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2. **Title**

   Physiological Roles of Endogenous Neurotoxin-like Proteins on Nicotinic Acetylcholine Receptor Function

3. **Period**

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4. **Summary**

   α 7 nicotinic acetylcholine receptors (nAChRs) are widely expressed in the central nervous system and regarded as potential therapeutic targets for several neurodegenerative conditions. However molecular physiological characterization remains poorly advanced because α7nAChR cannot be properly folded and sorted to the plasma membranes in most mammalian cell lines. We established a cell line, which stably and robustly express surface α7nAChRs by introducing α7nAChR, Ric-3, and NACHO cDNAs into HEK293 cells (Triple α7nAChR/RIC-3/NACHO cells; TARO cells). Potent α7nAChR inhibitors, α-Bgtx, retain a unique three-finger structure (TFS) that is essential for their binding with α7nAChR. In mammals, there are several TFS-containing proteins known as the Ly-6/neurotoxin superfamily (Ly6SF), some of which are anchored by glycosylphosphatidylinositol (GPI), and have been reported to modulate nAChRs. We have focused one of the Ly6SF member Ly6H because of high expression levels in brain and immune cells. We report in this study that Ly6H binds with α7nAChRs on the cell membrane and modulates the channel activity without affecting intracellular trafficking of α7nAChR. We speculate that Ly6H may fine-tune the cell surface α7 AChR activity in time- and cell-specific manners. α7nAChRs are known to transmit various intracellular signals responsible for neuroprotection and anti-inflammation. Our study suggests the possibility that Ly6H may act as a signaling modifier in α7nAChR-expressing neuronal or non-neuronal cells in physiological and pathological conditions.