**Background**

- Neuroinflammation is a hallmark of many central nervous system disorders, including Alzheimer's disease.
- SM07883 is an oral, brain-penetrant DYRK1A inhibitor that has been shown to reduce tau and amyloid pathology and glosis in neurodegenerative mouse models.1, 2
- This study assessed the potential of SM07883 to modulate innate immunity in vitro and in vivo using tau transgenic mice and inflammatory mouse models.

**Results**

**Figure 1. SM07883 reduced tau-induced glial activation in JNPL3 mice**

**Figure 2. SM07883 reduced neurodegeneration-induced glial activation in 3xTg-AD mice**

**Figure 3. SM07883 reduced acute neuroinflammation in vivo**

**Figure 4. SM07883 reduced chronic neuroinflammation in vivo**

**Figure 5. SM07883 reduced microglial cell activation in vitro**

**Figure 6. SM07883 reduced STAT3 translocation and NFAT cytoplasmic localization in vitro**

**Methods**

**In vivo**

- Ten-month-old JNPL3 mice (P301L human tau overexpression mutation) or eleven-month-old 3xTg-AD mice (APP, PSEN, P301L tau) were orally administered vehicle or SM07883 (JNPL3: 3 mg/kg, QD, 3 months; 3xTg-AD: 5 mg/kg, QD, 6 months). Glial activation was assessed using either a gliarial fibrillary acidic protein (GFAP) ELISA quantification assay in spinal cords of JNPL3 mice or by magnetic bead panel (IL-1β, TNF-α, IL-6, IFN-γ) and NO quantification from spinal cord homogenates (NOx, NO2, NO3). Activated microglial cells were identified by quantified by Iba1-positive staining (Fig. 1 and 2).
- Chronic inflammation: BV2 cells were incubated with SM07883 (30 µM) and then challenged with LPS (10 µg/ml) for 24 hours. Cells were collected and stained with fluorescently labeled anti-TNFα and analyzed for TNFα (Millipore Milliplex Magnetic Bead Panel). NOx (Griess reaction) (Fig. 4).

**In vitro**

- Mouse BV2 microglial cells were cultured overnight with SM07883 (1.1 µM) and challenged with LPS (100 ng/ml) for 6 hours. TNFα and NO2 expression was measured by qRT-PCR using TaqMan primers and normalized to GAPDH via β-Actin. BV2 cells were also cultured with serial dilutions of SM07883 and challenged with LPS (250 ng/ml) for 5 to 24 hours. Supernatants were tested for TNFα (MSDS) and NOx (Griess reaction) (Fig. 2).
- BV2 cells were exposed to SM07883 (1.1 µM) for 1 hour prior to overnight exposure to LPS (100 ng/ml). Cells were collected and stained with fluorescently labeled anti-murine CD45 or CD68 and analyzed by flow cytometry (Fig. 3).
- BV2 human monoclonal HMC-3 cells were incubated overnight with SM07883 (1.1 µM) and then treated with IL-1β (10 ng/ml) for 4 days. Cells were subjected to flow cytometry (FACS) (Fig. 4).

**References**


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