BALB/c-hTROP2

Strain Name： BALB/cJGpt-*Trop2*$^{em1Cin(hTROP2)}$/Gpt
Strain Type： Knock-in
Strain Number： T056432
Background： BALB/cJGpt

Description

TROP2 (tumor associated calcium signal transducer 2), also known as epidermal glycoprotein 1 (EGP-1), gastrointestinal tumor associated antigen (GA733-1), and surface marker 1 (M1S1), is expressed at very low levels in normal tissues and overexpressed in various malignant tumors . TROP2 is a single pass transmembrane protein that includes hydrophobic precursor peptides, extracellular domains, transmembrane domains, and cytoplasmic tails[1,2]. TROP2 promotes tumor cell growth, proliferation, and metastasis by regulating calcium signaling pathways, cyclin expression, and reducing fibronectin adhesion. It can also interact with β-catenin in the Wnt signaling cascade, thereby acting on the transcription of nuclear oncogenes and cell proliferation[3].

TROP2 is a cancer related antigen that is overexpressed in a variety of malignant tumors. It is mainly expressed in various human epithelial cancers, including breast cancer, lung cancer, stomach cancer, colorectal cancer, pancreatic cancer, prostate cancer, cervical cancer, head and neck cancer, and ovarian cancer[4]. Overexpression of TROP2 plays a key role in tumor growth, making TROP2 one of the potential targets for anti-cancer drug delvlopment. Mutations in this gene are responsible for glue drop-like corneal dystrophy (GDLD), an autosomal recessive disorder[5].

In Gempharmatech, the TROP2 gene was modified by using CRISPR/Cas9 technology to replace the mouse TROP2 gene signal peptide and extracellular region with the human gene signal peptide and extracellular region, preserving the intracellular signal transduction region of the mouse TROP2 gene. This model is an ideal animal model for studying diseases such as tumors.

Strategy

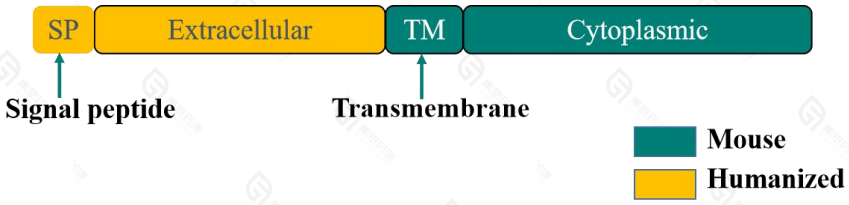

Fig 1. Schematic diagram of TROP2 humanization strategy on BALB/c-hTROP2 mice.

Applications

1. Efficacy and safety evaluation for Anti-TROP2 drugs.
2. Research on anti-tumor.

Supporting data

1. TROP2 mRNA expression analysis

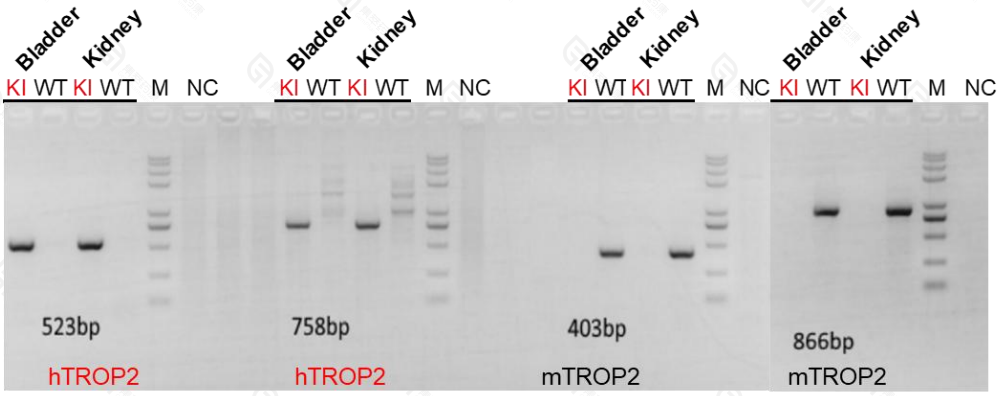

Fig 2. Expression of TROP2 mRNA in BALB/c-hTROP2 homozygous mice.

