B6-Rag1-KO

Strain Name：B6/JGpt*Rag1*^{em1Cd}/Gpt

Strain type：Knock-out

Strain number：T004753

Background: C57BL/6JGpt

Description

The protein encoded by Rag1 (Recombination activating gene 1) gene is involved in activation of immunoglobulin V-D-J recombination.[1]. Deficient of Rag1 gene in homozygous mice and therefore does not develop mature T or B cells expressing endogenous receptors. The homozygous mice did not have mature CD3+TCR+T cells, and the thymus contains 15 to 130 times fewer cells than heterozygous or wild-type siblings. The thymocytes are CD8-CD4- and most are IL2 receptor-positive.. Neither the spleen nor the bone marrow contain any IgM or IgD staining cells, indicating an absence of mature B cells [2]. Compared with Scid model which Prkdc gene is deletion, mature lymphocytes are more completely absent and no "leakage" in Rag1 kockout mice [3].

GemPharmatech use of gene editing technology to knock out the coding region of the Rag1 gene on C57BL/6JGpt Background.. This strain defects in T cells and B cells developmental. Compared with wild type mice, B6-Rag1-KO mice showed immunodeficiency as follows: thymus, spleen smaller, no mature T cells and B cells, the proportion of NK cells increased slightly. B6- Rag1-KO mice is an ideal model for tumor, immunity, inflammation and cell research.

Strategy

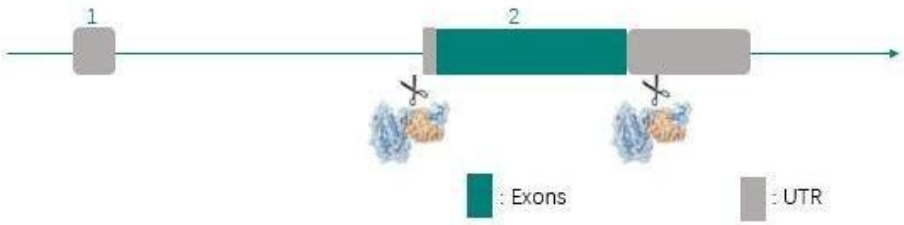


Fig.1 Schematic diagram of Rag1-KO mice.

Application

1. Research on immune system.
2. Infection and inflammation
3. Tumour transplantation
4. Efficacy evaluation of human BTLA inhibitors

Identification

1. Mouse Age：3W~4W
2. Genotype：KO/KO，homozygote
3. Genetic Locus：*Rag1*

Data support

1. Histopathology analysis

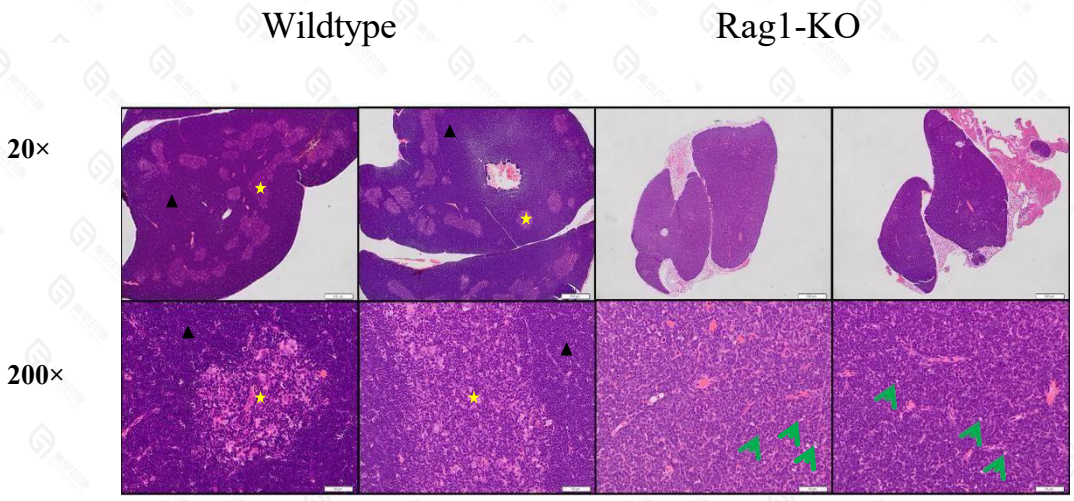


Fig.2 Histopathology of thymus from B6-Rag1-KO mice.

