# OPEN PEER REVIEW REPORT 1

**Name of journal:** Neural Regeneration Research
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**Title:** Luteolin induces hippocampal neurogenesis in the Ts65Dn mouse model of Down syndrome
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## COMMENTS TO AUTHORS

The study investigated the beneficial effects of luteolin, a natural flavonoid compound, on cognitive functions in a mouse model of Down Syndrome (DS). The study have found that 4 weeks of luteolin treatment improved learning and memory in Ts65Dn mice, which was associated with increased hippocampal neurogenesis and BDNF/ERK signaling pathways. The authors concluded that luteolin rescued behavioral performance and restored hippocampal neurogenesis defects of DS model mice. The study is significant because intellectual disability is common in DS but so far there is no treatment available. The study is well designed and the results have been appropriately presented to support the conclusion. However, a few inquiries and concerns need to be addressed.

1. The study used breeder pairs (Female Distal Chromosome 16 Trisomic x Male B6EiC3SnF1/J) to generate Ts65Dn mice. However, the genotyping method to determine the presence of the trisomy in the offspring was not described.

2. The author declared that two-tailed unpaired t-test or 1-way or 2-way ANOVA was used in the study. However, it is unclear how the statistic method was used for a specific result. For example, which method was used to test the results of morris mater maze? In addition, there are four groups of mice in the study and a "*" in the figures represents statistic significant. However, it is unclear which group was compared.

3. In figure 4B, BDNF levels in the Ts65Dn+Vehicle group was significant lower than the WT+ Vehicle group. However, the WB band of Ts65Dn+Vehicle group seems to be darker than the WT+ Vehicle group in figure 4A.

4. The behavioral tests "Water maze" should be "Morris Water Maze (MWM)" and the "new object recognition (NOR)" should be "Novel objection recognition (NOR)".

5. Several grammatical errors and typos need to be corrected

1) In the abstract line 4 "have showed"

2) In the Para 2 of introduction, there should be a conjunction before the sentence "this ability is of vital importance"

3) In the Para 3, Line 4 of introduction "neurogenes"

"some molecular markers of newborn neurons was increased"

The full name of "EGCG" is unknown.

4) In figure 1 legend, "Data shown as mean ± SEM"

In result 2.4 Line 4 "Compaired"

In result 2.4 Line 8 "we here found here"

5) In Para 1 of discussion "EGCG, acts as DYRK1A inhibitor"