

## **OPEN PEER REVIEW REPORT 1**

Name of journal: Neural Regeneration Research

Manuscript NO: NRR-D-20-00502

Title: Dopaminergic-cholinergic imbalance in movement disorders: A role for the novel striatal

dopamine D2-muscarinic acetylcholine M1 receptor heteromer

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## **COMMENTS TO AUTHORS**

Strength: well structured, compact, nice illustrative figures Weakness: not very novel though of some importance

The manuscript titled 'Dopaminergic-cholinergic imbalance in movement disorders: A role for the novel striatal dopamine D2-muscarinic acetylcholine M1 receptor heteromer" discusses successful detection of the novel D2R-M1R interaction in the mouse striatum and provides ideas about exploring these complexes in healthy controls versus PD patients. The approach to restore dopamine Ach balance by simultaneous D2R agonist and Ach antagonist might prove to be a promising therapeutic strategy for movement disorders including PD. Figures are well structured. However, few issues are here as follows:

- 1. "For instance, due to a reciprocal antagonistic D2R- M1R interaction, such as was previously described for the well-established D2R-A2AR 150 heteromer (Ferre et al., 2018)".... Needs clarification.
- 2. It has been mentioned that "The Alpha technology has recently been optimized and validated by our research group through the detection of D2R-A2AR heteromers in mice and post-mortem human brains. Is there any evidence of such presence in post-mortem brains from drug-induced PD? (mention with appropriate references).