Specific analysis of the expression of TROP2 gene in BALB/c-hTROP2 mice using RT-PCR. Mouse TROP2 mRNA was detectable only in bladder and kidney of wild-type mice, and human TROP2 mRNA was detectable only in the bladder and kidney of homozygous BALB/c-hTROP2 mice.

2. TROP2 protein expression analysis

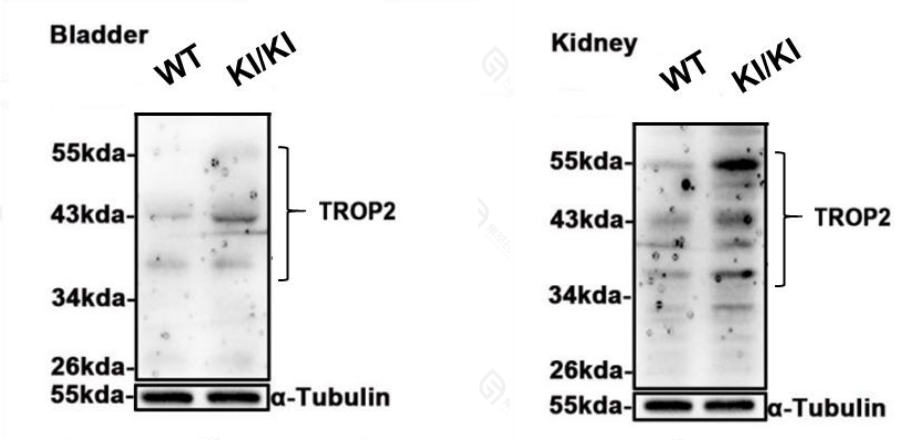

Fig 3. Expression of TROP2 in BALB/c-hTROP2 homozygous mice.

The cross-reaction antibody was used to detect the mouse endogenous and humanized TROP2 expression. In BALB/c-hTROP2 homozygous mice, human TROP2 was expressed in bladder and kidney tissue. (TROP2 could be glycosylated in multiple sites and has been predicted to have diverse molecular weight[6].)

