

BALB/c-hGPCR5D/hCD3EDG

Strain Name: BALB/cJGpt-Gprc5d^{em1Cin(hGPCR5D)}Cd3e, d, g^{tm1(hCD3E, D, G)}/Gpt

Strain Type: Targeted

Strain Number: T058817

Background: BALB/cJGpt

Description

GPCR5D (G protein-coupled receptor class C group 5 member D) was identified as an orphan receptor with no known ligand, a G protein-coupled receptor with seven transmembrane domains. The human GPCR5D is normally expressed in the hair follicles and lung tissue. Besides, the GPCR5D is also highly expressed in some multiple myeloma (MM) patients [1]. In addition, GPCR5D expression is heterogeneous and independent of BCMA expression [2].

Talquetamab is a general-purpose T cell redirected bispecific antibody targeting both GPCR5D and CD3. GPCR5D is a novel target for the treatment of multiple myeloma. Talquetamab can activate CD3 positive T cells and induce T cells to kill GPCR5D positive multiple myeloma cells.

The BALB/c- hGPCR5D/hCD3EDG was made by crossing the BALB/c-hCD3EDG with BALB/c-hGPCR5D by Gempharmatech, and the mice successfully expressed human GPCR5D and CD3E/D/G with a normal immune system. The GPCR5D/CD3EDG humanized mice are suitable models for preclinical studies of bispecific antibodies and related immunotherapies.

Strategy

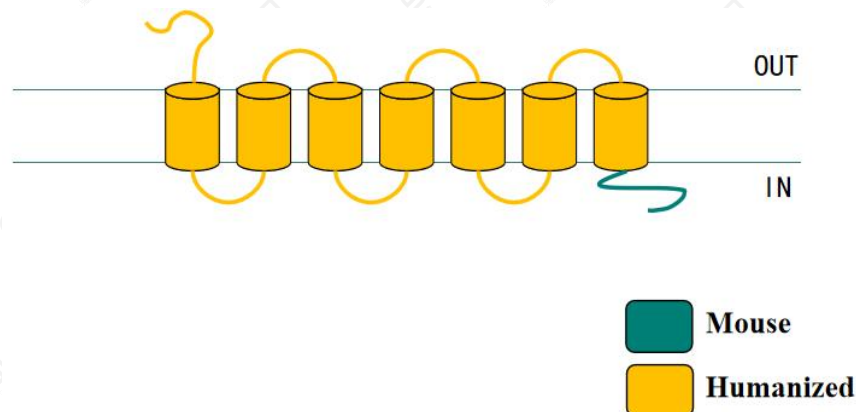


Fig.1 Schematic diagrams of GPCR5D humanization strategy.

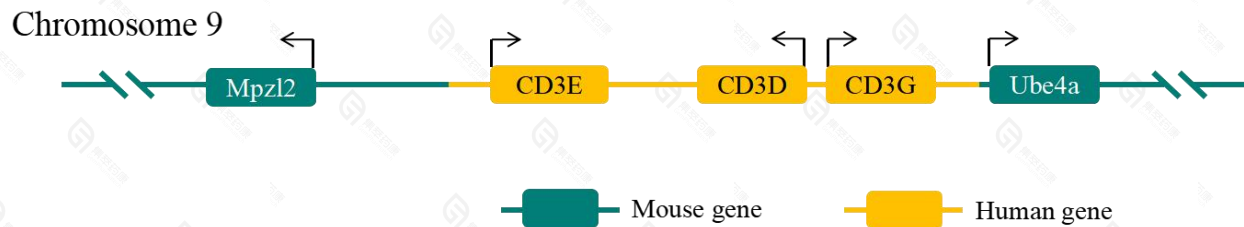


Fig.2 Schematic diagrams of CD3E/D/G humanization strategy.

Applications

1. Efficacy evaluation of bispecific antibody against human GPRC5D/CD3 targets
2. Anticancer drug research and development

Data support

1. Detection of hGPRC5D expression

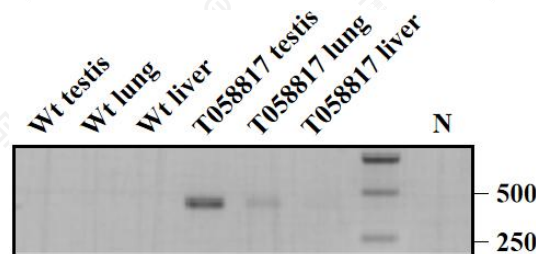


Fig 2. Detection of GPRC5D expression in BALB/c-hGPRC5D/hCD3EDG mice.

The expression of human GPRC5D mRNA in the testis, lung, and liver of BALB/c-hGPRC5D/hCD3EDG mice (hCD3 heterozygote /hGPRC5D heterozygote) was detected by RT-PCR. Human GPRC5D mRNA was successfully expressed in BALB/c-hGPRC5D/hCD3EDG mice. The protein expression of mice can be referred to the strain info of T055360 BALB/c-hGPRC5D.

2. Detection of hCD3 expression

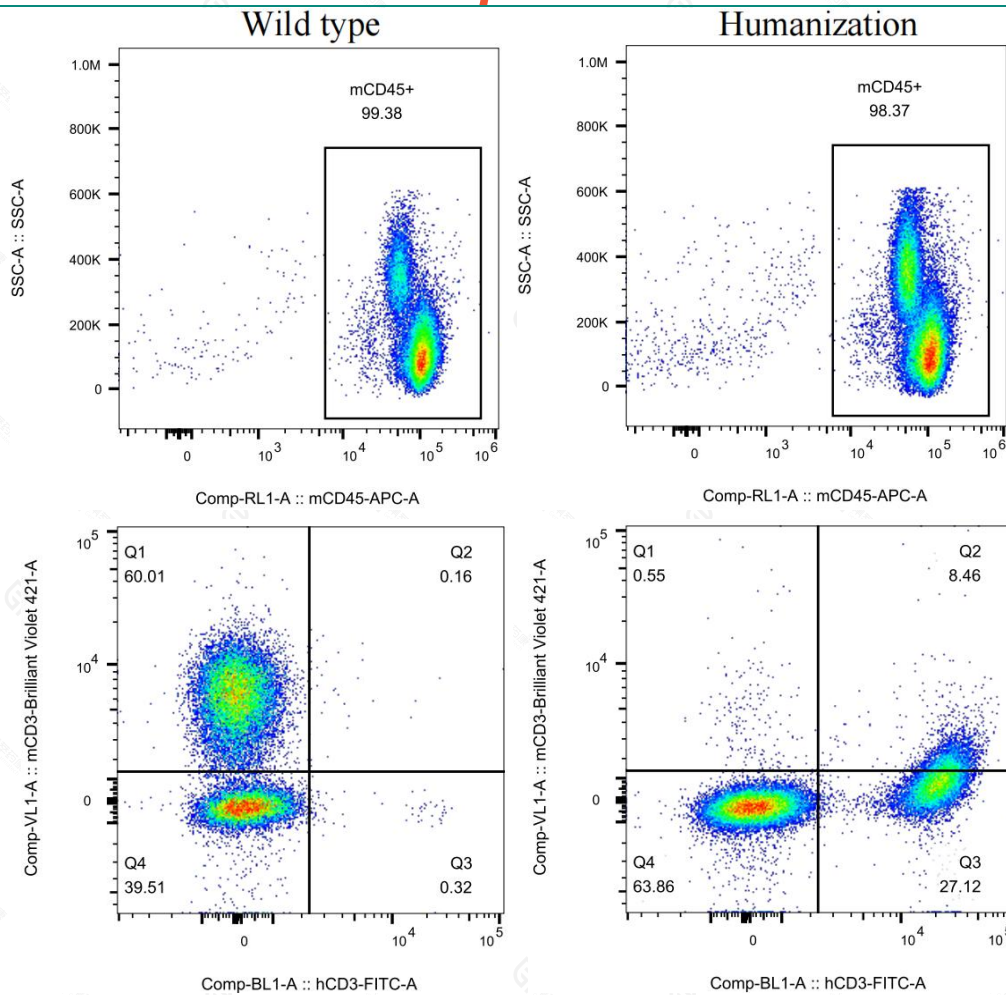


Fig 3. Detection of hCD3 expression in BALB/c-hGPC5D/hCD3EDG mice.

BALB/c-hGPC5D/hCD3EDG mice (hCD3 heterozygote /hGPC5D heterozygote) expressed human CD3E in T cells. Top panel: mCD45 ratio in live cells. Bottom panel: mCD3/hCD3 in CD45.

References

1. Pillarisetti, Kodandaram, et al. "A T-cell-redirecting bispecific G-protein-coupled receptor class 5 member D x CD3 antibody to treat multiple myeloma." *Blood* 135.15 (2020): 1232-1243.
2. Smith, Eric L., et al. "GPC5D is a target for the immunotherapy of multiple myeloma with rationally designed CAR T cells." *Science translational medicine* 11.485 (2019): eaau7746.