

Dear editor and reviewers,

Thank you for arranging a timely review for our manuscript. We have carefully evaluated the reviewers' critical comments and thoughtful suggestions, responded to these suggestions point-by-point, and revised the manuscript accordingly. With regard to the reviewers' comments and suggestions, we'd like reply as follows:

### **1. Peer-review report**

Reviewer #1: Following are the comments: • Very nice and well written manuscript with pioneering observations. It is worth publishing. However, there are few observations:

1. In abstract section – Core tip: the line “in adenocarcinomas, such as breast cancer, colorectal cancer and intrahepatic cholangiocarcinoma” is beyond the scope of study and it should be deleted.
2. In conclusion – Word ‘metastasis’ appears more appropriate than ‘migration’. Further the part of sentence after migration appears inappropriate, needs correction.
3. There is lot of repeats in article highlight which could be more precise.
4. In References: the name of journal is not abbreviated, hence checked according to the pattern of journal.
5. Minor grammatic or otherwise changes are mentioned within the manuscript.

Response to Reviewer #1:

1. We appreciate your thoughtful suggestion. The description of “in adenocarcinomas, such as breast cancer, colorectal cancer and intrahepatic cholangiocarcinoma” in Abstract section-core tip was deleted.
2. We appreciate your professional comments, and we have replaced “migration” word with “metastasis”. In addition, the conclusion has been redescribed as “FUCA1 cooperation with MMP-9 may have a major role in affecting the ESCC invasion and metastatic capability and serve as a valuable prognostic biomarker in patients who underwent esophagectomy for ESCC”.
3. Thank you for your professional comments. The description in article highlight was revised and the repetition was deleted.
4. The format of references complied with the “Guidelines for Authors” (<https://www.wjnet.com/bpg/gerinfo/204>) have been reedited in the manuscript.
5. Thank you for your professional comments. The minor grammatic or otherwise changes mentioned within the manuscript have been revised point-by-point.

Reviewer #2: # Checklist 1 Title. Does the title reflect the main subject/hypothesis of the manuscript? Yes, 2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? Yes 3 Key words. Do the key words reflect the focus of the manuscript? Yes 4 Background. Does the manuscript adequately describe the background, present status and significance of the study? Yes 5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? Yes 6 Results. Are the research objectives achieved by the experiments used in this study? What are the contributions that the study has made for research progress in this field? Yes, the research objectives was achieved by the experiments. 7 Discussion. Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? @ see below specific comments 8 Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Do figures require labeling with arrows, asterisks etc., better legends? Figures and tables were sufficient and good. 9 Biostatistics. Does the manuscript meet the requirements of biostatistics? The authors had provided the certificate regarding statistical review. 10 Units. Does the manuscript meet the requirements of use of SI units? Yes 11 References. Does 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? Yes 12 Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented? Is the style, language and grammar accurate and appropriate? >> Appropriate 13 Research methods and reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. Did the author prepare the manuscript according to the appropriate research methods and reporting? @ see below specific comment 14 Ethics statements. For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? >> Ethic approval was provided in the files for review. # Specific comments The original findings of this manuscript was that the authors found high FUCA1 expression was significantly correlated with MMP-9 expression and was associated with worse OS in patients with resected esophageal squamous cell carcinoma. The quality and importance of this manuscript was acceptable.

Response to Reviewer #2:

Thank you for your support and recognition of my work.

The reviewer can't find the STROBE Statement in the files for review.

1. We have uploaded the STROBE Statement via the submission website for review again.

In conclusion, we speculate that the molecular mechanisms of FUCA1 in ESCC are entirely different in adenocarcinoma. The increased FUCA1 protein plays a key role in ESCC invasion and migration, but this effect may be reversed by a specific FUCA1 inhibitor (deoxyfuconojirimycin) or FUCA1 siRNA." The reviewer wondered if these was the appropriate conclusion. Nether "Adenocarcinoma" nor "deoxyfuconojirimycin" were investigated in the methods. The statement in the abstract ("FUCA1 cooperation with MMP-9 may have a major role in affecting the ESCC invasion and metastatic capability and serve as a valuable prognostic biomarker in patients who underwent esophagectomy for ESCC.") may be a better statement.

2. Thank you for your professional comments. As you mentioned, the esophageal adenocarcinoma and deoxyfuconojirimycin were not investigated in the study. Therefore, the statement of "FUCA1 cooperation with MMP-9 may have a major role in affecting the ESCC invasion and metastatic capability and serve as a valuable prognostic biomarker in patients who underwent esophagectomy for ESCC." was revised as the conclusion.

The limitations of the study included [but not limited to] the omission of potential confounders [such as the serum level of Alpha-L-fucosidase]. Suggest to comment that serum level of (Alpha-L-fucosidase-1) had been reported to be a prognostic factor [ref-5 = Journal of thoracic disease 2019; 11(9): 3980-3990] but was not considered in the Cox regression analyses used in the current manuscript.

3. Thank you for your professional comments. As you mentioned, we have reported that patients who received surgery for pT1N0M0 ESCC between 2005 and 2012 with lower serum FUCA1 level ( $\leq 17.95$  U/L) showed longer OS. However, the level of serum FUCA1 was included in blood biochemical examination as a routine test item only before 2012. In the present study, we enrolled 119 patients who underwent esophagectomy for ESCC between January 1, 2014, and December 31, 2014. Therefore, the correlation of the serum level of FUCA1 and the IHC expression was not compared. We have described the limit of these potential confounders, including the serum level of FUCA1, in Discussion section.

## 2. Editorial Office's comments

**1) Science Editor:** The authors stated that high FUCA1 expression was significantly associated with worse OS, which illustrated that FUCA1 might have the ability to promote tumor cells invasion and metastasis among patients with ESCC. This study provides additional evidence that the molecular mechanisms of FUCA1 in ESCC are entirely different in adenocarcinomas, such as breast cancer, colorectal cancer, and intrahepatic cholangiocarcinoma. It is well written and organized article. Reviewers indicate only minor concerns. For example, In conclusion – Word 'metastasis' appears more appropriate than 'migration.' Further, the part of the sentence after migration appears inappropriate, needs correction. The number of references is small. Regarding this manuscript, 1) high novelty, 2) good relevance, and 3) areas for improvement are significant. It is accepted conditionally.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade B (Very good)

Response to Science Editor:

Thank you for your support and recognition of my work.

**2) Editorial Office Director:** I recommend the manuscript to be published in the World Journal of Gastrointestinal Oncology.

Response to Editorial Office Director:

Thanks for your recognition and generosity to us, and it would be our great honor to publish article in World Journal of Gastrointestinal Oncology.

**3) Company Editor-in-Chief:** I recommend the manuscript to be published in the World Journal of Gastrointestinal Oncology.

Response to Company Editor-in-Chief:

We hope that our manuscript could be considered for publication in your journal. Thank you very much for your help.