3. Analysis immune cell subpopulations in BALB/c-hTROP2 mice

3.1 Analysis of blood immune cell subpopulations

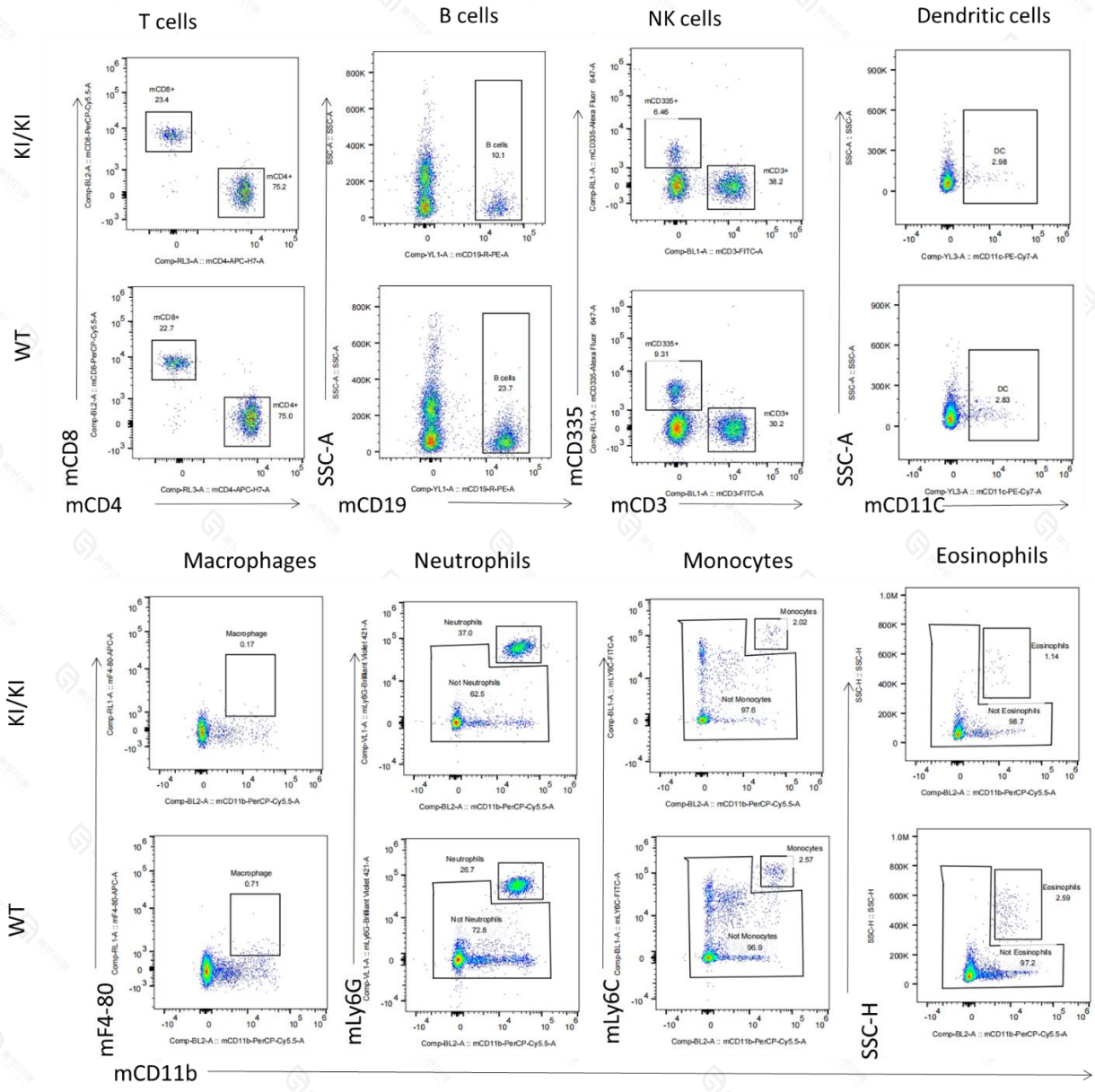

Fig 4. Immune cell subpopulations analysis in BALB/c and BALB/c-hTROP2

Blood was taken from BALB/c and BALB/c-hTROP2 mice for flow cytometric analysis to assess immune subpopulations. As shown in Figure 4, the percentages of T cells, NK cells, dendritic cells, macrophages, neutrophils, monocytes, and eosinophils in BALB/c-hTROP2 mice were similar to those in BALB/c, indicating that the replacement of mTROP2 by hTROP2 did not alter the development, differentiation, and distribution of these cells in blood.

