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   2021G021

2. Title
   Study of the Molecular Mechanism of Lysosomal Activation via Nicotine Receptors in Neurodegeneration

3. Period
   2021-2025

4. Summary

This research aimed to elucidate the molecular mechanisms of lysosomal activation via α7 nicotinic receptors and to clarify their neuroprotective effects against neuronal damage caused by abnormal protein accumulation and viral infections.

Using α-synuclein accumulation cell models and bimolecular fluorescence complementation (BiFC) assays, we demonstrated that treatment with the α7 nicotinic receptor agonist PNU282987 significantly reduced the intracellular aggregation of both wild-type and mutant α-synuclein, thereby preventing neuronal cell death. Mechanistically, we revealed that the activation of α7 nicotinic receptors enhances autophagy mediated by transcription factor EB (TFEB) and stabilizes the retromer complex through the induction of vacuolar protein sorting-35 (VPS35).

Furthermore, in a herpes simplex virus type 1 (HSV-1) infection model, we found that the activation of these receptors effectively suppressed viral proliferation and significantly attenuated time-dependent neuronal injury.

In conclusion, our findings indicate that the activation of α7 nicotinic receptors exerts robust protective effects against neurotoxicity induced by both misfolded protein aggregation and viral infections. These results suggest that targeting α7 nicotinic receptors to modulate lysosomal and retromer functions represents a promising novel therapeutic and preventive strategy for neurodegenerative diseases.