OPEN PEER REVIEW REPORT 1

Name of journal: Neural Regeneration Research

Manuscript NO: NRR-D-18-00916

Title: Strategies to Promote the Maturation of ALS-associated SOD1 Mutants: Small Molecules Return to the Fold

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COMMENTS TO AUTHORS

The manuscript title "Strategies to Promote the Maturation of ALS-associated SOD1 Mutants: Small Molecules Return to the Fold sought to suggest that a copper (Cu)-based small molecule (Cu) II ATSM (CuATSM) effective in treating multiple transgenic mouse models expressing human SOD1-FALS protein but fail to rescue the toxicity associated with the expression of SOD1 metal-binding-region (MBR) mutants in cultured cellsindicating that CuATSM may not be as effective for patients carrying SOD1-fALS MBR mutations. Specifically, the article goes through the brief over view and description about strategy to prevent SOD-1 associated toxicity through promotion of maturation or blockade of aggregation by small molecules.

This article could help researcher quickly know about the copper (Cu)-based small molecule called (Cu)IIATSM (CuATSM) and its effectiveness in treating multiple transgenic mouse models expressing human SOD1-FALS protein; however, the overall description is too general and lack scientific rigors and insights. To meet the quality of NRR, I highly suggest the author to first add purpose of the study and add some descriptions and discussions to address the following issues:

1. What are the challenge and issues of studying the copper (Cu)-based small molecule called (Cu)IIATSM (CuATSM) and its impact on brain heath?

2. The insights and constructive suggestions should be added in the manuscript.

3. Author should add an additional paragraph describing role of (Cu)IIATSM (CuATSM) in motor neuron calcium homeostasis as it play a major role in ALS (For review search Keller BU articles in PubMed)

4. Besides to that I also suggest the author to correct the references (several missing references) with new updates in the field