Humanized TIGIT Mouse

Strain Name: C57BL/6-*Tigit* $^{em1(hTIGIT)Smoc}$ Strain Background: C57BL/6 Cat. No. : IT-HU-00053

TIGIT (T-cell immunoreceptor with Ig and ITIM domains) is identified as a co-inhibitory molecule in the PVR family of immunoglobulin (Ig) proteins. Upon the interaction of TIGIT with its ligand, TIGIT can inhibit the functions of anti-tumor immune cells at multiple steps. The blockade of TIGIT has been shown to restore the cytotoxicity of NK cells, thereby facilitating the elimination of tumor cells.

Construction strategy

The humanized TIGIT mouse model was developed on the C57BL/6 background. A chimeric expression cassette that encodes the extracellular domain of human TIGIT as well as the transmembrane and intracellular domains of murine Tigit was inserted immediately downstream of the start codon of the mouse endogenous Tigit gene, followed by a poly(A) signal. Thereby, the extracellular domain of the mouse Tigit was replaced by its human counterpart while the rest of the mouse gene was retained.

Validation data

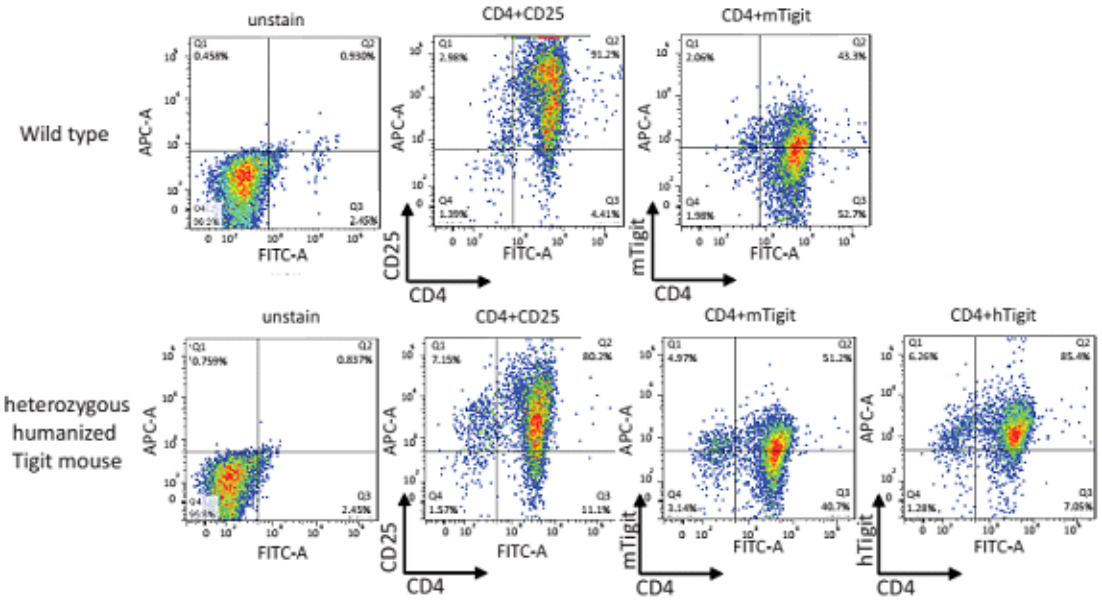

Figure 1. Expression of human TIGIT in the polarized CD4+ T cells of humanized TIGIT mice is detected by FACS. Spleen Naive CD4+ T cells were isolated from heterozygous humanized TIGIT mice. After in vitro stimulation, activation and expansion by cytokines and antibodies, the CD4+ T cells were re-stimulated with PMA/ionomycin before the expression of human TIGIT in polarized CD4+ T cells was detected by FACS. The results showed that the active expression of human TIGIT could be detected in polarized CD4+ T cells collected from humanized TIGIT mice, and the expression trend of human TIGIT was similar to that of murine TIGIT.