Thymus examined by HE staining for pathology, there was no obvious abnormality in the wild type mice. Compared with wild type mice, thymus of B6-Rag1-KO mice had a smaller volume, and a small amount of fat cells infiltrated under the capsule. The boundary of cortex and medulla is blurred, the lymphocytes were reduced, the mesenchymal is increased, loosely arranged, and hypoplasia.

Note: red arrow: infiltration of adipocytes; black triangle: the cortical area; yellow pentagram: the medulla area.

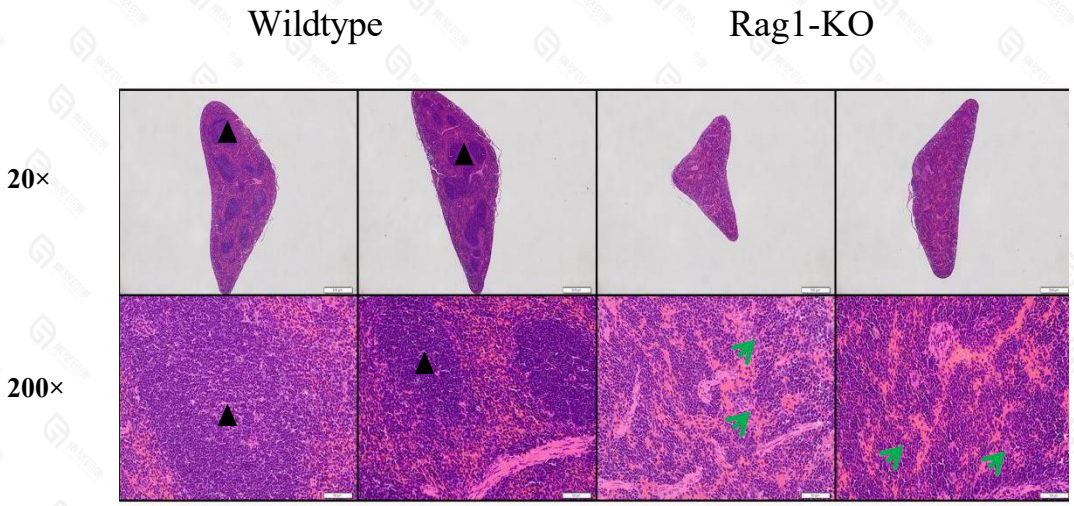


Fig.3 Histopathology of spleen from B6-Rag1-KO mice.

Spleen examined by HE staining for pathology, there was no obvious abnormality in wildtype mice. Compared with wildtype mice, the basic structure of spleen was disappeared in B6-Rag1-KO mice, no obvious medulla and splenic corpuscle, the central artery was surrounded with immature lymphocytes. polynuclear giant cells increased, bleeding occurs.

Note: The black triangle: splenic corpuscle; the green arrow shows the polynuclear giant cell.

