NCG-B2m-KO

Strain Name：NOD/ShiLtJGpt-*Prkdc*^{em26Cd52}*Il2rg*^{em26Cd22}*B2m*^{em21Cd4}/Gpt

Strain type：Knock-out

Strain number：T004670

Background：NOD/ShiLtJGpt

Description

Severe immune-deficient strain NCG is established by CRISPR/Cas9 technology. Prkdc (Protein kinase, DNA activated, catalytic polypeptide) and Il2rg (Common gamma chain receptor）genes are knocked out on NOD/ShiltJGpt background. NOD/ShiltJGpt mice have natural immunodeficiency, such as complement system and macrophage defects [1]. At the same time, the Sirpa on NOD/ShiltJGpt has high affinity with human CD47, making it more suitable for colonization of human grafts (e.g. tumors and human cells) than other strains [2]. Loss of Prkdc gene leads to the inability of V(D)J recombination to occur, resulting in the inability of T cells and B cells to mature. Il2rg is a common subunit of various interleukin cytokine receptors, and the inactivation of Il2rg leads to the loss of six different cytokine signaling pathways[4], resulting in NK cell defects [3]. Therefore, NCG is the most thorough mouse model of the immune-deficient to date, and is very suitable for Cell derived xenograft (CDX), Patient derived xenograft (PDX), human peripheral blood mononuclear cells (PBMC) and human hematopoietic stem cell(hCD34+HSC) transplantation for immune reconstitution. The NCG has a long life cycle of >89 weeks, which is beneficial for long term transplantation and pharmacodynamic evaluation.

B2M, (also known as Ly-m11, beta2m, beta2-m, β2-microglobulin), an component of MHC complex, is essential for MHC class I protein transport to cell membrane [5]. B2M knockout homozygous mouse express few MHC class I protein on cell membrane, accompany with phenotypes of NK cell deficiency, NK+ T cell deficiency, and decreased level of serum Ig.

The Proprietary B2M gene Knockout mouse (NCG-B2m-KO) was constructed on NCG background by GemPharmatech Co., Ltd using gene editing technology. Besides the severe immune-deficient characteristics, this strain has highly resistant to graft-versus-host disease (GvHD), which indicates a useful mouse model to study the GvHD mechanism of heterograft in vivo and assess preclinical efficacy of therapeutic agents rapidly.

Application

1. For the preparation of human mouse models, such as PBMC or HSC.
2. For human cell tissue transplantation.
3. Human tumors were inoculated for screening of related drugs.

