

## **34815-Answering Reviewers**

### ***COMMENTS***

ID: 00401043

The Author, Dr. Maguire, describes a host of extrinsic factors, including the exposome, that leads to neurodegeneration in the motor tracts. A treatment regimen is reported using the stem cell released molecules from a number of types of adult stem cells to provide tissue dependent molecules that restore homeostasis, including proteostasis, in the ALS patient. The manuscript seems too long and redundant. The authors should shorten the text, by omitting somewhat peripheral material. What about dysregulation of spatacsin in ALS (Orlacchio et al, 2010) and a possible therapy with stem cells? Finally, a minor language polishing is required.

ID: 03656580

Author reviewed ALS that is a disease of protein dysfunction without an RNA or DNA component. Once the proteins in the nervous system misfold, the misfolded proteins self template themselves and act in a prion-like manner to spread and destroy neurons. The best way to treat this disease of degraded ECM and misfolded proteins is to restore homeostasis, and in particular, proteostasis, so that the ECM and proper folding of proteins is restored. Homeostatic renormalization is accomplished by administering S2RM stem cell molecule technology to the nervous system.

### ***RESPONSE***

I appreciate the helpful comments of the reviewers. I have eliminated the peripheral material, edited the language, and included reference to the Orlacchio et al, 2010 paper.