of PLGA-PEG (si-LINC00958) NPs has been added on Page 21, lines 480-481.
- A legend about the m6A icon has been added in Figure 2.
- Figure 5 is subdivided into 4 sections (A to D), and citations to each part have been added to the manuscript (see Page 21, line 478; Page 21, line 484; Page 22, line 489; Page 22, line 495) and the explanation of each part has been added to the legend of Figure 5.
- The references in Figure 4 have been updated.

Comment:

In the text, the references should be cited **numerically and consecutively in the order of appearance**. Therefore, reference 38 should be cited before reference 39. Please check through and revise.

Comment:

The citation of reference 61 is missing in the main text. Please check and revise.

Reply:

We have checked and revised the above citations of references.

Comment:

Please note that citations in one place should **not** exceed 25 references. Please remove the citation.

Fig. 4 m6A-related non-coding RNAs serve as prognostic markers for tumors in different cancer types (124-157).

Reply:

We have revised the format of references in Figure 4 and removed some pre-2022 references, reducing the number of references to 24. (references 124-147). The revised image has been added to the attachment of the email.

Comment:

Please check if any references should be added since you mentioned studies.

1.Previous studies on m6A primarily focused on coding RNAs, but recent discoveries have revealed the significant regulatory role of m6A in non-coding RNAs.

2.Recent studies have shown that m6A regulatory factors play a role in regulating the metabolism of tumor cells by modulating the stability of lncRNAs.

Reply:

1.We sincerely appreciate your valuable comments. However, this sentence is in the ‘Abstract’ section of the article, so we didn't label references. If we have a misunderstanding, we hope you can contact us.

2.We have added a bibliographic citation to this sentence (reference 45).

Change in the text: Page 6, line 126.