Reviewer #1:

The authors attempted to study the related mechanisms of Tanshinone IIA (Tan-IIA) by applying its neuroprotective effect to Alzheimer's disease. The study is interesting, but there are some issues to revise.

1. A Methodology should describe how the AD mouse model was established.

Response: The AD model was not constructed for this study, but was a mouse model of AD purchased directly from an animal testing center. For this reason, we refer to the AD model construction method from a previous study in the "Animal Models and NSCs Isolation" section.

2. Scale bars are missing in Figure 1b.

Response: We have added the scale in Figure 1B for a clearer representation.

3. Figure 2 is difficult to read due to poor readability.

Response: We've reorganized the layout and size of figure 2 to make it easier to read.

4. A description of the theoretical background for Aβ1-42 is missing.

Response: Thanks to your correction, we have now added a description of the theoretical background of A β 1-42 in the introduction section.

5. In Figure 2, although the increase in SOD by 5uM of Tan-IIA is not clear, the amount of ROS is relatively well reduced as compared with a low dose of Tan-IIA or Aβ1-42 treated group. This is illogical.

Response: The relationship between Tan-IIA concentration and its biological effects such as modulation of SOD activity and ROS reduction may not be linear or proportional. It is possible that at 5 μM, Tan-IIA induces maximal or near maximal ROS scavenging activity, leading to a substantial reduction in

ROS levels. This effect may be facilitated by mechanisms other than direct activation of SOD, such as up-regulation of other components of the antioxidant defense system such as GSH, or increased efficiency of the ROS neutralization pathway.

6. According to Figure 3, the expression of NEAT1 is associated with increased ROS, and AD is associated with decreased mir-291a-3p. However, it is wondering why NEAT1 shows a tendency to increase with the expression of mir-291a-3p in Figure 3q and r. This comment also applies to the results in Figure 4e. Does this indicate that expression is suppressed by mir-291a-3p binding of the relevant factors? If so, this phenomenon should already be spontaneously presented in NCS under the AD condition.

Response: Depicted in Figure 3 is that overexpression of NEAT1 reduces ROS accumulation (Figure 3E), where the mechanism may be the regulation of miR-291a-3p by NEAT1 (Figure 3Q). The RNA pull-down assay confirmed that NEAT1 with a Biotin-labeled label could pull down miR-291a-3p (Figure 3R). And overexpressed NEAT1 could also inhibit the expression of miR-291a-3p. This series of experiments confirmed the ceRNA mechanism between NEAT1 and miR-291a-3p and that NEAT1 negatively regulates miR-291a-3p expression.

7. In Figure 5, changes in factors resulting from the introduction of mir-291a-3p in diseased condition cells should have been investigated.

Response: miR-291a-3p acts more as a link in the ceRNA machinery, and its overexpression in the ov-NEAT1/mir-291a-3p mimic/si-Rab22a interaction regulates AD model cells in vitro. In addition, due to lack of funding and time, it is not possible at this time to individually investigate the role of miR-291a-3p in in vitro AD model cells.

EDITORIAL OFFICE'S COMMENTS

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Response: We have made revisions to Figure legends.

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Response: As per your request, we have revised both Figures as well as Figure legends.

(4) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text (and directly before the References).

Response: We had add "Article Highlights" section as your request.