江苏集萃药康生物科技有限公司
GemPharmatech Co.,Ltd

BALB/c-hCD3E-hKDR

Strain Name：BALB/cJGpt-Tg(hCD3E BAC)102/Gpt-*Kdr*$^{em1Cin(hKDR)}$/Gpt

For short：BALB/c-hCD3E/hKDR

Strain Type：Knock-in

Strain Number：T017537

Background：BALB/cJGpt

Description

KDR is also known as VEGFR2, and is a receptor tyrosine kinase (RTK). It belongs to the VEGFR superfamily and express on the cell surface of endothelial cells to promote angiogenesis through stimulating the proliferation and survival of endothelial cells. However, recent studies have revealed that VEGFR2 also overexpress in tumor to stimulate tumor survival, progression, and metastasis. VEGF/VEGFR2 can inhibit the function of T cells via PLCγ-calcineurin-NFAT pathway to induce inhibitory checkpoint PD-1 expression, and increase the recruitment of regulatory T cells (Tregs) and myeloid-derived suppressor cells (MDSCs), and hinder the differentiation and activation of dendritic cells (DCs).It is necessary to update the role of targeting VEGF/VEGFR in antitumor immunity. Therefore, the VEGFR2 humanization can be used as a good animal model for the evaluation and toxicity of antibody drug against this target. It will gradually broaden the market and the future will be expected.

Using gene editing technology, the signal peptide and extracellular region of the mouse-derived VEGFR2 gene in BALB / c background mice were replaced with corresponding fragments of human-derived VEGFR2, and gene targeting was performed on the background of existing BALB/c-hCD3E transgenic mice to form Some humanized VEGFR2 mice can be used as animal models to evaluate drug toxicity such as bispecific antibody VEGFR2 x CD3.

Strategy

Fig.1 Schematic diagram of CD3E humanization strategy in BALB/c-hCD3E-hKDR mice.

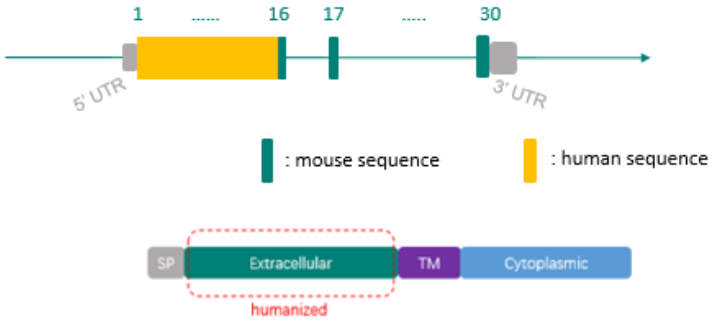

Fig.2 Schematic diagram of KDR humanization strategy in BALB/c-hCD3E-hKDR mice.

Application

1. Efficacy evaluation of human bispecific antibody VEGFR2 x CD3
2. Assessment of human bispecific antibody VEGFR2 x CD3 safety
3. Research on immune system

References

1. Thibault Voron, et al.VEGF-A modulates expression of inhibitory checkpoints on CD8+ T cells in tumors. J. Exp. Med. 2015 Vol. 212 No. 2 139–148.
2. Ju Yang, et al. Targeting VEGF/VEGFR to Modulate Antitumor immunity. Front Immunol. 2018; 9: 978.
3. Chinnasamy, et al.Gene therapy using genetically modified lymphocytes targeting VEGFR-2 inhibits the growth of vascularized syngenic tumors in mice. The Journal of clinical investigation 120.11 (2010): 3953-3968.