

B6-hTIGIT

Strain Name: B6/JGpt-*Tigit*^{em1Cin(hTIGIT)}/Gpt

Strain Type: Knock-in

Strain Number: T003366

Background: C57BL/6JGpt

Description

TIGIT (T cell Ig and ITIM domain; also called Vsig9, Vstm3, or WUCAM), is an immune receptor on NK cells, activated T cells, memory T cells and a subset of regulatory T cells (Tregs).

TIGIT has two ligands, CD155 (PVR) and CD112 (PVRL2, nectin-2), with the costimulatory molecule CD226. They comprise a pathway that is strongly similar with the well-known B7/CD28/CTLA-4 pathway. Multiple studies have shown that TIGIT contributes to immune tolerance by delivering inhibitory signals to effector T and NK cells ^[1-2]. Blockade of TIGIT can reverse the exhaustion of cytotoxic T lymphocyte (CTL)-mediated anti-tumor immunity and inhibit tumor growth in preclinical tumor models ^[3].

The coding sequence of TIGIT extracellular region was replaced with human counterpart by CRISPR/Cas9 technology on B6 mouse. Intracellular region of murine *Tigit* was completely retained and normal intracellular signal transduction was guaranteed. Levels of Human TIGIT expression in homozygous B6-hTIGIT mice are similar to murine TIGIT expression in wildtype. These mice are ideal models for anti-TIGIT drug evaluation and immunotherapy drug development.

Strategy

Strategy of humanized TIGIT mouse

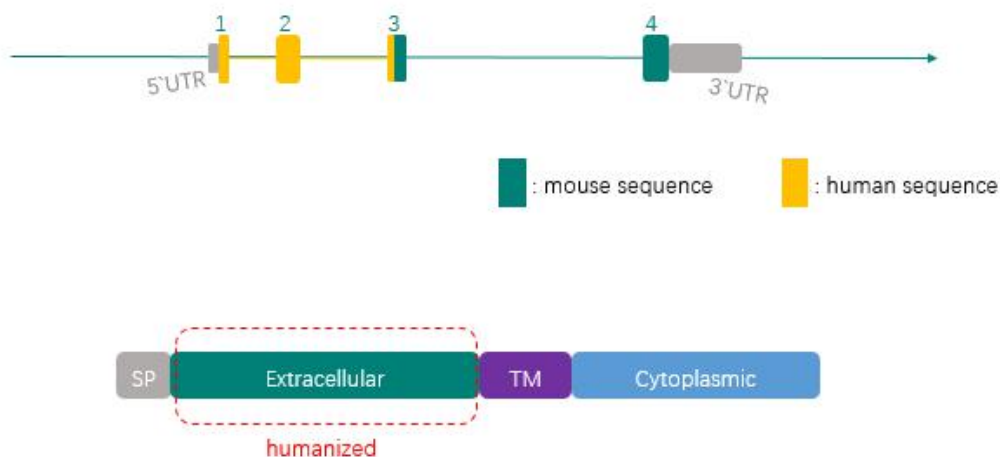


Fig.1 Schematic diagram of TIGIT humanization strategy in B6-hTIGIT mice.

Application

1. Efficacy evaluation of human TIGIT inhibitors
2. Safety assessment of human TIGIT inhibitors
3. Research on immune system

