**Response to reviewer’s comments**

In general terms, it is an interesting work that has merits to be considered for publication. However, I consider that it needs some improvements before of being finally accepted, which are detailed below:

- The English must be proofread (e.g. page 3, paragraph 3, line 23: "see for review the WOKS" instead of WORKS; page 6, paragraph 2, line 11: CAMBER instead of CHAMBER)

* Response: Thank you for this reminder. We proofread the manuscript accordingly and changed those specific typographical errors mentioned as well as other overlooked English-related errors.

- As I can guess, the final aim of this kind of works is to supplement children with ginseng in the future, but not all people investigates with mice. It is convenient to describe in the discussion the equivalent human ages of mice in order to depict a clinical scenario. This description should be applied for duration of treatment as well as for ages at which experiments were applied.

* Response: We agree with your opinion that we’ve tried to represent the clinical setup using preclinical studies in mice. Thus we added a new paragraph of discussion in page 15, 1st paragraph, stated as: “To roughly depict the clinical scenario of the treatment regimen of KRG in autistic patients, we used juvenile mice to represent school-age and puberty stages in humans. Previous research studied the ages of mice in comparison to human life stages showing that a one-month-old mouse is equivalent to a 12.5 years old child (69). Thus, the age of mice when KRG treatment started (P21) was approximately equivalent to the beginning of the school-age stage in humans. Moreover, the experimental period between P28-P38 could be highly similar to the puberty stage of human development in which the treatment regimen was still ongoing Thus, the treatment period in this study well-represent a clinical set up where long-term treatment of KRG started at an age when a child is usually diagnosed with ASD.”

- It is not completely clear what was the logical thinking to apply the described order of the experiments. I can guess that the most stressful experiments had to be performed at the end, but not the others.

* Response: The order of experiments were planned considering the validation of ASD symptoms and the degree of stress they can induce in the animals. We first conducted the social test as this is crucial to determine whether the VPA-induced mice show a validated core symptom of autism. We followed it up with open field test for the measurement of locomotor activity and marble burying test for repetitive behaviors based on their relevance to ASD and the complexity of the experimental methods. Y-maze and rotarod tests determine the variable symptoms accompanying the ASD in terms of spatial working memory and motor coordination, respectively. The experiments ended with the electroshock seizure threshold test, which is obviously most stressful to the animals.
* We added these statements in the first paragraph of the discussion section (page 14, lines 6 to 13).

- I disagree with use of parametrical tests (e.g. ANOVA) if you did not demonstrate normal distribution of data. Moreover, this kind of experiments requires small groups, for which is convenient to use interquartile ranges and non-parametric tests.

* Thank you for this critical comments. We reanalyzed the data using a non-parametric Kruskal-Wallis test followed by Dunn’s Multiple Comparisontest for all pairwise comparisons. Please refer to Statistical analysis methods on page 9, last paragraph, for these changes.

- In the discussion part, you mentioned that dysregulation of mGluR pathways is responsible of ASD symptoms in rat models. You must cite the corresponding work to support that.

* We cited the corresponding work by Kim et al. (2014) in the mentioned statement that “dysregulation of mGluR pathways is responsible for ASD symptoms in rat models” in page 16, lines 22-23 of the discussion section. To make the statement clearer, we also added a connecting previous sentence which reads “A role of mGluR antagonism on the alleviation of repetitive behaviors in VPA mice model was previously demonstrated (59).”

- The line 6 in the 2nd paragraph of page 16 describes "...the Tbx1 heterozygous (HT) mice possessing the 22q11.2 gene" which is, at least, unclear. The Tbx1 gene in mice is located in chromosome 16A3 region, which is homolog to TBX1 human gene. This gene is located in 22q11.2 region, which contains many genes apart from TBX1. This sentence must be corrected.

* We clarified the sentence accordingly as to avoid confusion about the genes and locations. We corrected the line as “…the Tbx1 heterozygous (HT) mice, in which the mutated Tbx1 gene is part of the chromosome region 22q11.2 in humans,…”. We appreciate your helpful correction.

- You declared no conflicts of interests, but your work was supported by a Ginseng company and none of authors’ works at that company. To me, that is a clear conflict of interest that you should declare.

* Thank you for pointing this out. Instead of declaring “no conflict of interest”, we stated that “CYShin was funded by the Korean Ginseng Corporation for this study, through a grant from the Korean Society of Ginseng.”