

Dear Professor and dear reviewers,

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "Targeting oxidative stress with natural products: A novel strategy for esophageal cancer therapy" (ID: 88792). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in red in the paper. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Responds to the editor's and the reviewers comments:

The quality of the English language of the manuscript does not meet the requirements of the journal. Before final acceptance, it is recommended that the authors provide the English Language Certificate issued by a professional English language editing company.

Response: Thanks for your suggestion, we had a new syntax to modify and polish, and upload the certificatehoping to make the overlap of the article within an acceptable range for publication.

Reviewer #1: Comments:

In the last decade interest in natural medicine sources has increased importantly to hit oxidative stress and continuous chronic inflammation courses of disorders. Nature is giving a lot of treasure to fight out many disorders. I would like to suggest continuing that innovative review and including high phenolic compounds of the early harvest extra virgin olive oil such as oleocanthal, oleacein, and squalene to complete the natural sources against free radicals and body inflammation. Congratulations on your initiative of the idea science article.

Response: We are very grateful to the reviewers for your constructive questions. In this study, natural products used to treat esophageal cancer through antioxidant stress pathways are mostly polyphenolic compounds. Previous studies have shown that polyphenolic compounds can interact with lipid hydrophobic chains, eliminate

free radicals formed during lipid peroxidation, and have significant antioxidant and anti-inflammatory properties, including early harvested extra virgin olive oil, such as oleic acid, which can be processed through Ras/MAPKs/PPAR- γ . The signaling pathway inhibits inflammation and oxidative stress, while squalene can weaken oxidative stress and activate the AKT/mTOR pathway. They exert their anti-tumor effects through the antioxidant stress pathway. However, it is worth noting that further research is needed to determine whether these substances can target oxidative stress for the treatment of esophageal cancer.

We tried our best to improve the manuscript and made some changes in the manuscript. And here we did not list the changes but marked in red in revised paper.

We appreciate for Editors/Reviewers' warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.