

Peer Review File

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Reviewer A:

Comment1: The authors should add more detail explanation of m7G-related genes in the Introduction section. I did not understand what are the m7G- “related” genes. Are these associated with m7G regulator genes? I misread that m7G-related genes are regulator genes including METTL1 etc. For example, m6A- “regulators”, such as METTL3 and FTO, are reported as m6A- “related/associated” genes (reference A, below). In addition, are there any evidence that 11 genes detected in this study are accompanied by m7G methylation? Thus, I think that many readers have confusion of m7G-related genes and regulator.

Reference A: Kelei Guan, Xin Liu Jianhao Li, Yanxia Ding, Juan Li, Guangying Cui, Xichun Cui, Ranran Sun. Expression Status and Prognostic Value Of M6A-associated Genes in Gastric Cancer. *J Cancer*. 2020 Mar 4;11(10):3027-3040. doi: 10.7150/jca.40866. eCollection 2020.

Reply1: Thank you for your comments to our study. The two terms “m7G regulators” and “m7G-related genes” proposed in this paper are indeed confusing sometimes. As your understanding, “m7G regulators” were obtained from previously published research including METTL1, WDR4, NSUN2 and so on. “M7G-related genes” were obtained by cluster analysis of GC samples based on the 29 m7G regulators. We have added detail explanation of m7G-related genes in the Introduction (see Page 2, line 66-69). Since m7G methylation is a novel research field, few studies have been reported about it and the role of these 11 m7G-related genes in m7G modification has not been reported at present, which deserves further exploration in the future.

Changes in the text: M7G-related genes were obtained from the differential expression genes between the two clusters which were classified according to the expression level of 29 m7-G regulators in GC samples (see Page 2, line 66-69).

Comment2: In Figure 1, Flow chart. I did not understand the means of three m7G-related genes model. Where should we check the “three m7G-related genes model” in the text and Figure?

Reply2: Thank you for pointing out this vital mistake in this paper and we have revised “three m7G-related genes model” to “11 m7G-related genes model” in Figure 1 and remade it (see Page 7, line 153).

Changes in the text: Figure 1 was remade and resubmitted (see Page 7, line 153).

Reviewer B

Comment1: The abstract needs to be revised to clarify the difference between 29 m7G regulators and 11 m7G-related genes.

Reply1: Thank you for your valuable comments and we have modified our text as

advised (see Page 1, line 16-20).

Changes in the text: According to the expression similarity of m7G regulators, the samples obtained from the TCGA-STAD were further classified in two clusters which demonstrate different OS rates and genetic heterogeneity and the differentially expressed genes between these two clusters are defined as m7G-related genes. (See Page 1, line 16-20)

Comment2: Results may be revised to show what “Based on the m7G regulator of tumor classification” means in line 135.

Reply2: Thanks for your advice and we have explained the meaning of “Based on the m7G regulator of tumor classification” in the results (See Page 6, line 145-147).

Changes in the text: According to the expression parallelism of the 29 m7G regulators, the consensus clustering method was applied to cluster the STAD samples of the TCGA (See Page 6, line 145-147).

Comment3: TCGA data for GC specimens may be specified with data name or citation.

Reply3: Thank you for your valuable advice and we have specified with data name of GC samples in this paper.

Changes in the text: TCGA-STAD (See Page 1, line 17; Page 9, line 183).

Comment4: Differential expression and prognostic value of m7G-related genes in risk model may be revised to cite the Gene Expression Profiling Interactive Analysis (GEPIA) in lines 102-106.

Reply4: Thank you for your advice and we have cited the paper (See Page 20, line 441-442).

Changes in the text: [17] Tang Z, Li C, Kang B, et al. GEPIA: a web server for cancer and normal gene expression profiling and interactive analyses. *Nucleic Acids Res*, 2017,10.1093/nar/gkx247(See Page 20, line 441-442).

Comment5: In line 305, some of these m7G-related genes may be specified with gene names.

Reply5: Thanks very much for reviewer’s comments and suggestion and we have received it as the suggestion (See Page 16, line 326-329).

Changes in the text: A previous study shown the promoter-associated CpG island of ST6GALNAC3 is significantly hypermethylated in prostate cancer and may act as a relevant biomarker for prostate cancer prognosis (See Page 16, line 326-329).