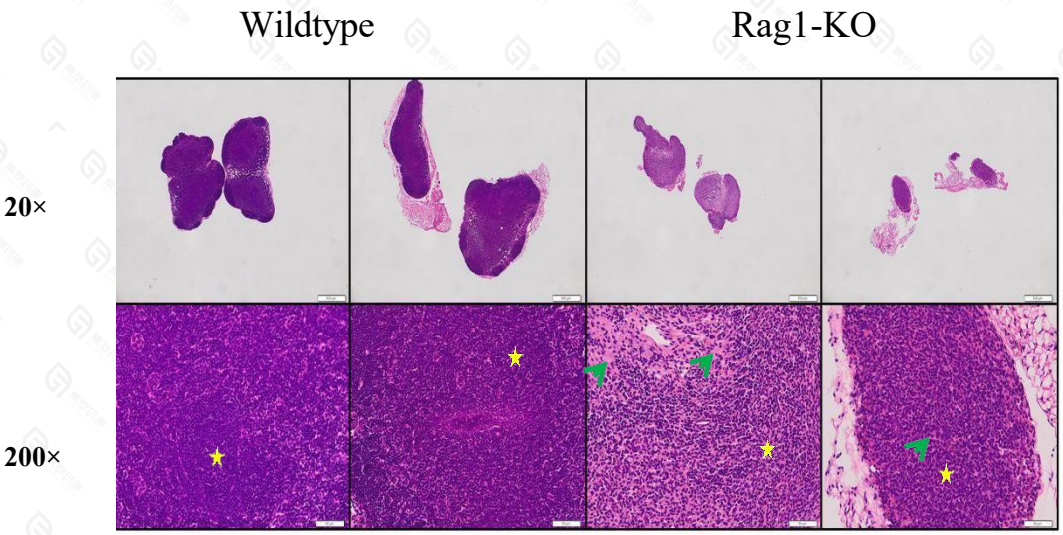


Fig.4 Histopathology of Inguinal lymph node from B6-Rag1-KO mice.

Inguinal lymph node examined by HE staining for pathology, there was no obvious abnormality in wildtype mice. Compared with wildtype mice, the B6-Rag1-KO group disappeared in the basic structure, the volume decreased, the lymphocytes decreased significantly, the arrangement was loose, and the interstitial increased.

Note: Yellow pentagrams are shown as lymphocytes, and green arrows are shown as mesenchyme.

2. Analysis of immune cell subpopulations

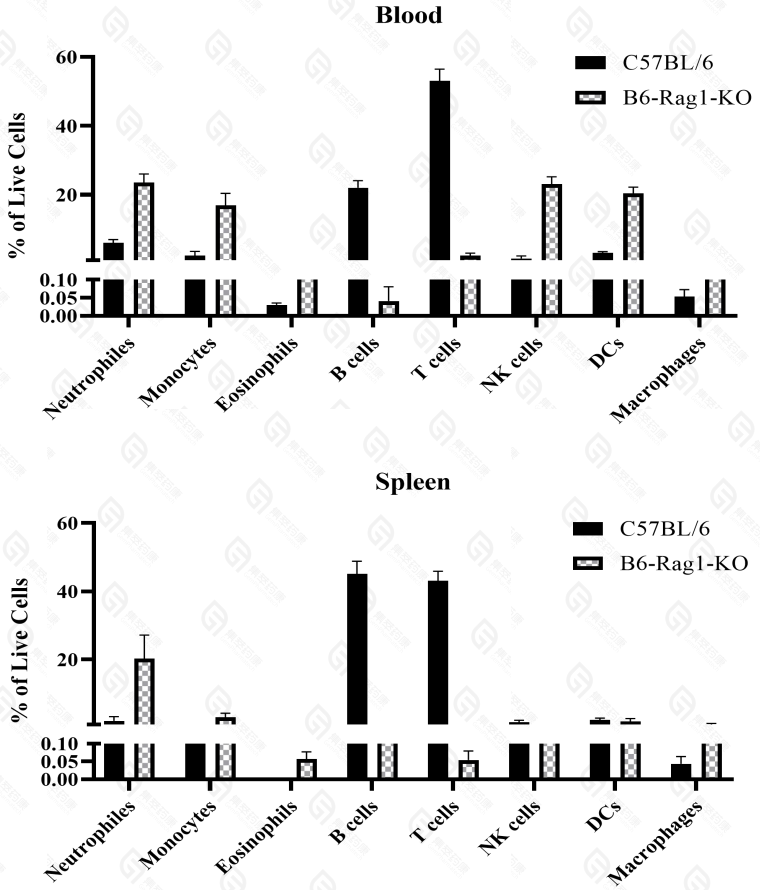
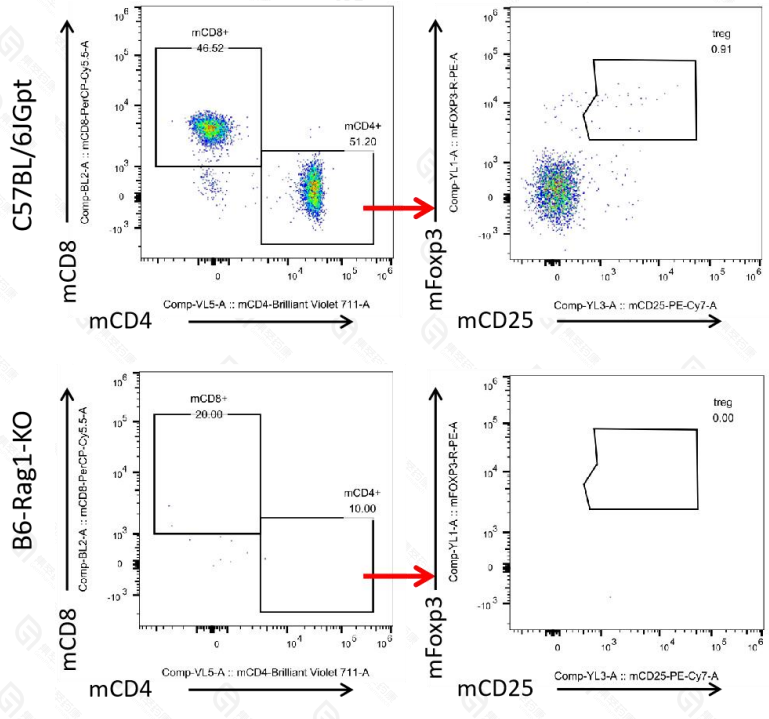