Data support

1、 TIGIT expression level detection

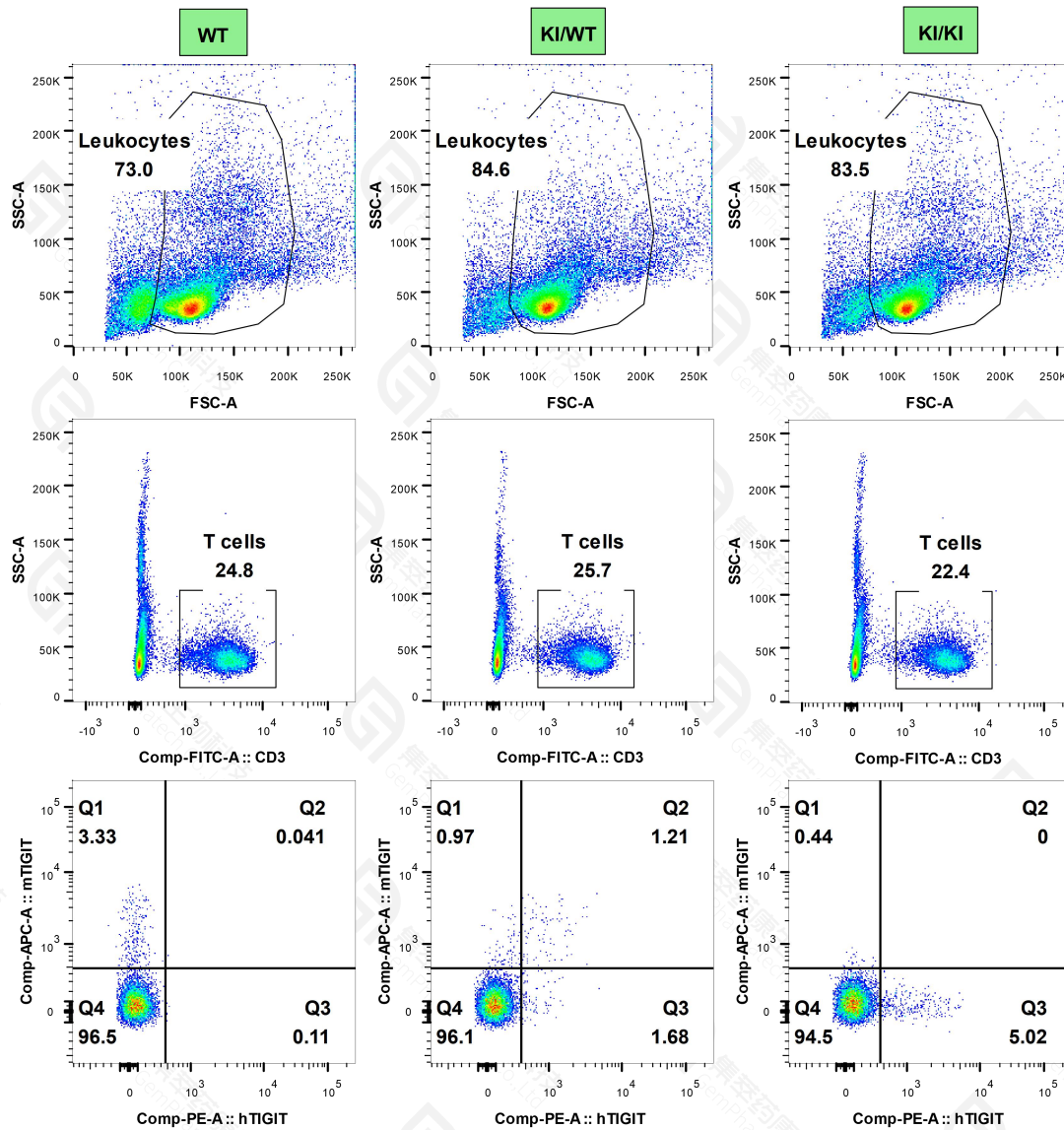


Fig 2. Detection of expression in mice.

B6-hTIGIT mice can successfully express hTIGIT on the surface of T cells, and the expression level of hTIGIT in B6-hTIGIT mice is similar with mTIGIT expressed in wild-type mice.