4. For human hematopoietic system and immune system research.
5. Studies on graft versus host disease (GvHD).

Data support

1、MHC I detection

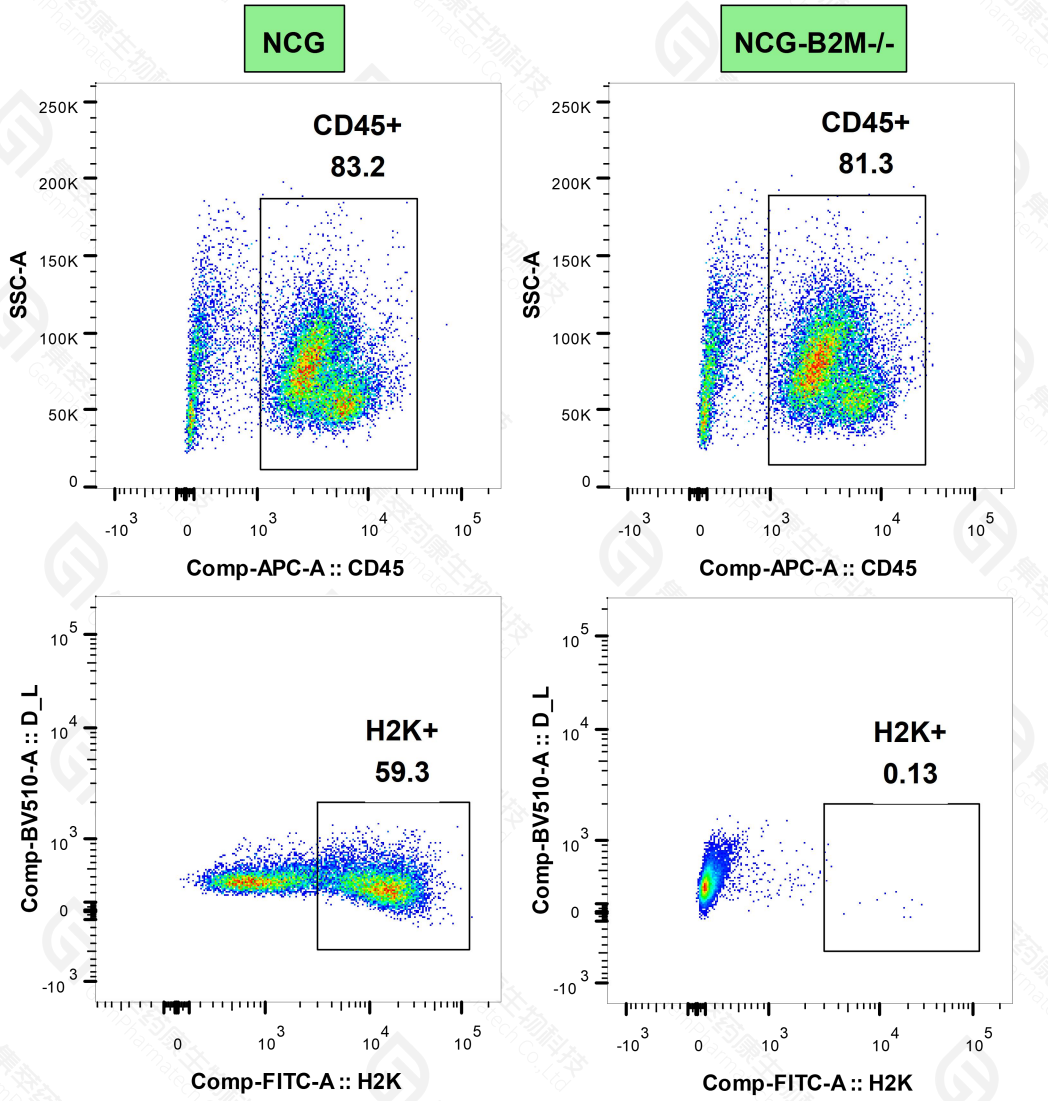

Fig.2 Detection of MHC I in NCG-B2m-KO mice.

H2K antibody was used to detect MHC I, and H2K (59.3% of CD45+ cells) was detected in NCG control mice, but not in spleen cells of NCG-B2m-KO mice.

2、HuPBMC reconstruction

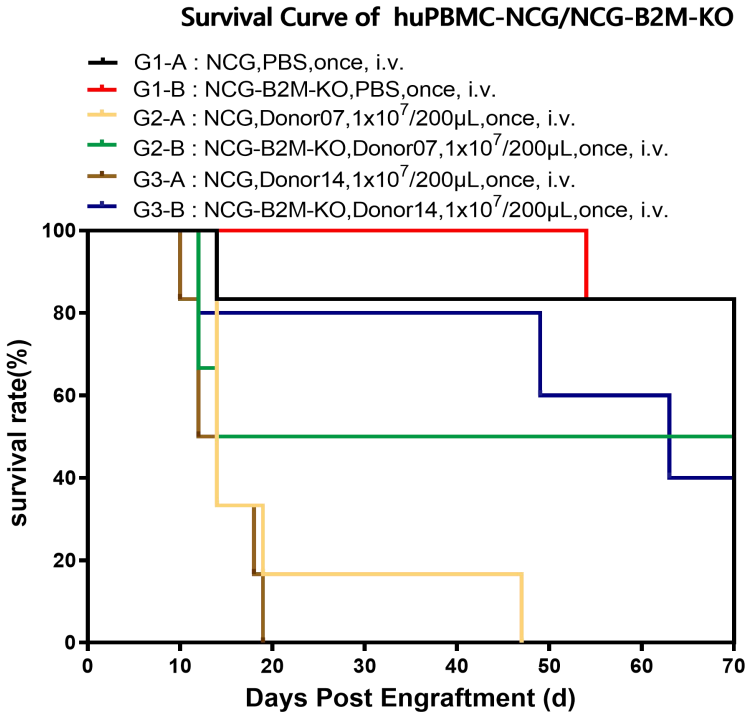

Fig.3 Survival curve of huPBMC NCG/NCG-B2m-KO mice.

After 100cGy irradiation and inoculation with PBMC, the NCG-B2m-KO strain significantly reduced GvHD.

References

1. Shultz LD, Schweitzer PA, Christianson SW, et al. (1995). “Multiple defects in innate and adaptive immunologic function in NOD/LtSz-scid mice”. J. Immunol. 154 (1): 180–91.
2. Takenaka K, Prasolava TK, Wang JC, et al. (2007). “Polymorphism in Sirpa modulates engraftment of human hematopoietic stem cells”. Nat. Immunol. 8 (12): 1313–23.
3. Greiner DL, Hesselton RA, Shultz LD (1998). “SCID mouse models of human stem cell engraftment”. Stem Cells. 16 (3): 166–177.
4. Cao X, Shores EW, Hu-Li J, et al. (1995). “Defective lymphoid development in mice lacking expression of the common cytokine receptor gamma chain”. Immunity. 2 (3): 223–38.
5. Sprent, Jonathan, and Susan R. Webb. "Function and specificity of T cell subsets in the mouse." Advances in immunology. Vol. 41. Academic Press, 1987. 39-133