Fig.5 Analysis of immune cell subpopulations by FACS.

Blood cells and Splenocytes were isolated from C57BL/6 and B6-Rag1 KO mice (n=8, 6-week-old).

Compared with wild-type mice, B6-Rag1-KO mice lacked mature T and B cells, while percent of all the other cells, including NK cells, dendritic cells, neutrophiles, monocytes, eosinophils and macrophages were compensatively increased, both in blood and spleen.

Values are expressed as mean ± SD.



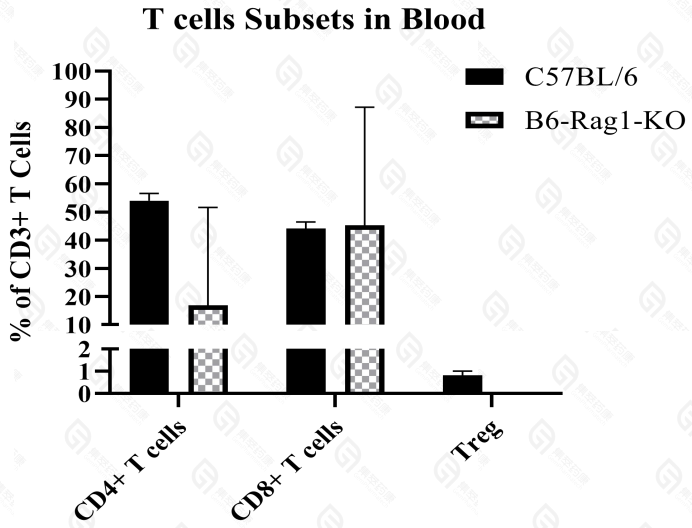


Fig.6 Analysis of T cell subsets by FACS in blood.

Blood cells were isolated from C57BL/6 and B6-Rag1 KO mice (n=8, 6-week-old).

Results of FACS analysis. Percent of CD4+ T cells, CD8+ T cells and Tregs in B6-Rag1 KO mice were significantly decreased compared to those in the C57BL/6 mice.

Values are expressed as mean ± SD.

