B6-hPD1/hCSF1R

Strain Name: B6/JGpt-*Pdcd1*$^{em1Cin(hPDCD1)}$ *Csf1r*$^{em1Cin(hCSF1R)}$/Gpt

Strain Type: Knock-in

Strain ID.: T006213

Background: C57BL/6JGpt

Description

Colony-stimulating factor 1 receptor (CSF1R) is a cell-surface tyrosine kinase receptor expressed on macrophages and other cells of the myeloid lineage. The CSF1R/ CSF1 interaction can promote the growth and differentiation of macrophages. High CSF1 or CSF1R expression levels in a variety of tumors, such as breast cancer, hepatocellular carcinoma, etc., were positively correlated with poor survival prognosis.

A variety of small molecules and monoclonal antibodies (mAbs) directed at CSF1R or its ligand CSF1 are in clinical development both as monotherapy and in combination with standard treatment modalities such as chemotherapy as well as other cancer-immunotherapy approaches.

The coding sequence of extracellular region of CSF1R is replaced with human counterpart by gene editing technology on B6-hPD1 mice. Intracellular region of murine CSF1R is completely retained and normal intracellular signal transduction can be guaranteed. These mice are ideal models for anti-CSF1R drug evaluation and combination with anti-PD1 drug evaluation.

Strategy

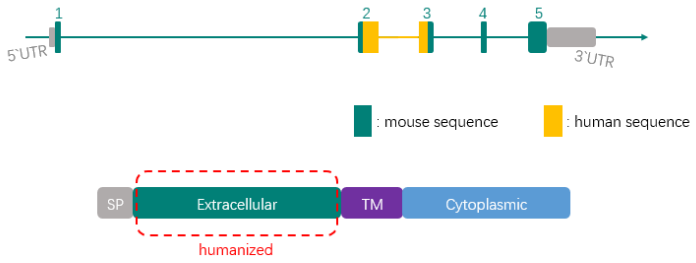

Fig.1 Schematic diagram of PD1 humanization strategy in B6-hPD1/hCSF1R mice.

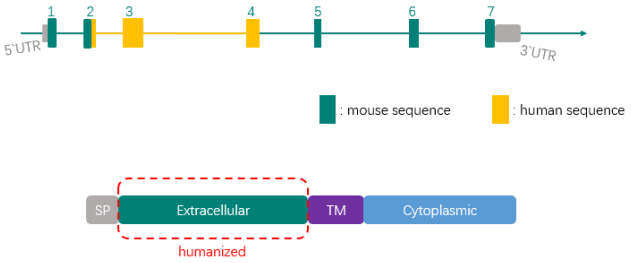

Fig.2 Schematic diagram of CSF1R humanization strategy in B6-hPD1/hCSF1R mice.

Application

1. Screening and performance evaluation of CSF1R inhibitors and PD1 inhibitors, such as tumor treatment drugs or neutralizing antibodies;
2. Screening of immune tolerance inhibitors;
3. Preclinical evaluation of toxicology;
4. Screening and development of CSF1R targeted drugs combined with PD1 drugs;
5. Research on the immune system.

Data Support

1. PD1, CSF1R protein expression analysis

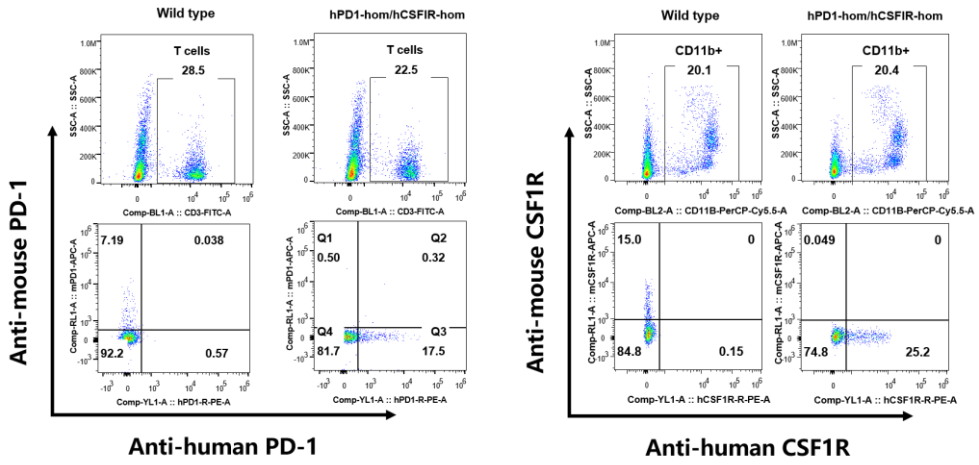

Fig.3 Detection of PD1 and CSF1R expression in B6-hPD1/hCSF1R mice. B6-hPD1/hCSF1R mice can successfully express hPD1 on the surface of T cells, hCSF1R can be successfully expressed on the surface of macrophages.

