Review of: "Neuronal membrane proteasomes homeostatically regulate neural circuit activity in vivo and are required for learning-induced behavioral plasticity"

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This manuscript intended to demonstrate the functional role of neuronal membrane proteasomes (NMPs) in the activity-dependent nascent protein homeostasis and experience-dependent circuit plasticity. The authors found that inhibiting NMPs in tectal neurons significantly increased nascent proteins but abolished visual experience-dependent plasticity. The authors also used BMI to enhance nascent protein synthesis by increasing neural activity, further indicating that NMPs may degrade newly-synthesized proteins, such as CaMKII and PSMD2. Calcium imaging data showed that BMI and BE treatment increased neuronal activity, suggesting that NMPs may regulate spontaneous network activity. The research of this manuscript is clear and well-designed. The novel findings of NMPs in activity-dependent circuit function would make a great contribution to the research fields of protein homeostasis and plasticity. There are few suggestions that the authors may consider.

1. In the Xenopus tectum, there are some other non-neuronal cell types including radial glia cells. Is there any evidence showing the specificity NMPs locations in the tectal brain?

3. In Figure 1C, the expression of GluA1 was variable in different groups. Is it possible that the change in the expression of synaptic receptors is the result of NMPs, or changes in neuronal activity?

4. The authors mainly used BE to inhibit NMPs to study the functions. Is there any way to enhance NMPs in the brain? It will be great to show the result that NMPs themselves can regulate homeostasis of the nascent proteins.