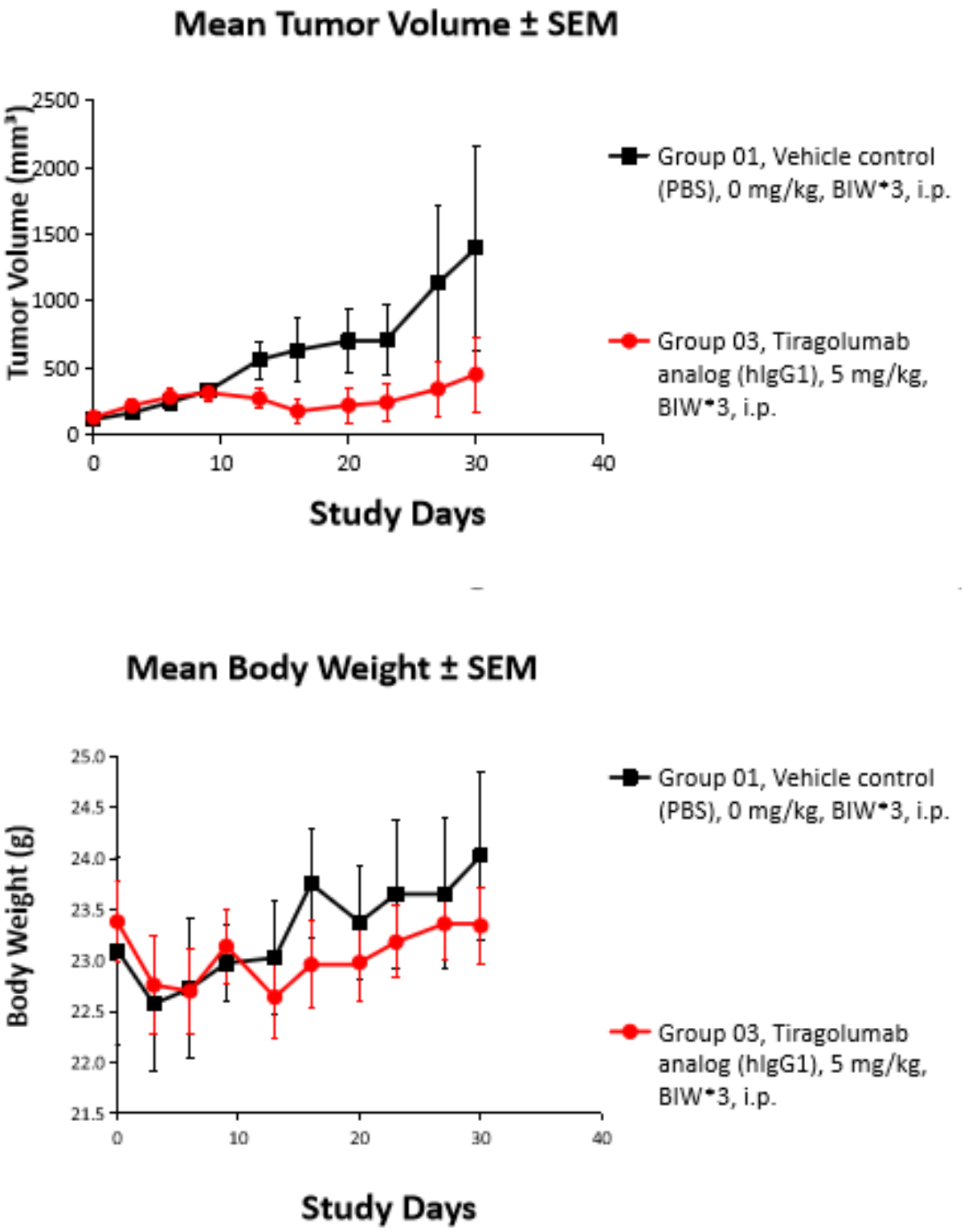

Figure 2. In vivo validation of anti-tumor efficacy in a Hepa1-6 tumor-bearing model of humanized TIGIT mice. Homozygous humanized TIGIT mice were inoculated with Hepa1-6 cells. After the tumors grew to 110 mm^3, the animals were randomly assigned into a control group and a treatment group. The results showed a significant anti-tumor effect was observed when the antibody targeting human TIGIT. (Completed in collaboration with CrownBio).