2. T/B/NK/Macrophage cells ratio detection

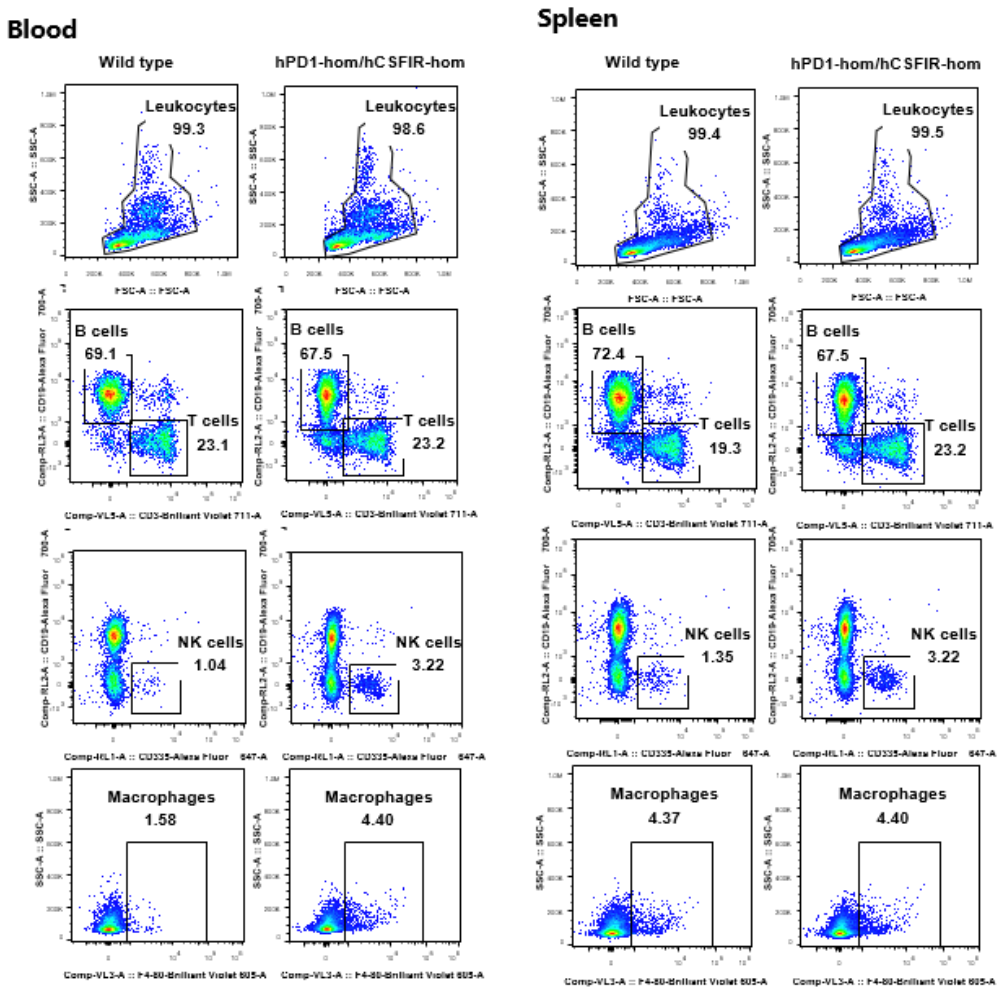

Fig.4 Detection of the T/B/NK/macrophage cells ratio in B6-hPD1/hCSF1R mice. There was no obvious difference of T/B cells proportion between wild type and homozygote mice. The proportion of NK cells in blood and spleen increased; the proportion of macrophages in blood increased, but the proportion of spleen did not change significantly.

References

1. Robinson, John L., et al. "Common neuropathological features underlie distinct clinical presentations in three siblings with hereditary diffuse leukoencephalopathy with spheroids caused by CSF1R p. Arg782His." *Acta neuropathologica communications* 3.1 (2015): 42.

2. Stanley, E. Richard, and Violeta Chitu. "CSF-1 receptor signaling in myeloid cells." *Cold Spring Harbor perspectives in biology* 6.6 (2014): a021857.

3. Perry, Curtis J., et al. "Myeloid-targeted immunotherapies act in synergy to induce inflammation and antitumor immunity." *Journal of Experimental Medicine* 215.3 (2018): 877-893.