Trem2-KO

Strain Name: C57BL/6JGpt-*Trem2*^{em1Cd3332in1}/Gpt
Strain Type: Knock-out
Strain Number: T003346
Background: C57BL/6JGpt

Description

Triggering receptor expressed on myeloid cells 2 (TREM2) is a single-pass transmembrane immune receptor that is mainly expressed on microglia in the brain and macrophages in the periphery [1-2]. Signaling transduction of TREM2 is complex. In general, TREM2 binds to the adaptor proteins DNAX activation protein 10 (DAP10) and DAP12 through oppositely charged residues in their transmembrane domains. TREM2 has been found to regulate inflammatory signaling [3] and microglial metabolism, which could promote microglial phagocytosis, activation, survival, and proliferation [4-6]. Thus, TREM2 is essential for normal immune function and cell viability in the brain. TREM2 is a confirmed genetic risk factor for Alzheimer's disease (AD) [7].

TREM2 has a variety of ligands, most of which are hallmarks of tissue damage, mainly free negatively charged molecules bound to the plasma membrane, including bacteria, DNA, lipoproteins, and phospholipids. In the physiological state, the activity of TREM2 is restricted to specific tissues, whereas in the pathological state, TREM2 signaling acts as an immune signaling hub to sense tissue damage and inhibit it [8].

GemPharmatech constructed a Trem2-KO mouse model on the background of C57BL/6JGpt. Trem2-KO homozygous mice had no TREM2 protein expression in brain.

Strategy

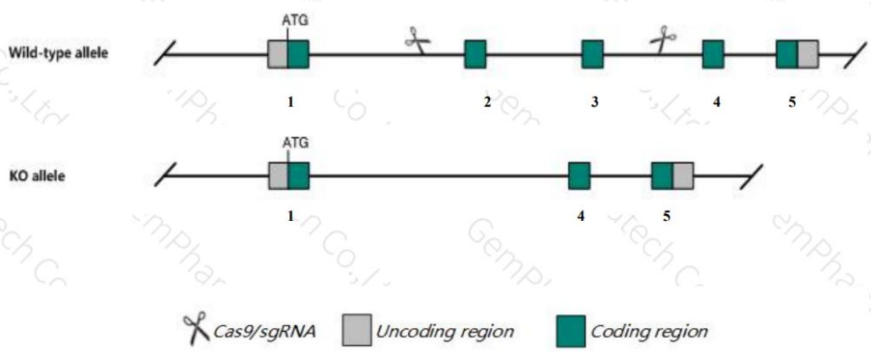

Fig 1. Schematic diagram of C57BL/6JGpt-Trem2-KO model strategy.

Applications

1. Research related to deficiency of TREM2 protein.
2. Research related to Alzheimer's disease.

Data support

1. IHC analysis of TREM2

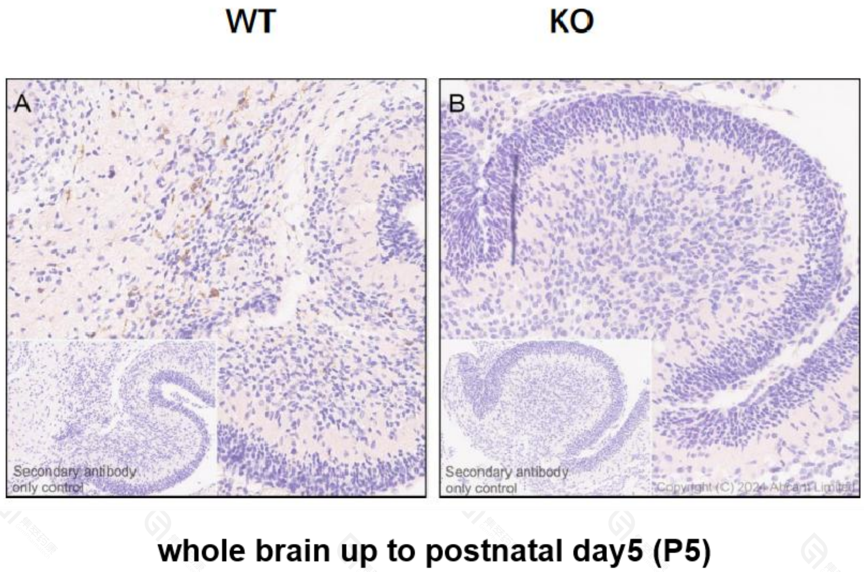

Fig 2. Representative IHC results of TREM2 in mouse pancreas.