3.2 Analysis of spleen immune cell subpopulations

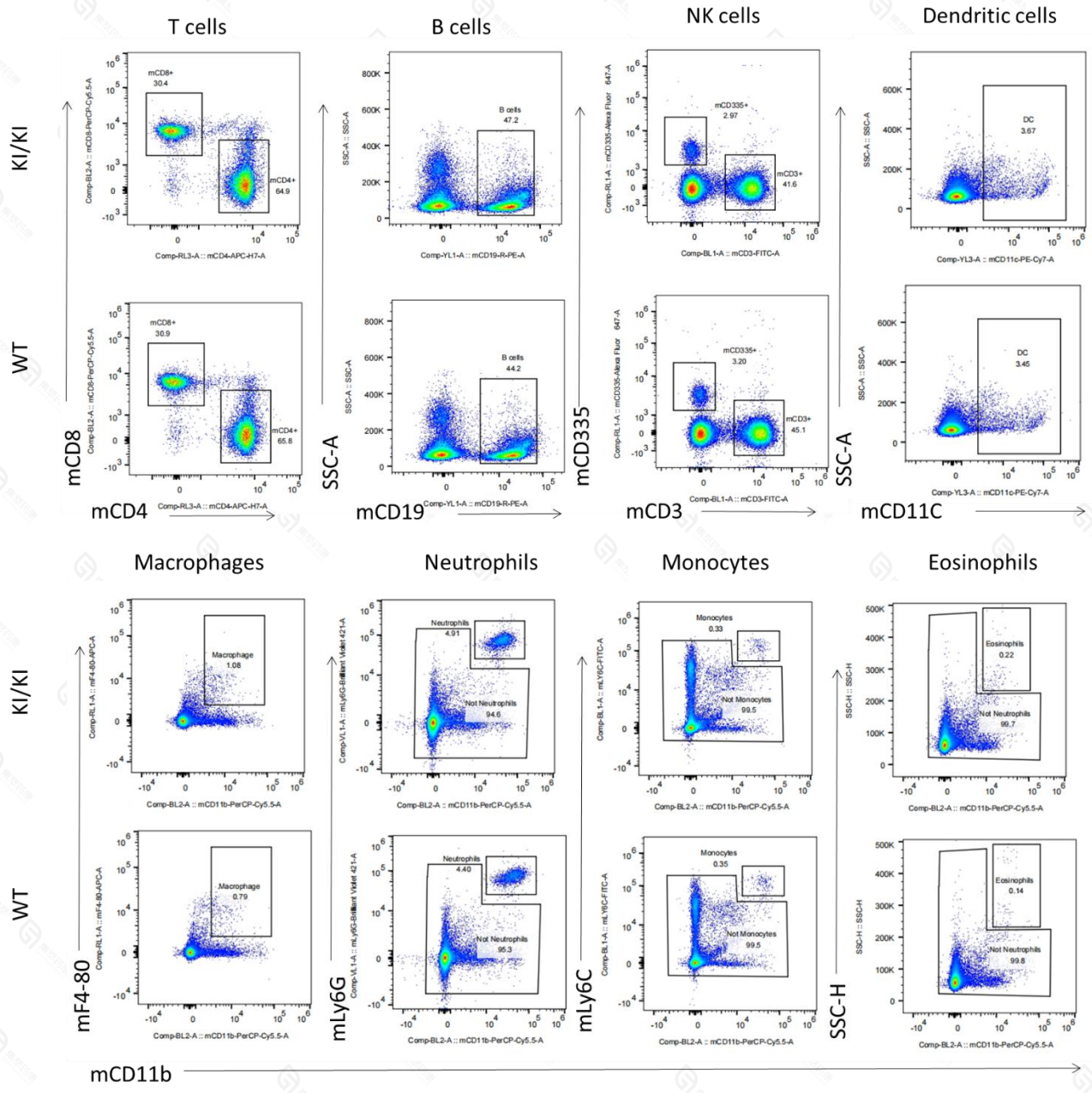

Fig 5 .Leukocyte subpopulations analysis in spleen of BALB/c and BALB/c-hTROP2

Splenocytes were taken from BALB/c and BALB/c-hTROP2 mice for flow cytometric analysis to assess immune subpopulations. As shown in Figure 5, the percentages of T cells, B cells, NK cells, dendritic cells, macrophages, neutrophils, monocytes, and eosinophils in BALB/c-hTROP2 mice were similar to those in BALB/c, indicating that the replacement of mTROP2 by hTROP2 did not alter the development, differentiation, and distribution of these cells in spleen.

References

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6.Stepan, Lara P et al. Expression of Trop2 cell surface glycoprotein in normal and tumor tissues: potential implications as a cancer therapeutic target. The journal of histochemistry and cytochemistry : official journal of the Histochemistry Society vol. 59,7 (2011): 701-10.