

Cover Letter

Dear Editors and Reviewers,

Thank you very much for your efficient work and thank you for your letter and comments. Accordingly, we have revised the manuscript entitled "Aberrant methylation of SPARC gene and its significance in Gastric Cancer" (Manuscript NO:50829), and would like to resubmit it for your consideration. We have addressed the instructive comments raised by the reviewers, and the amendments are highlighted in yellow in the revised manuscript. Point by point responses to the reviewers' comments are listed for your consideration. We would like to express our sincere thanks to the editors and reviewers for the constructive and meaningful comments.

We are so grateful that you have offered us this opportunity to resubmit our manuscript. We hope that the revised version of the manuscript is now acceptable for publication in your journal.

Please address correspondence to: Dong-Qiu Dai, Professor, Chief Physician. Department of Gastrointestinal Surgery and Cancer Center, the Fourth Affiliated Hospital of China Medical University & Cancer Research Institute of China Medical University, Shenyang 110032, Liaoning, China. E-mail: daidq63@163.com.

We shall look forward to hearing from you at your earliest convenience.
Yours sincerely,

Dong-Qiu Dai

Response to Reviewers

Reviewer # 1 (Number ID: 02839880)

Comment 1: This is an interesting paper that aimed to observe the status of promoter methylation and the effects of SPARC gene in gastric cancer cells and tissues. Overall the manuscript is well written and the findings are interesting. Please check all the abbreviations and acronyms, and define them in the text (i.e. in the title and keywords, "GC"). The statistical analysis has been well carried out (please in the statistical analysis paragraph check for correctness " χ^2 " and " $M \pm SD$ " which should be " χ^2 " and "mean \pm standard deviation" respectively). Tables and Figures are clear and exhaustive. I would suggest to include more discussion on the role of methylated biomarkers, emphasizing the importance of SPARC, for the prediction and diagnosis of gastrointestinal tumors (e.g. Vacante M et al, World J Clin Cases 2018). I would also include a statement in the conclusion paragraph on the possible future clinical and/or surgical applications of the results of the study.

Response 1: We are grateful for your meaningful comments. and we fully understand and agree with you, and we fully agree with you and apologize for the mistakes. Accordingly, we have corrected them in the manuscript and all abbreviated nouns that appear in the article for the first time will follow the full name of the noun. We have revised it according to your suggestion (See in the "DISCUSSION" and "CONCLUSION" section). We hope this may address your concerns.

Reviewer # 1 (Number ID: 03261241)

Comment 1: The authors investigated the function of Secreted Protein, Acidic and Rich in Cysteine (SPARC) genes in gastric carcinoma (GC) cells and tissues. In this study, the expression of SPARC was detected through qRT-PCR and Western blotting, and methylation status was analyzed by Methylation specific-PCR (MSP). They mentioned that low levels of SPARC expression and high levels of methylation in GC tissues were associated with poor clinical features and prognosis, and concluded that SPARC expression may play an important role involved in the regulation development and progression of GS. In general, this is a well-written paper that presents interesting data. It will be of interest to readers of this journal, especially to the oncologists in the field. The paper requires minor revision, which are listed below.

1. The word GC should be spelled out on the first occurrence with the abbreviated form shown in parentheses.

Response 1: Thank you very much for your meaningful comments and we are fully appreciative for your understanding and approval to our research, and we fully agree with you and apologize for the mistakes. Accordingly, we have corrected them in the manuscript, and all abbreviated nouns that appear in the article for the first time will follow the full name of the noun. Hopefully, this may address your concerns.