IHC analysis of TREM2 in brain using specific antibody (Abcam, ab305103). WT: C57BL/6JGpt wildtype mice, KO: Trem2-KO homozygous mice. (Data source: Abcam collaborative verification).

2. mRNA expression of *Trem2*

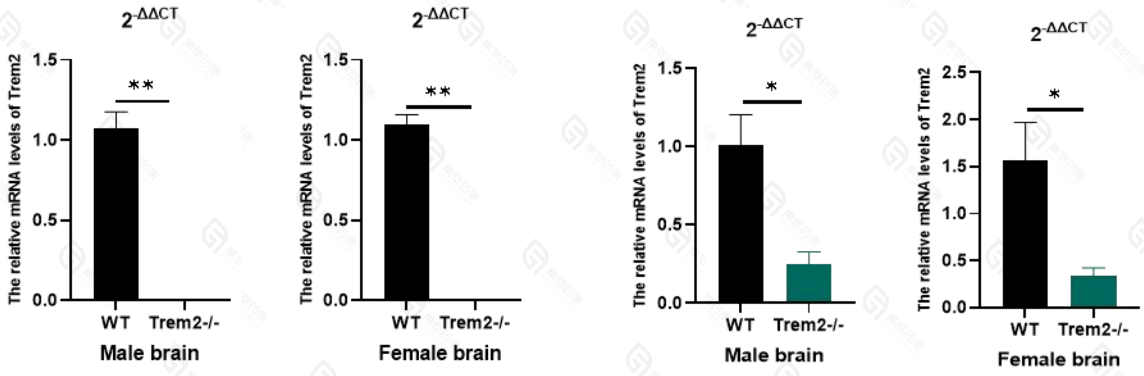

Fig 3. mRNA expression of mouse *Trem2*

The total RNA of mouse brain was extracted for qRT-PCR analysis of *Trem2* mRNA level, and the results showed that *Trem2* mRNA was depleted in the brain of Nppa-KO homozygous mice. Primers are designed within the knockout region (left) and outside the knockout region (right). n=3, *P<0.05, **P<0.01.

References

1. Wang, Yaming, et al. "TREM2 lipid sensing sustains the microglial response in an Alzheimer’s disease model." *Cell* 160.6 (2015): 1061-1071.
2. Chung, Dong‐Hui, William E. Seaman, and Michael R. Daws. "Characterization of TREM‐3, an activating receptor on mouse macrophages: definition of a family of single Ig domain receptors on mouse chromosome 17." *European journal of immunology* 32.1 (2002): 59-66.
3. Kobayashi, Masaaki, et al. "TREM2/DAP12 signal elicits proinflammatory response in microglia and exacerbates neuropathic pain." *Journal of Neuroscience* 36.43 (2016): 11138-11150.
4. Poliani, Pietro Luigi, et al. "TREM2 sustains microglial expansion during aging and response to demyelination." *The Journal of clinical investigation* 125.5 (2015): 2161-2170.
5. Zheng, Honghua, et al. "TREM2 promotes microglial survival by activating Wnt/β-catenin pathway." *Journal of Neuroscience* 37.7 (2017): 1772-1784.
6. Jay, Taylor R., et al. "TREM2 deficiency eliminates TREM2+ inflammatory macrophages and ameliorates pathology in Alzheimer’s disease mouse models." *Journal of Experimental Medicine* 212.3 (2015): 287-295.
7. Jonsson, Thorlakur, et al. "Variant of TREM2 associated with the risk of Alzheimer's disease." *New England Journal of Medicine* 368.2 (2013): 107-116.
8. Deczkowska, Aleksandra, Assaf Weiner, and Ido Amit. "The physiology, pathology, and potential therapeutic applications of the TREM2 signaling pathway." *Cell* 181.6 (2020): 1207-1217.