mGluR5 Modulator For Treatment of Alzheimer’s Disease

OCR Number: OCR 5708

Description:

- **Background**: mGluR5 has been identified as part of a cell-surface complex that binds to Ab oligomers, which leads to synaptic loss and neuronal death.
- A small molecule silent allosteric modulator (SAM) has been identified that blocks Ab binding, but does not interfere with normal glutamate signaling.
- Treatment of AD mice with SAM improves memory and learning (Fig.1), and ameliorates synaptic loss (Fig.2).
- **Mechanism of Action**: SAM-Induced conformational changes in mGluR5 strongly reduce its interaction with cellular prion protein (PrPC), a cell-surface anchor for Alzheimer’s Aβ0, without affecting glutamate signaling.
- **IP status**: Extensive patent portfolio covers novel composition of matter and is available for licensing.
- **Lead Innovator**: Stephen M. Strittmatter, M.D., Ph.D.

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Fig. 1. SAM reverses learning and memory deficits in APP/PS1 transgenic mice after 4 weeks of treatment. Spatial learning in Morris-Water Maze.

Fig. 2. SAM recovers loss of synaptic markers in APP/PS1 mice after 5 weeks of treatment. PSD95 area.