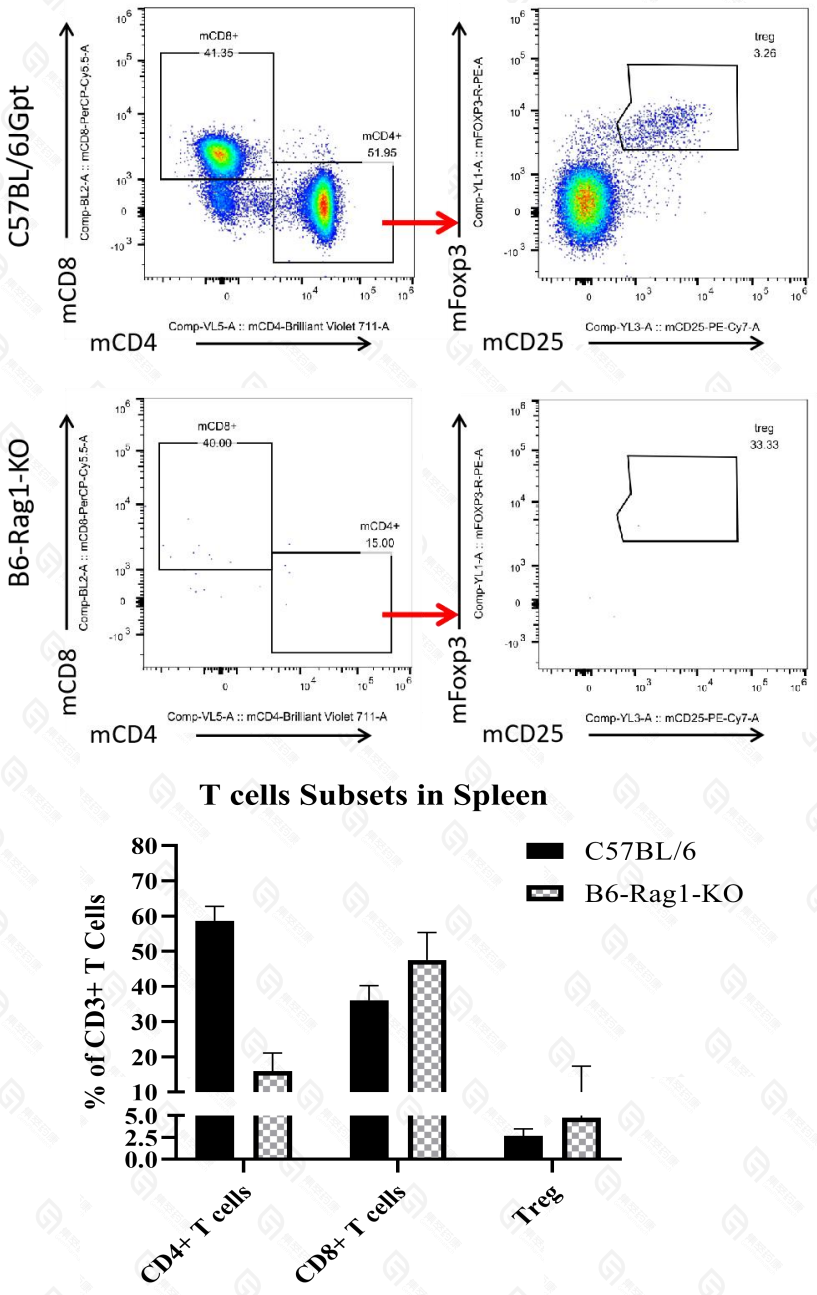


Fig.7 Analysis of T cell subsets by FACS in spleen.

Splenocytes were isolated from C57BL/6 and B6-Rag1 KO mice (n=8, 6-week-old).
Results of FACS analysis. Percent of CD4+ T cells, CD8+ T cells and Tregs in B6-Rag1 KO mice were significantly decreased compared to those in the C57BL/6 mice.
Values are expressed as mean ± SD.

Breeding and Conservation

1. Ordinary feed（6% fat content）
2. Reproductive Performance：normal
3. Foster Nursing Ability：normal
4. Description: This strain is an immunodeficient mouse. It is necessary to pay attention to the gentle operation in daily to reduce the stress

References

1. Oettinger, Marjorie A., et al. "RAG-1 and RAG-2, adjacent genes that synergistically activate V (D) J recombination." *Science* 248.4962 (1990): 1517-1523.
2. Mombaerts, Peter, et al. "RAG-1-deficient mice have no mature B and T lymphocytes." *Cell* 68.5 (1992): 869-877.
3. Bassing, Craig H., Wojciech Swat, and Frederick W. Alt. "The mechanism and regulation of chromosomal V (D) J recombination." *Cell* 109.2 (2002): S45-S55.