

Dear Editors and Reviewers:

We would like to submit the revised manuscript entitled “Expression and diagnostic value of HE4 in esophageal squamous cell carcinoma”, which we wish to be considered for publication in *“World Journal of Gastrointestinal Oncology”*.

On behalf of my co-authors, we thank you very much for giving us an opportunity to revise our manuscript, we appreciate editor and reviewers very much for their positive and constructive comments and suggestions on our manuscript entitled “Expression and diagnostic value of HE4 in esophageal squamous cell carcinoma”(ID: 55710). We have studied reviewer’s comments carefully and have made revision in the revised manuscript. We have tried our best to revise our manuscript according to the comments. Attached please find the revised version, which we would like to submit for your kind consideration.

We deeply appreciate your consideration and revision of our manuscript again, and we look forward to receiving comments from the reviewers. If you have any queries, please don’t hesitate to contact me at the address below.

Thank you and best regards.

Yours sincerely,

Shiyuan Liu.

## **SPECIFIC COMMENTS TO AUTHORS**

HE4 is a 25 kDa secreted glycoprotein, is specifically expressed in epididymis, lung and trachea tissues. HE4 carries protease inhibitor activity through interactions with serine proteases, Prss35 and Prss23, which are implicated in kidney fibrosis in a mouse model. The prognostic value of serum HE4 as a biomarker for ovarian and endometrial cancers has also been well recognized. Serum HE4 could be a potential diagnostic marker for small cell lung cancers, non-small cell lung cancer, breast, ovarian, endometrial cancers. HE4 was found to be of little benefit in diagnosis, prognosis and other clinical settings of several human cancers. But there is little research focus on the diagnostic value of HE4 in ESCC. In this study, the authors evaluated the associations between serum HE4 levels and clinicopathological parameters in a cohort of ESCC patients. The design of the study is very well. Sample size is large, and methods are described in detail. Results are interesting and well discussed. References are updated. Please check the data in tables. And figures should be moved to the end of the text. A minor editing is required according to the journals' guidelines. Thank you very much.

**Reply:** Thank you very much for your comments. We have revised the manuscript carefully, include the tables, figures and the language editing.