2、 T/B/NK cell ratio assay

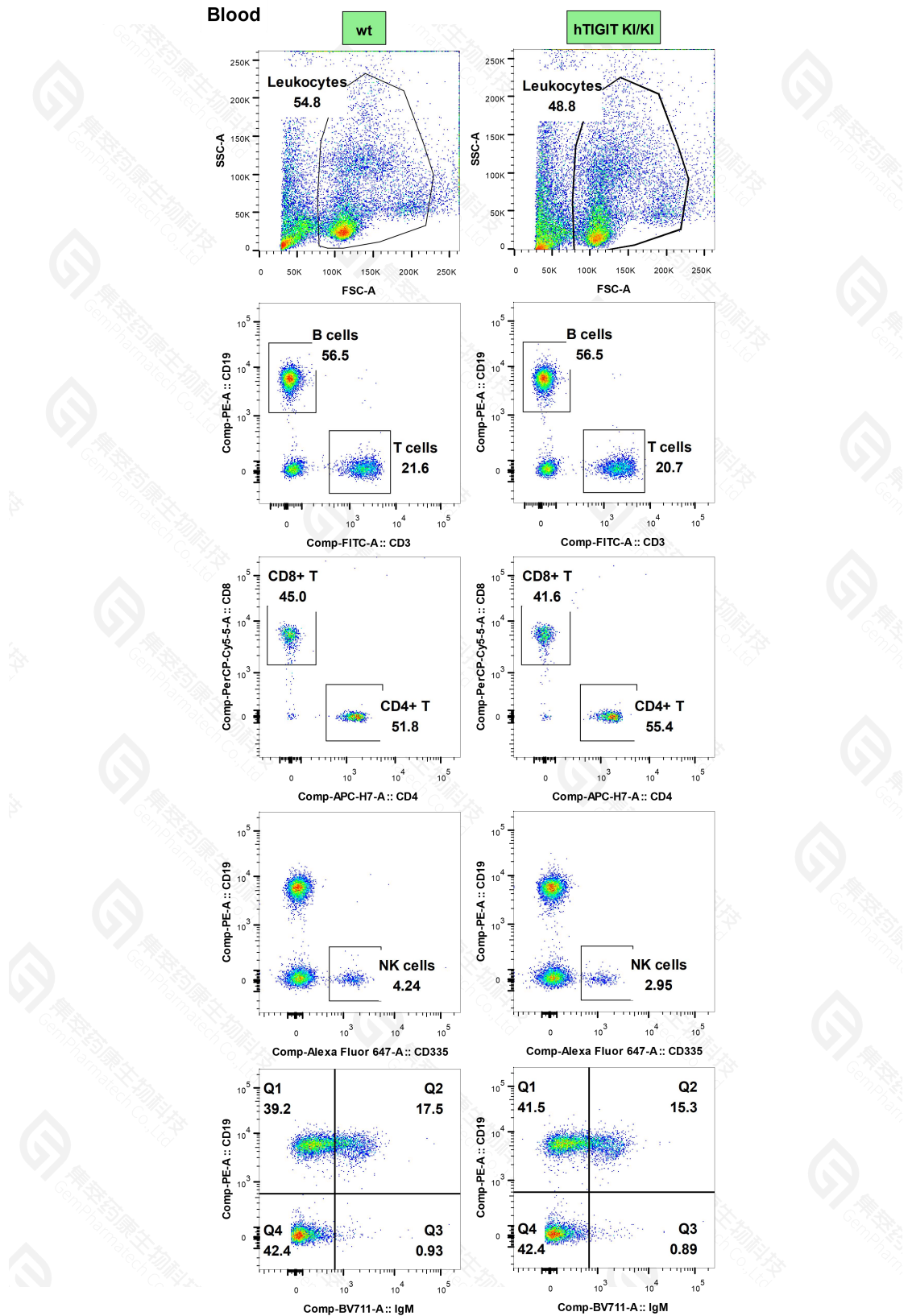


Fig 3. Detection of T/B/NK cells proportion in B6-hTIGIT mice

There was no obvious difference of T/B/NK cells proportion between wild-type and B6-hTIGIT homozygous mice.

References

1. Yu, Xin, et al. "The surface protein TIGIT suppresses T cell activation by promoting the generation of mature immunoregulatory dendritic cells." *Nature immunology* 10.1 (2009): 48.
2. Zhang, Qing, et al. "Blockade of the checkpoint receptor TIGIT prevents NK cell exhaustion and elicits potent anti-tumor immunity." *Nature immunology* 19.7 (2018): 723.
3. Johnston, Robert J., et al. "The immunoreceptor TIGIT regulates antitumor and antiviral CD8+ T cell effector function." *Cancer cell* 26.6 (2014): 923-937.