

Point-to-point responses to the reviewers' comments

We would like to express our sincere thanks to the reviewer for the constructive and positive comments.

(1) Is the overall structure of the manuscript complete? A complete manuscript will contain title, abstract, key words, introduction, materials, methods, experimental procedure, results, discussion, conclusion, acknowledgements, and references.

Answer: complete

(2) What is the scientific question proposed in the manuscript? This should be clearly presented in the Introduction section, along with the pertinent background, rationale, aim, major findings and potential significance of the study. Collectively, this information should inform whether the manuscript would be interesting enough to warrant readers' attention?

Answer: This study is the differential expression of cholinergic nicotinic receptors in the esophagus of healthy volunteers versus patients with esophageal squamous cell carcinoma. This study is interesting.

(3) Which special (unique, innovative and/or timely, appropriate) methods and techniques are adopted in the manuscript? This should be clearly presented in the Methods section. In addition, does the manuscript provide adequate details of methods (including experimental design, subjects or materials, data collection methods, and statistical methods) to allow a reader to repeat the research?

Answer: Methods provide necessary details.

(4) Is the source of the data that is presented reliable? This will be indicated by the information presented in the Results section. The information in the results section will also indicate the academic significance of the main findings (including figure and tables).

Answer: Results seem to be reliable.

(5) What are the results obtained from the data that is presented in the manuscript? This information will make up the Discussion section. It will also answer the questions of whether the results answered the proposed scientific question, achieved the aim of the study, or confirmed or rejected the hypothesis proposed in the manuscript.

Answer: Hypothesis not clearly stated. The study shows expression of *CHNR* subunits $\alpha 3$, $\alpha 5$, $\alpha 7$ and $\beta 4$, but not $\alpha 1$, $\alpha 4$, $\alpha 9$ and $\alpha 10$ in normal esophageal mucosa. In ESCC, *CHRNA5* and *CHRNA7* subunits were found overexpressed when compared to matched surrounding mucosa. *CHRNA4* was differentially expressed between healthy esophagus and normal-appearing ESCC adjacent mucosa. *CHRNA5* expression is an independent prognostic factor in ESCC. Patients with high *CHRNA5* expression showed an increased overall survival in comparison with those with low expression.

The authors included a paragraph in the Introduction Section to clearly state the hypothesis.

(6) What are the conclusions of the manuscript? These should be clearly presented in the Conclusion section. In addition, the section should present the contributions of the conclusions to the field and the weaknesses of the study, and provide future research directions.

Answer: The authors conclude that there is homogenous expression of CHRN₁ along the esophagus and their deregulation in ESCC, suggesting the role of these receptors in its development and progression. Weaknesses and future directions are not included.

The authors included a paragraph in the Discussion Section presenting the weaknesses and future directions.

(7) Does the manuscript cite all important, relevant and timely references?

Answer: Did not evaluate.

(8) Is there any indication of academic misconduct in the manuscript?

Answer: No

(9) Does the manuscript conform to the academic rules and norms and include a human and animal rights statement, institutional review board statement, informed consent statement, clinical trial registration statement, institutional animal care and use committee statement, animal care and use statement, biostatistics statement, and conflict-of-interest statement?

Answer: Yes

(10) Does the manuscript describe any important new methods, problems in or directions of research?

Answer: yes

(11) Does this manuscript contribute to understanding the pathogenesis of disease, disease diagnosis, and treatment or prevention?

Answer: yes

(12) Does the title of the manuscript contain key words, and is the title interesting enough to attract readers' attention?

Answer: Yes

(13) Does the topic of the manuscript fall within the scope of World Journal of Gastroenterology?

Answer: Yes

(14) Does the language of the manuscript reach the standard of publishing?

Answer: Minor corrections needed.

The authors submitted the manuscript to an editing service by Filipodia. The language certificate is enclosed.

3 Peer-reviewers' conclusions

The peer-reviewer should use the considerations above to determine the following conclusions about the manuscript's potential for publication:

(1) Are there any weaknesses or deficiencies in the manuscript?

Answer: the abstract uses abbreviations without spelling out the full form. For example, CHRN is not spelled out. The authors need to be consistent in use of subunits for CHRN – is it $\alpha 4$ or A4?

The authors corrected this in the manuscript. All abbreviations are spelled out and the abbreviation for the nicotinic cholinergic receptors is now standardized.

(2) Does the content of the manuscript have value for publication? If not, rejection should be recommended.

Answer: yes

(5) Is the manuscript concise, clear, comprehensive, and convincing?

Answer: Yes