

May 3th, 2018

Dear Editors,

Thank you for giving us the opportunity to revise our manuscript entitled **“Bioinformatics analysis of aberrantly methylated-differentially expressed genes and pathways in hepatocellular carcinoma”** (NO. 38793). We thank the reviewers for their positive comments and constructive suggestions. We value the opportunity and have done our best to revise the manuscript. This letter addresses the comments raised by the reviewers.

### Responses to Reviewers:

**Reviewer #1: This is an interesting study. In this study, the authors studied the methylated-differentially expressed genes in HCC and to explore the hub genes and potential pathways. The expression profiling of GSE25097, and methylation profiling of GSE57956 were gained from GEO Datasets. Pathway analysis illustrated that Hyper-LGs were enriched in cancer, Wnt and chemokine signalling pathways, while Hypo-HGs were related to cell cycle and steroid hormone biosynthesis pathways. After the PPI networks, PTGS2, PIK3CD, CXCL1, ESR1, and MMP2 were identified as hub genes for Hyper-LGs and CDC45, DTL, AURKB, CDKN3, MCM2, and MCM10 for Hypo-HGs by combining 6 ranked methods of cytoHubba. Overall, the study is well designed and the results are interesting. I suggest to publish this manuscript in the journal after a language editing.**

Response: Thank you for the encouraging comment about our research. The manuscript has been revised again for proper English language usage, including grammar, spelling, and overall style, by highly qualified native English speaking editors at American Journal Experts, as shown in the following figure.

 AMERICAN JOURNAL EXPERTS

### EDITORIAL CERTIFICATE

This document certifies that the manuscript listed below was edited for proper English language, grammar, punctuation, spelling, and overall style by one or more of the highly qualified native English speaking editors at American Journal Experts.

**Manuscript title:**  
Bioinformatics analysis of aberrantly methylated-differentially expressed genes and pathways in hepatocellular carcinoma

**Authors:**  
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**Reviewer #2:** 1 Title reflects the main subject/hypothesis of the manuscript. 2 Abstract summarizes and reflects the work described in the manuscript. 3 The manuscript adequately describes the background, present status and significance of the study. 4 The manuscript describes methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail. 5 The research objectives achieved by the experiments used in this study. The study discovered methylated-differentially expressed genes (MDEGs) in hepatocellular carcinoma. 6 The results were well discussed with updated references. 7 Illustrations and tables are good. 8 The manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? 9 There are some minor language polishing which requires a revision. 10 The manuscript meet the requirements of ethics.

Response: First, thank you for the encouraging comment about our research. In view of the eighth comment, we have again retrieved articles related to our research, and the current references are the latest, important and authoritative references in the introduction and discussion sections. In addition, the manuscript has been revised again for proper English language usage, including grammar, spelling, and overall style, by highly qualified native English speaking editors at American Journal Experts, as shown in the following figure.



**Reviewer #3:** First of all, this manuscript is novel, professional, and has a certain significance on the accurate diagnosis and treatment of liver cancer. It discloses numerous novel genetic and epigenetic regulations and offer vital molecular groundwork to understand pathogenesis of HCC. These findings may help to provide new insights into clinical treatment to prevent the development of hepatocellular carcinoma. However, there are some grammatical errors in the article that need to be corrected. In conclusion, this manuscript could be published with minor changes and expect the author to have a more in-depth study of the mechanisms described in the article.

Response: Thank you for the encouraging comment about our research. The

manuscript has been revised again for proper English language usage, including grammar, spelling, and overall style, by highly qualified native English speaking editors at American Journal Experts, as shown in the following figure.



We hope that these revisions meet with your approval and that the manuscript is suitable for acceptance.

Sincerely yours,  
Dr. XueMei Wang