Dear editor,

Thank you very much for your letter on the review of the manuscript entitled "**Let-7-related polymorphisms are associated with susceptibility to and prognosis of gastric cancer**" (No. 44516) for consideration for publication in ***World Journal of Gastroenterology***.

We are very grateful to the reviewers' reviewing and their comments. They are very helpful in preparing this revised submission. We have carefully considered each of the comments from all the reviewers and the editor, and made changes to the manuscript accordingly. Below are our point-to-point responses, in which our responses are highlighted in red.

Reviewer #1:

The authors have investigated the role of let-7 related polymorphisms in tumorigenesis and survival of gastric cancer. They found that the C allele of rs3811463 of LIN28A was associated with lower risk of gastric cancer and rs10889677 of IL23R was corresponded to the prognosis of gastric cancer patients.

Response: Thank you for your reviewing and comments.

I have just minor comments; 1. A total of 898 patients and 992 tumor-fee controls were enrolled in this study. In table 2, 4 and 5, case numbers were different in each SNP site and variables. The authors should explain the reason.

Response: Some variables have missing values, so the total number of these variables is less than the number of subjects included. For Table 2 and 4, we added the number of genotyping-failure for each SNP (13 subjects for rs13293512,10 for rs562052, 10 for rs547008, 26 for rs1143770, 2 for rs629367, 53

for rs10877887, 7 for rs10889677, 6 for rs7963551, 31 for rs712, respectively, failed to genotype. On Page 8). For the clinicalpathological parameters in Table 5, we added the number of missing in the note section under the table (Some of the variables have missing values (The missing number was not shown in the variables with missing (The missing number was 4 for the variable of WHO type, 18 for differentiation, 7 for T stage, 7 for N stage, 7 for TNM stage, 11 for lymphovascular invasion, 11 for neural invasion and 4 for Helicobacter pylori, respectively.). On Page 27).

2. They found that rs10889677 of IL23R was associated with overall survival of gastric cancer patients. Is there any correlation between this variant and clinicopathologic parameters including T stage, TNM stage and lymph node metastasis?

Response: We did not observe any significant correlations between rs3811463 of LIN28A or rs10889677 of IL23R and clinicopathologic parameters of gastric cancer, neither under the additive genetic model nor the dominant model. Below is some of the results in patients included in survival analysis.

Table 1 Association between rs10889677 and clinicopathologic parameters of gastric cancer patients (Dominant model: A/C+C/C vs A/A).

Variables	Classification	A/A	A/C+C/C	*P*
WHO type	Tubular adenocarcinoma	317 (84.1)	296 (84.1)	0.964
	Signet ring cell	36 (9.5)	35 (9.9)	
	Other	24 (6.4)	21 (6.0)	
Differentiation	Poor	275 (73.9)	231 (67.3)	0.0586
	Moderate and high	97 (26.1)	112 (32.7)	
T stage	T1-T2	105 (28.0)	97 (27.6)	0.934
	T3-T4	270 (72.0)	254 (72.4)	
N stage	N0	115 (30.7)	104 (29.6)	0.808
	N1-N3	260 (69.3)	247 (70.4)	
TNM	I	71 (18.9)	66 (18.8)	0.919
	II	141 (37.6)	137 (39.0)	
	III	163 (43.5)	148 (42.2)	
Lymphovascular	Negative	111 (29.8)	102 (29.1)	0.87

invasion				
	Positive	261 (70.2)	248 (70.9)	
Neural invasion	Negative	170 (45.6)	158 (45.3)	0.941
	Positive	203 (54.4)	191 (54.7)	
Helicobacter pylori	Negative	117 (31.1)	110 (31.2)	1.000
	Positive	259 (68.9)	243 (68.8)	

Table 2 Association between rs3811463 and clinicopathologic parameters of gastric cancer patients (Dominant model: T/C+C/C vs T/T).

Variables	Classification	T/T	T/C+C/C	*P*
WHO type	Tubular adenocarcinoma	468 (84.8)	146 (81.6)	0.219
	Signet ring cell	55 (10.0)	17 (9.5)	
	Other	29 (5.3)	16 (8.9)	
Differentiation	Poor	392 (72.3)	116 (66.3)	0.127
	Moderate and high	150 (27.7)	59 (33.7)	
T stage	T1-T2	153 (27.8)	49 (27.5)	1.000
	T3-T4	397 (72.2)	129 (72.5)	
N stage	N0	158 (28.7)	61 (34.3)	0.188
	N1-N3	392 (71.3)	117 (65.7)	
TNM	I	102 (18.5)	35 (19.7)	0.818
	II	208 (37.8)	70 (39.3)	
	III	240 (43.6)	73 (41.0)	
Lymphovascular invasion	Negative	160 (29.2)	53 (30.1)	0.849
	Positive	388 (70.8)	123 (69.9)	
Neural invasion	Negative	252 (45.9)	76 (43.4)	0.601
	Positive	297 (54.1)	99 (56.6)	
Helicobacter pylori	Negative	181 (32.7)	47 (26.4)	0.115
	Positive	372 (67.3)	131 (73.6)	

3. What is the "other" in variable "WHO type" in Table 5?

Response: The WHO type was used for the pathological type. Among 881 patients with this variable (17 patients had no definite diagnosis on this parameter), the most common type is tubular adenocarcinoma (n=737) and the second is signet-ring cell cancer (n=91). We classified all the other types

including mucinous adenocarcinoma (n=42), papillary adenocarcinoma (n=9), adenosquamous carcinoma(n=2), to the group of "Other" because of the rarity.

4. Please insert "rs10877887" in Table 4.

Response: Sorry for the typo. We have added it in the revised manuscript.

Reviewer #2:

The authors investigated the role of microRNA let-7 related polymorphisms in tumorigenesis and prognosis of gastric cancer in Chinese population. They concluded that Let-7 related polymorphism, rs3811463 in LIN28A, is associated with the susceptibility to and rs10889677 in IL23R, is associated with the prognosis of gastric cancer. This is interesting and important study for genotypes of SNPs and prognosis of gastric cancer. So, this article will be acceptable.

Response: Thank you for reviewing and your comments on our manuscript.

Reviewer #3:

The authors raised an exciting and original issue that is currently considered one of the top of research interest. The methodological approach is appropriate and the manuscript is clear, well organized and easy to read. The authors have been able to condense the wide literature in a coherent, well-structured sequence that leads the reader step-by step to a logical understanding of the genetic mechanisms underlying gastric cancer. In conclusion, the study is interesting with a valuable clinical message. The criteria for the preparation of the manuscript have been fulfilled and frankly I don't have any criticism.

Response: Thank you for reviewing and your comments on our manuscript.