Reviewer’s report

Title: The NF-kappa B inhibitor celastrol could enhance the anti-cancer effect of Gambogic acid on oral squamous cell carcinoma

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Reviewer: Qing Ren

Reviewer’s report:

This is a well designed study investigating the synergistic anti-tumor effects of two potential chemotherapeutic agents derived from Chinese traditional medicine. The idea is to enhance the Gambogic Acid-induced apoptosis in the oral squamous cancer cells (Tca8113) by inhibiting NF-κB activity with Celastrol. The authors suggested a well-defined hypothesis and performed relevant experiments to support it. The abstract, background, methods, results and discussion sections are adequate and concise. The paper is supported by sufficient amount of published and unpublished work. However, using only one established oral squamous cancer cell line to generalize what will happen in oral cancer is insufficient. Furthermore, there are places in the paper demonstrated inadequate English writing.

• Major Compulsory Revisions:
  Figure 3a and Figure 5a: There was no obvious NF-κB nuclear translocation exhibited in these figures. In fact, there was only intensified immunofluorescence staining in the cytoplasm upon GA treatment.
  It will be helpful to use TNF-α as a positive control since TNF-α is known to induce NF-κB activity in almost all cell systems.

• Minor Essential Revisions
  There are many grammatical mistakes in the writing. It will be a good idea to prove read the paper if not by a native speaker.

• Discretionary Revisions
  The authors used an oral cancer cell line relatively unknown to the cancer research field outside of China. It will be beneficial to conduct similar studies in additional oral cancer cell lines in order to relate to other studies in the field. Furthermore, it will be interesting to see if Celastrol can also improve the anti-tumor effect on other chemotherapeutic drugs commonly used in oral cancer in the clinics.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being
published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests