BALB/c- hCD3EDG/hCD22

Strain Name: BALB/cJGpt-*Cd3e, d, g*$^{tm1(hCD3E, D, G)}$*Cd22*$^{em1Cin(hCD22)}$/Gpt
Strain Type: Targeted
Strain Number: T058940
Background: BALB/cJGpt

Description

CD22, or cluster of differentiation-22, is a molecule belonging to the SIGLEC family of lectins. It is mainly expressed on the surface of mature B cells, and involved in the regulation of the expression of surface IgM on B cells. CD22 is also found on the surface of most B-cell leukemias and lymphomas and therefore has been explored as a target for Ab-based therapies [1]. Inotuzumab ozogamicin (InO) is a calicheamicin-conjugated antibody targeting CD22 on B-cell ALL cells, and is approved for R/R B-cell precursor ALL. And there are many drugs that target CD22 in the clinical stage for treating B-cell Lymphoma.

In addition, a lot of studies have shown that CD22 contributes to the regulation of autoimmunity. Some recent data suggest that targeting CD22 can suppress pathogenic B cell response, such as Epratuzumab (Emab) as therapies for autoimmune diseases, particularly for SLE.

Bispecific antibodies (BsAbs) combine specificities of two antibodies and simultaneously address different antigens or epitopes. BsAbs with 'twotarget' functionality can interfere with surface receptors or associated ligands belonging to multiple pathways simultaneously, for example, cancer, proliferation or inflammatory processes. BsAbs can also place targets into close proximity, either to support protein complex formation on one cell, or to trigger contacts between cells. CD3-target-based bispecific antibodies (CD3-TCB) are designed to simultaneously bind to T cells and target cell antigens, leading to T-cell activation, proliferation, and target cell death.

The BALB/c- hCD3EDG/hCD22 was made by crossing the BALB/c-hCD3EDG with BALB/c-hCD22 by Gempharmatech, and the mice successfully expressed human CD22 and CD3E/D/G with a normal immune system. The CD3EDG/CD22 humanized mice are suitable models for preclinical studies of bispecific antibodies and related immunotherapies.

Strategy

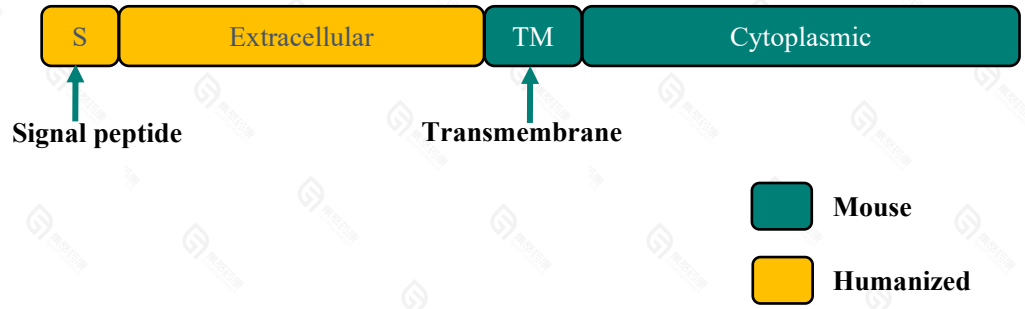

Fig.1 Schematic diagram of CD22 humanization strategy in BALB/c-hCD22 mice.
The extracellular domain was substituted with its human counterpart.

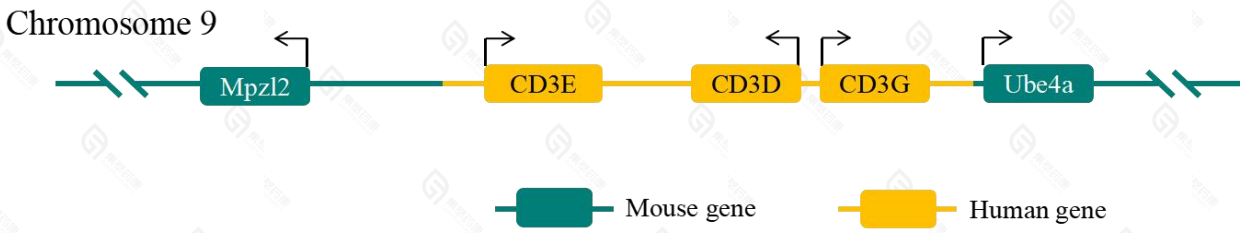

Fig.2 Schematic diagrams of CD3E/D/G humanization strategy.

Applications

1. Efficacy evaluation of bispecific antibody against human CD22/ CD3 targets
2. Anticancer drug research and development
3. Research on autoimmune diseases

Data support

1. CD22 Protein expression analysis

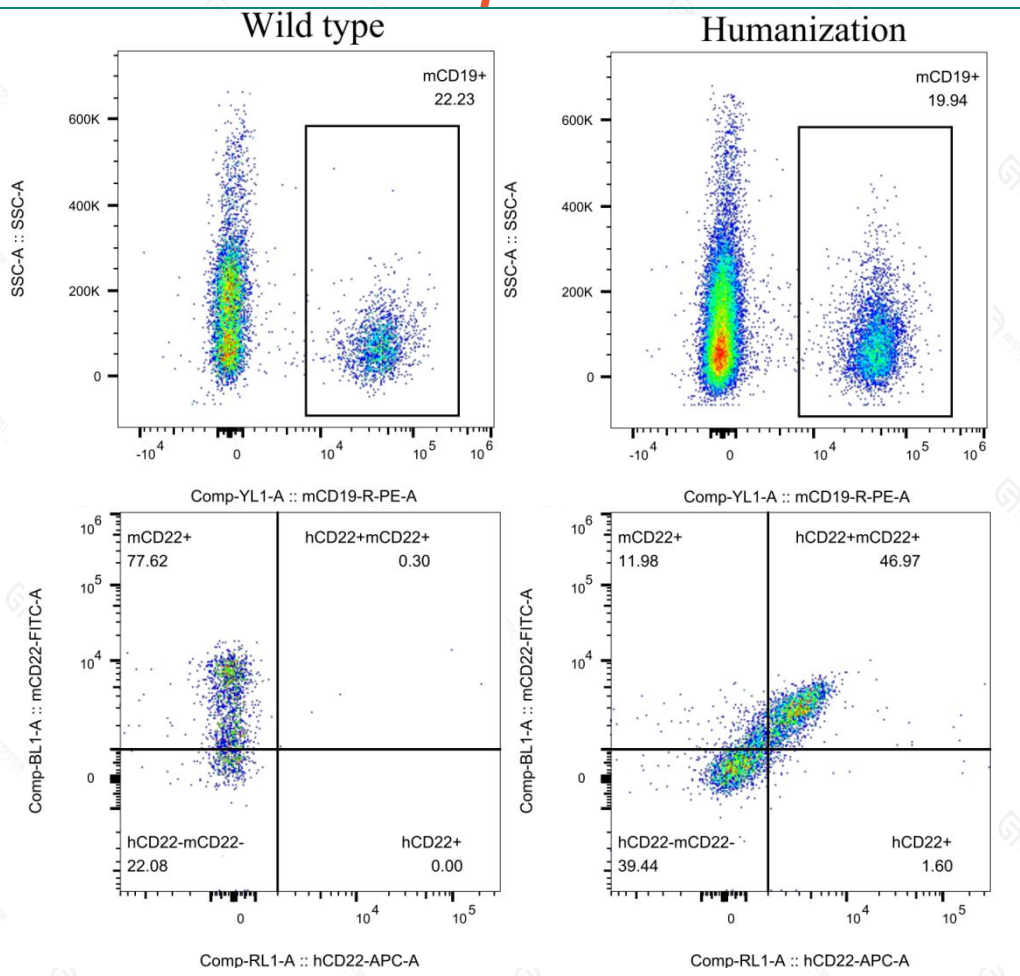

Fig.3 Detection of CD22 expression in BALB/c-hCD3EDG/hCD22 mice.

BALB/c-hCD3EDG/hCD22 mice (CD22 heterozygote /CD3 homozygote) expressed human CD22 on the B cell surface of peripheral blood. Top panel: mCD19 expressing ratio in lymphocytes. Bottom panel: mCD22+/hCD22+ expressing ratio in B cells.

2. CD3 Protein expression analysis

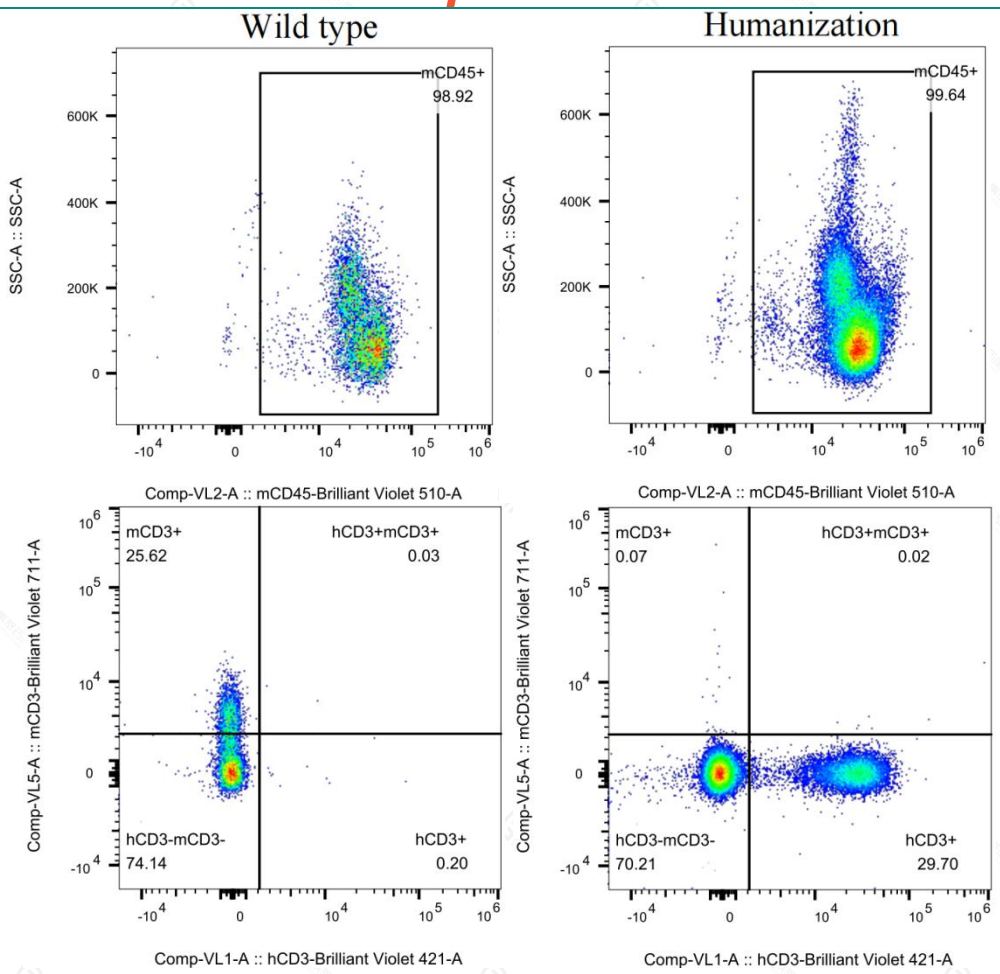

Fig.4 Detection of CD3 expression in BALB/c-hCD3EDG/hCD22 mice.

BALB/c-hCD3EDG/hCD22 mice (CD22 heterozygote /CD3 homozygote) expressed human CD3E in T cells, and mouse CD3E expression could not be detected. Top panel: mCD45 ratio in live cells. Bottom panel: mCD3/hCD3 in T cells.

References

1. Leonard J P, Goldenberg D M. Preclinical and clinical evaluation of epratuzumab (anti-CD22 IgG) in B-cell malignancies[J]. Oncogene, 2007, 26(25): 3704-3713.
2. Geh D, Gordon C. Epratuzumab for the treatment of systemic lupus erythematosus[J]. Expert review of clinical immunology, 2018, 14(4): 245-258.