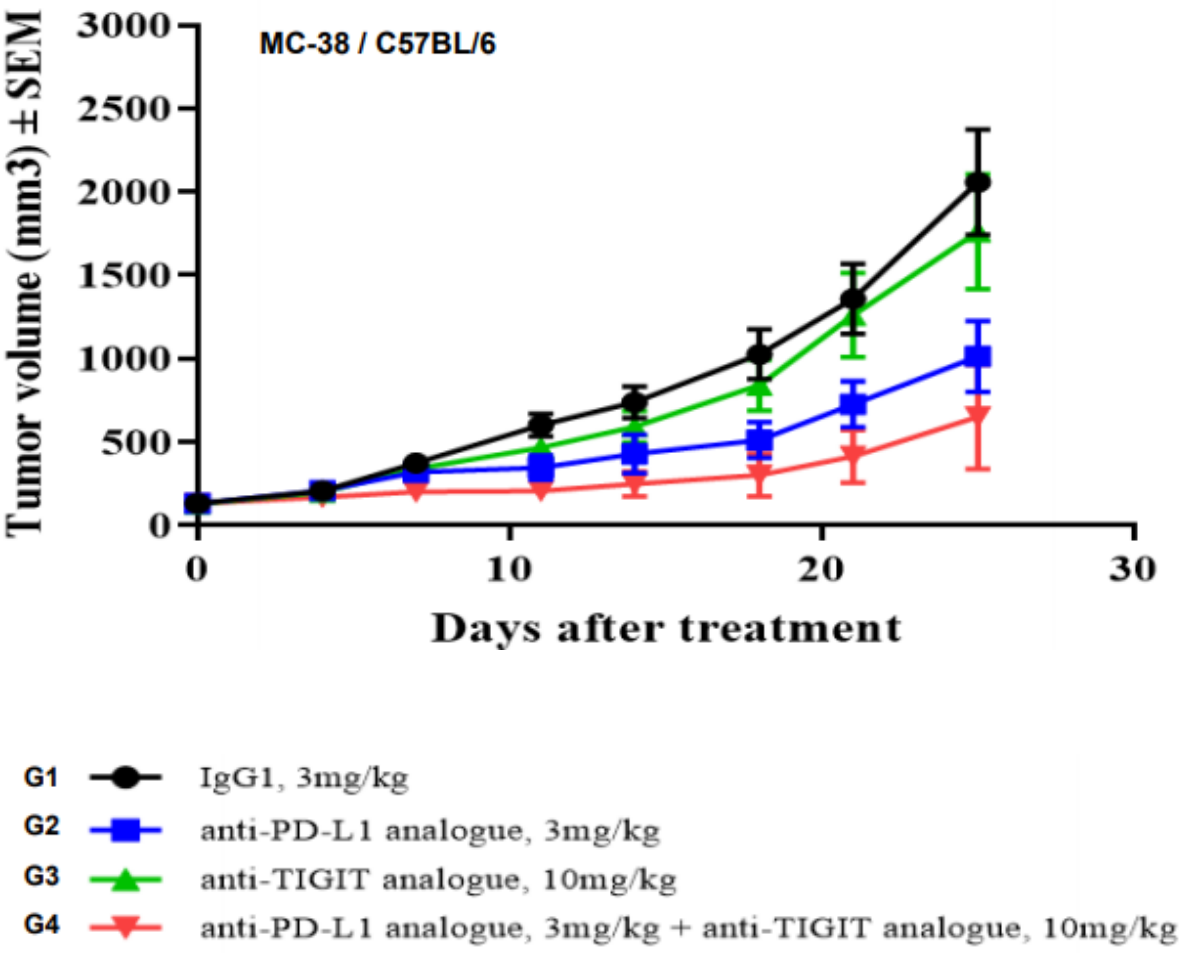

Figure 3. In vivo validation of anti-tumor efficacy in a MC38 tumor-bearing model of humanized TIGIT mice. Homozygous humanized TIGIT mice were inoculated with MC38 colon cancer cells. After the tumors grew to 130 mm^3, the animals were randomly assigned into a control group and a treatment group (n=7). The results showed a significant anti-tumor effect was observed when the antibody targeting human TIGIT was administered together with Anti-PD-L1 analogue.(Completed in collaboration with Harbour BioMed).

Immune Checkpoint Humanized Mouse Models

Being recognized as a top scientific breakthrough in 2013, cancer immunotherapy is predicted to be one of the most promising research areas for improving patient outcomes. Although many immunotherapy breakthroughs may still lie ahead, important clinical advances have been made in the past few years for some of the deadliest cancers, reaffirming the potential of immunotherapy for many types of patients.

However, it is worth noting that drug candidates developed to interfere with human proteins may not comparably interact with their murine counterparts. It is therefore critical to develop humanized mouse models to enable in vivo efficacy evaluation of cancer immunotherapies.

Immune Checkpoint Humanized Mouse Models available at ingenious targeting laboratory

4-1BB
CD40
CD47
CD73 (NT5E)
CTLA4 (C57BL/6)
CTLA4 (BALB/c)
KDR
LAG3
OX40
OX40/CTLA4
PD-1 (C57BL/6)
PD-1 (BALB/c)
PD-1/4-1BB
PD-1/CD40
PD-1/CTLA4
PD-1/LAG3
PD-1/OX40
PD-1/PD-L1
PD-1/TIGIT
PD-1/TIM3
PD-L1
PD-L1/CTLA4
PD-L1/LAG3
PD-L1/OX40
PD-L1/TIGIT
SIRPA
SIRPA/CD47
TIGIT
TIM3 (C57BL/6)
TIM3 (BALB/c)
TNFRSF1B
And more to come!

To get to know more about these models, visit our website **www.genetargeting.com** or contact our scientific experts at **inquiry@genetargeting.com**

About ingenious targeting laboratory

ingenious targeting laboratory (**ingenious**) has been a leading global provider of custom genetically modified mouse, rat, and rabbit models for over 20 years. As one of the very first mouse gene targeting companies, our trusted service is built on two decades' worth of successful animal model creation for investigators, organizations, and companies worldwide. Our models have been published in hundreds of journals including *Science*, *Nature*, and *Cell*, making us one of the most validated and respected production companies in the industry. We are excited to add catalog mouse models to our service repertoire by means of our collaboration with Shanghai Model Organisms Center (SMOC).

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